(b) (4)

FULLY REDACTED PAGES WITHHELD IN FULL FOLLOWING THIS PAGE. SEE BATES-NUMBERS ON BOTTOM OF PAGES TO IDENTIFY RANGE OF PAGES WITHHELD IN FULL.

16.1.3.1 List of IECs and IRBs

List of IECs and IRBs

Site Number or Identifier	Name of IRB or IEC
Site 01: Mendell	Nationwide Children's Hospital Institutional Review Board 700 Children's Drive Columbus, Ohio 43205 Chairman: (b) (4) , MD
Site 02: (b) (4)	(b) (4)
Site 03: (b) (4)	(b) (4)
Site 04: Byrne	(b) (4)
Site 05: (b) (4)	(b) (4)
Site 07: (b) (4)	(b) (4)
Site 08: Heydemann	Rush University Medical Center IRB Research and Clinical Trials Administration Office 1653 West Congress Parkway Chicago, Illinois 60612-3833 Chair of Pediatric Neurology IRB – (b) (4) MD, PhD
Site 09: (b) (4)	(b) (4)

	(b) (4)
Site 10: (b) (4)	(b) (4)
Site 11: Connolly	The Washington University in St. Louis Human Research Protection Office 660 South Euclid Ave Campus Box 8089 St. Louis, MO 63110 Chair: (b) (4) , MD
Site 12: (b) (4)	(b) (4)
Site 13: (b) (4)	(b) (4)

16.1.3.2 Representative Written Information for Patient and Sample Consent Forms

Representative Written Information for Patient and Sample Consent Forms

Representative Written Information and Consent/Assent Version	Date
Optional Fourth Biopsy Approved ICF Nationwide	04 November 2014
Parental Permission Form and HIPAA Authorization Version 07	14 August 2014
Parental Permission Form and HIPAA Authorization Version 06	23 April 2014
Parental Permission Form and HIPAA Authorization Version 05	25 June 2013
Parental Permission Form and HIPAA Authorization Version 04	18 Oct 2012
Parental Permission Form and HIPAA Authorization Version 03	16 May 2012
Parental Permission Form and HIPAA Authorization Version 02	03 May 2012
Parental Permission Form and HIPAA Authorization Version 01	14 March 2012
Optional Fourth Biopsy Approved Assent Nationwide	04 November 2014
Children's Assent Form V4.0	14 August 2014
Children's Assent Form V3.0	23 April 2014
Children's Assent Form V2.0	12 July 2013
Children's Assent Form V1.0	14 March 2012

NATIONWIDE CHILDREN'S
When your child needs a hospital, everything matters.

Study Title: Open-Label, Multiple-Dose, Efficacy, Safety, and Tolerability Study of Eteplirsen in Subjects with Duchenne Muscular Dystrophy who Participated in Study 4658-us-201

Protocol No.: 4658-us-202 **Study Sponsor:** Sarepta Therapeutics, Inc.

Study Doctor: Jerry Mendell, MD **Contact Telephone Number:** 614-722-2203
(24 hours a day, 7 days a week)

CONSENT - To Participate In A Clinical Research Study
Optional Biopsy Consent

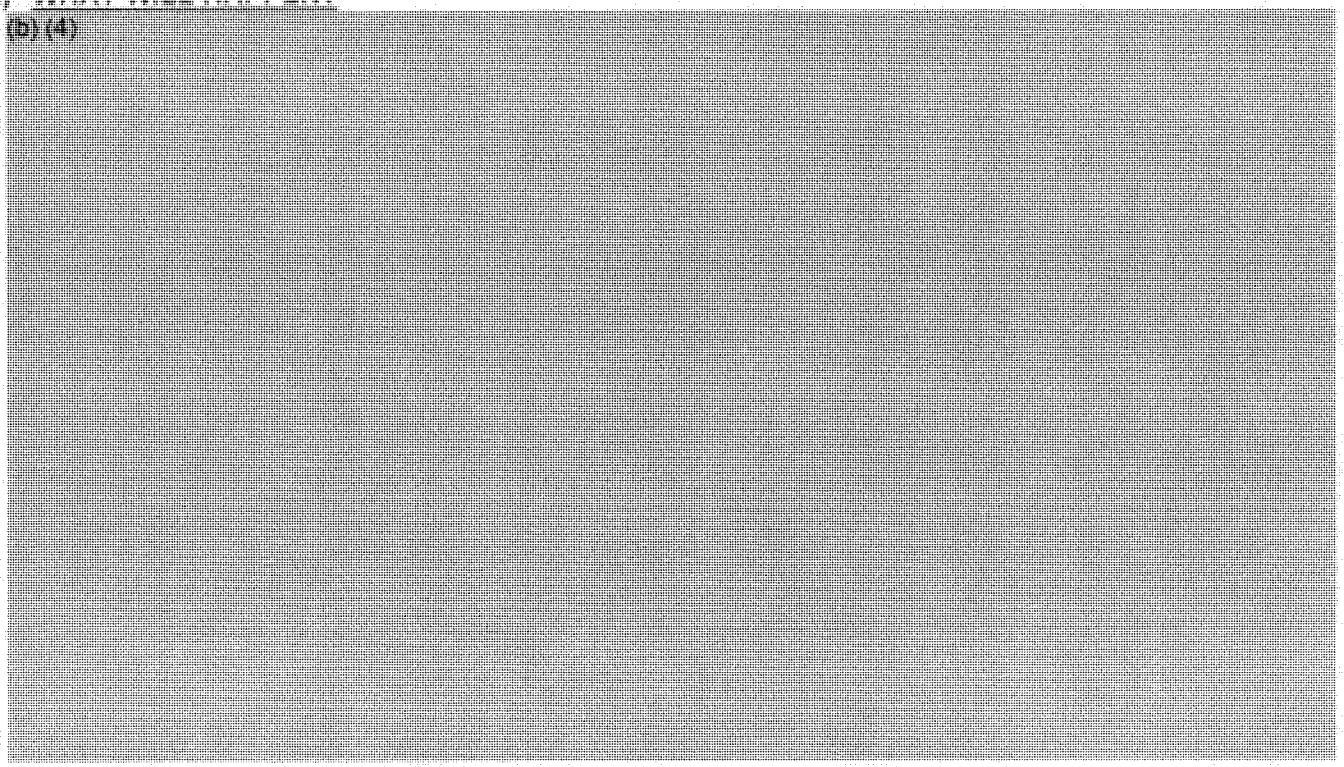
SUBJECT'S NAME: _____ **DATE OF BIRTH:** _____

1) INTRODUCTION

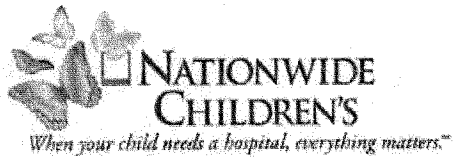
You are being asked to allow your child to have an additional biopsy done as an **optional** part of this study. Collection of this biopsy sample is entirely voluntary. Your child can still participate in the main study if you do not agree to allow him to have the biopsy. If you agree to allow your child to take part, and then change your mind, you may withdraw your consent before the procedure is done and your child will not lose any benefits to which your child would have and your child may continue to take part in the main study. Listed below is a description of how the sample will be collected, what it will be used for and any possible risks.

2) WHAT WILL HAPPEN?

(b) (4)



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Initials



Study Title: Open-Label, Multiple-Dose, Efficacy, Safety, and Tolerability Study of Eteplirsen in Subjects with Duchenne Muscular Dystrophy who Participated in Study 4658-us-201

Protocol No.: 4658-us-202 **Study Sponsor:** Sarepta Therapeutics, Inc.

(b) (4)

3) **WHAT WILL THE SAMPLES BE USED FOR?**
The optional biopsy is being done to collect additional information on the long-term effect of receiving eteplirsen and how it effects the production of new dystrophin within your child's muscles.

4. **WHAT ARE THE RISKS:**
Common side effects of muscle biopsies may include discomfort, a scar, bruising, numbness near the biopsy site delayed wound healing and infection. Although infection is rare, signs of infection include oozing, redness and an increase in pain over time. If you or your child see any of these signs, you should report this to the study staff right away.

After use of conscious sedation, your child may get a headache or feel nauseous or dizzy. It is possible that your child will have a reaction to the sedative medication used.

5. **WHAT GOOD THINGS CAN POSSIBLY HAPPEN DURING THIS STUDY?**
There will be no benefit to your child from being having the additional biopsy but we might learn something from your child's information that could help others.

6. **WILL THERE BE ANY COSTS TO ME:**
There will be no cost to you for allowing your child to participate in the additional biopsy sample collection portion of the study. You will not be paid to provide this optional sample.

Some new products might be developed and sold because of the research done on your child's biopsy sample but you will not receive money for this.

NATIONWIDE CHILDREN'S
When your child needs a hospital, everything matters.™

Study Title: Open-Label, Multiple-Dose, Efficacy, Safety, and Tolerability Study of Eteplirsen in Subjects with Duchenne Muscular Dystrophy who Participated in Study 4658-us-201

Protocol No.: 4658-us-202 **Study Sponsor:** Sarepta Therapeutics, Inc.

Subject's Name _____ **Date of Birth**_____

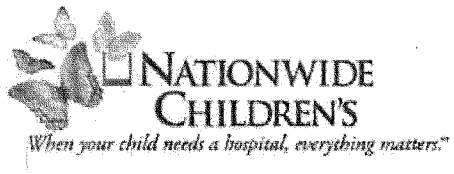
SUBJECT'S PARENT OR PERSON AUTHORIZED TO CONSENT ON BEHALF OF THE CHILD (SUBJECT TO THE SUBJECT'S GENERAL MEDICAL CARE)

I have read this consent form for the optional biopsy and have had a chance to ask questions about this research study involving the optional biopsy. These questions have been answered to my satisfaction. If I have more questions about participation in this study or a research-related injury, I can review the informed consent for the main study and may contact the Principal Investigator. By signing this consent form, I certify that all health information I have given for my child is true and correct to the best of my knowledge.

Since this is an addendum to the main consent form, I understand that what I agreed to in the main consent form is still in effect. If I have any questions about this optional study or the main study, I know that I can talk to the study team at any time. I have been given a copy of the Nationwide Children's Hospital Notice of Privacy Practices. I understand that my right to my child's patient information that is created or collected by Nationwide Children's Hospital in the course of this research can be temporarily suspended for as long as the research is in progress. I also understand that my right to access will be reinstated upon completion of this research.

I agree to participate in this optional study/I give permission for my child to participate in this optional study. I will be given a copy of this consent form for the optional biopsy with all the signatures for my own records.

Printed name of subject or subject's legal representative	Signature of subject or subject's legal representative
	Date and time AM/PM
N/A Printed name of subject or subject's legal representative Permission of the second parent not obtained because (select all that apply). __X__ Not required by the IRB (risk level 1 or 2). _____ Other parent is deceased. _____ Other parent is unknown. _____ Other parent is not reasonably available. _____ Only one parent has legal responsibility for the care and custody of subject	N/A Signature of subject or subject's legal representative
	N/A N/A Date and time AM/PM



Study Title: Open-Label, Multiple-Dose, Efficacy, Safety, and Tolerability Study of Eteplirsen in Subjects with Duchenne Muscular Dystrophy who Participated in Study 4658-us-201

Protocol No.: 4658-us-202 **Study Sponsor:** Sarepta Therapeutics, Inc.

Investigator/Research Staff

I have explained the research to the subject's guardian or authorized representative before requesting the signature above. There are no blanks in this document. A copy of this form has been given to the participant or his/her representative.

Printed name of person obtaining consent	Signature of person obtaining consent
	Date and time AM/PM

APPROVED: Sep 09, 2014
COPERNICUS GROUP IRB

copernicus group independent review board
Approved:

PARENTAL PERMISSION FORM AND HIPAA AUTHORIZATION

STUDY TITLE: Open-Label, Multiple-Dose, Efficacy, Safety, and Tolerability Study of Eteplirsen in Subjects with Duchenne Muscular Dystrophy who Participated in Study 4658-us-201

PROTOCOL NUMBER: 4658-us-202

PROTOCOL AMENDMENT: 07 Dated 14 Aug 2014

STUDY SPONSOR: Sarepta Therapeutics, Inc.

STUDY DOCTOR:

RESEARCH SITE ADDRESS(ES):

DAYTIME TELEPHONE NUMBER(S):

24-HOUR TELEPHONE NUMBER(S):

SUBJECT'S NAME: _____

INTRODUCTION

The purpose of this Parental Permission Form is to give you the information you will need to help you decide whether or not to allow your child to be in this study. Please read this form carefully. You should ask questions about what your child will be asked to do, the risks, the benefits, your child's rights as a subject, or anything else about the research or this form that is not clear to you. When all of your questions have been answered to your satisfaction, you can decide if you want your child to take part in this study or not. If you agree to allow your child to take part in this study and you sign this permission form, you will be given a copy for your records. If your child is 10 years of age or older, he will sign a separate informed consent form called an "Assent." You and your child will be given a copy for your records.

You are being asked to allow your child to be in this research study because your child has a muscle disorder called Duchenne muscular dystrophy (DMD). DMD is caused by a mutation (a change) in the gene that makes dystrophin protein. Dystrophin is important for protecting your child's muscles from stress and damage during activity. Because of the mutation in your child's gene, your child's body is not able to make enough working dystrophin to protect your child's muscles.

This study is investigating a study drug called eteplirsen, which is designed to skip a certain fragment of the dystrophin gene called exon 51. In people with changes, called deletions, in certain parts of the dystrophin gene (including exons 45-50, 47-50, 48-50, 50, 52, or 52-63), skipping exon 51 is believed to allow the body to produce a shortened, but still working, form of dystrophin protein. This may result in improved muscle function for people with DMD.

In this study, all subjects will receive eteplirsen once a week and take part in study-specific tests for 212 weeks.

Participation in this study is voluntary. Please learn enough about this research study, its risks and benefits, to decide whether you should agree to allow your child to take part. The study team will explain the study to you, and give you a chance to ask questions about anything you do not understand. This process is called "informed consent." It is up to you to choose if you want your child to be in this study. You may refuse to allow your child to be in this study or your child may quit this study at any time, and standard medical care will still be available here or at a doctor of your choice without a penalty or loss of benefits to your child. If your child is between 10 and 17 years of age and agrees to take part in the study, he will be asked to sign an Assent Form. You will be given a signed and dated copy of this Parental Permission Form and the Assent Form.

Note: A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you or your child. At most, the Web site will include a summary of the results. You can search this Web site at any time.

WHY ARE WE DOING THIS RESEARCH STUDY?

This study will examine the effects of continued treatment with eteplirsen in children with DMD who have successfully completed the 28-week eteplirsen study, Study 4658-us-201. To better understand how eteplirsen works over a long period of time; the sponsor will use data from both studies (4658-us-201 and 4658-us-202) to compare how your child does in this study to how he was doing before he started eteplirsen in Study 4658-us-201.

Sarepta Therapeutics, Inc. is developing eteplirsen for the treatment of DMD by intravenous (IV, meaning through a vein) administration. Eteplirsen is designed to skip exon 51, which is believed to allow for the production of a shortened, but still working, form of the dystrophin protein and therefore result in improved muscle function for people with DMD.

Eteplirsen is considered to be an experimental drug. Experimental means that this study drug is currently being tested. Eteplirsen has not been approved for marketing by the Food and Drug Administration (FDA) for use in the United States.

WHERE WILL THE STUDY BE DONE AND HOW MANY PARTICIPANTS WILL TAKE PART?

This study will only be open to the 12 subjects who took part in the previous eteplirsen study, Study 4658-us-201. This study will be done at Nationwide Children's Hospital (the central site) and at up to 12 sites closer to the homes of participating subjects (satellite sites).

To take part in the study your child will need to meet all of the inclusion criteria and none of the exclusion criteria that your child's study doctor will discuss with you. The study doctor will also speak with you about some medicines that should not be taken by your child while participating in this study.

To be enrolled in the study, your child must:

1. Have completed 28 weeks of treatment in Study 4658-us-201
2. Have a parent(s) or legal guardian(s) who is able to understand and comply with all of the study requirements
3. Have a parent(s) or legal guardian(s) who is willing to provide written informed consent for the subject to take part in the study
4. Be willing, if at least age 10, to provide informed assent (agreement)

If your child has a prior or ongoing medical condition that the study doctor believes might affect his safety, or make it difficult for him to attend all of the required study visits and receive all of the study drug, or might affect the results of this study, your child will not be able to take part in this study.

WHAT WILL HAPPEN DURING THE STUDY AND HOW LONG WILL IT LAST?

During this study, your child will receive IV infusions of either 30 or 50 mg/kg eteplirsen once a week for 212 weeks (approximately 4 years). Your child will receive the same dose of eteplirsen in this study that he received in Study 4658-us-201. That means if your child received the high dose (50 mg/kg) of eteplirsen in 4658-us-201, then he will receive the high dose in this study, and if he received the low dose of eteplirsen in 4658-us-201 (30 mg/kg), then he will receive the low dose in this study. Remember that the dose of eteplirsen that your child receives (high or low) was randomly assigned to him (picked by chance like tossing a coin in the air) during Study 4658-us-201. There was an even chance (50/50) that he would be assigned to the high or low dose.

This study is open-label. Open-label means that the study doctor, the study nurse, the study sponsor (Sarepta Therapeutics, Inc.), you, your child, and everyone else who might work with your child in this study will know your child is receiving eteplirsen.

Your child will receive all weekly infusions at the identified satellite site that is closer to your home. The personnel there are trained, and the site is approved to take part in this study. You and your child will be asked to sign new Parental Permission and Assent Forms when you transfer to the satellite site.

Option for Home infusions:
After your Week 124 visit, you may be given the option to have a home infusion visiting nurse come to your house to give your child their weekly infusions. If you are interested in this option, you will need to discuss this with your study doctor. Your study doctor can provide more information about the home infusion option and help you to decide whether or not this is a good option for your child. If you and your study doctor agree to have your child infused at home, you and your child will still need to return to the study site about once every month for study assessments and an infusion. You will also be responsible for continuing to communicate with the study doctor about how your child is doing.

You and your child will still need to travel to Nationwide Children's Hospital approximately once every 24 weeks so your child can complete certain study-specific tests.

The procedures and tests that will take place at each of the weekly study visits are presented below.

If a situation occurs that your child is unable to attend a scheduled visit and your child is at risk of missing a weekly dose, you must immediately notify the study doctor. It is very important that no more than 2 doses are missed in a 6-month period. If your child misses more than 16 doses during the 212 week study, he may be withdrawn from the study.

Screening/Baseline Period
Because this is an extension study for children who successfully completed Study 4658-us-201, there will be no formal screening period for this study. Instead, the study doctor will review the details of this study with you, obtain your consent and your child's agreement (assent) to take part in this study, and make sure this study is right for your child at the last visit (Week 28) of Study 4658-us-201.

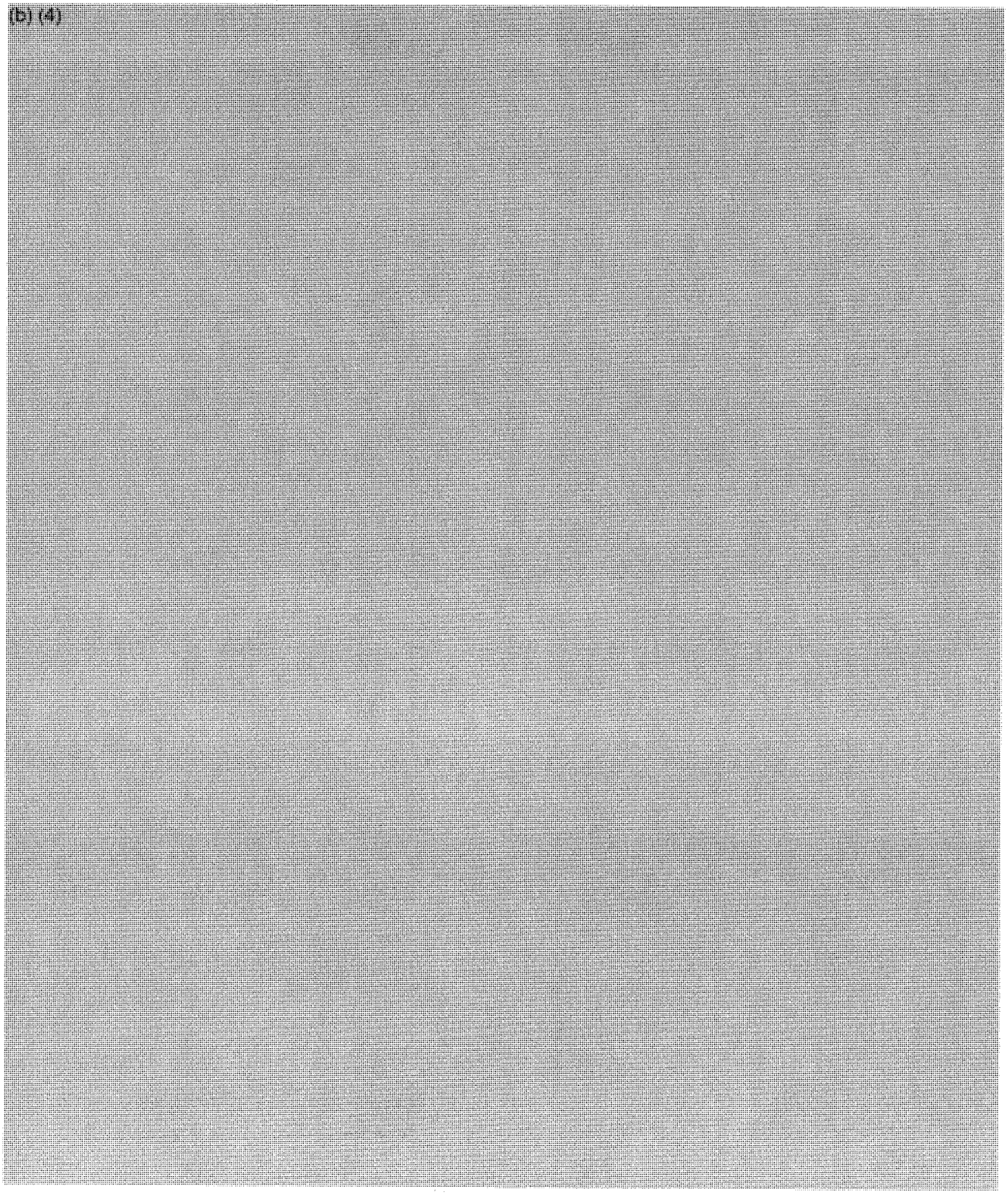
In addition to procedures and tests specific to Study 4658-us-201, the following procedures will be performed at (b) (4) of Study 4658-us-201:

(b) (4)

Parental/Legal Guardian Initials _____

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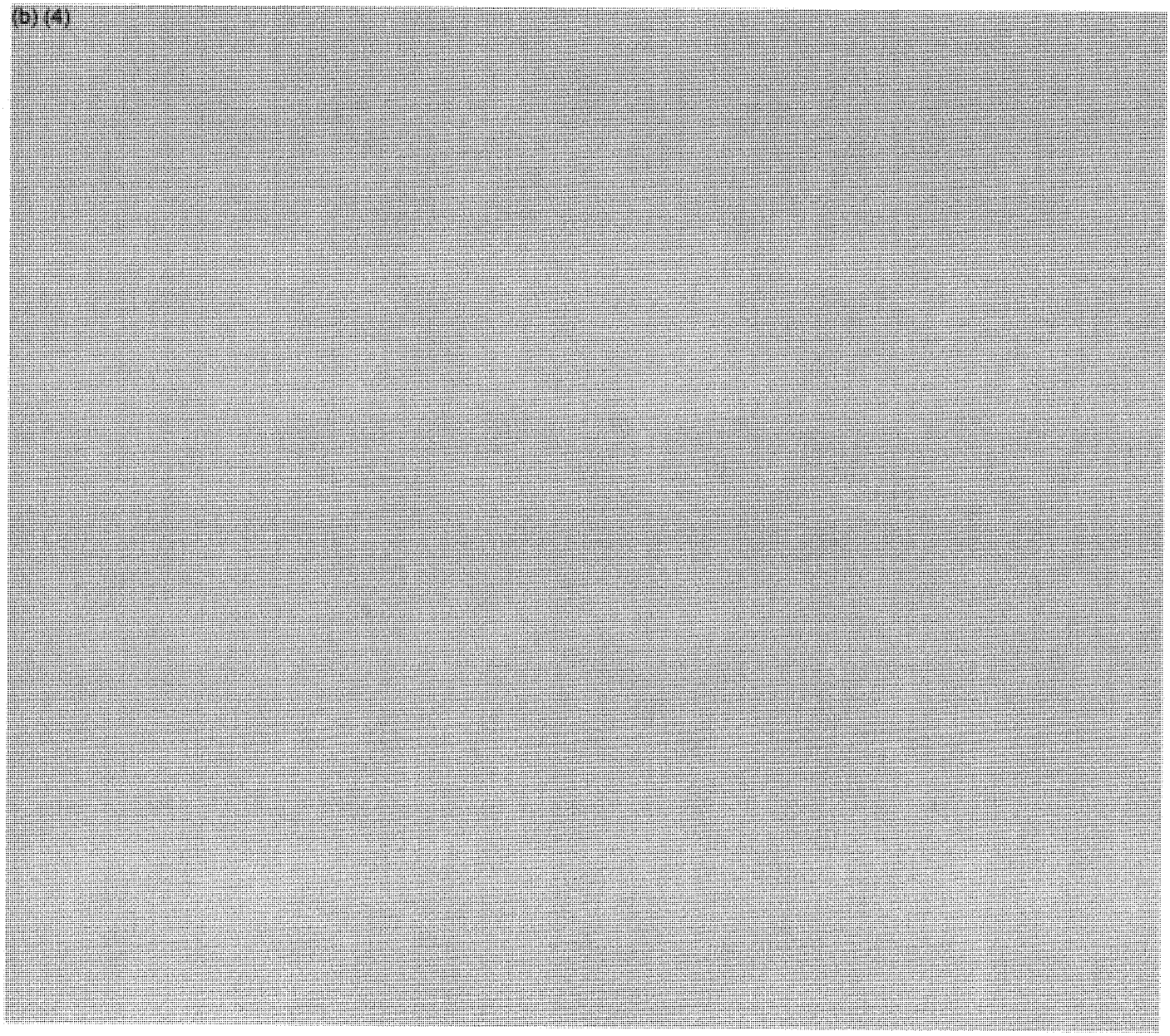
(b) (4)



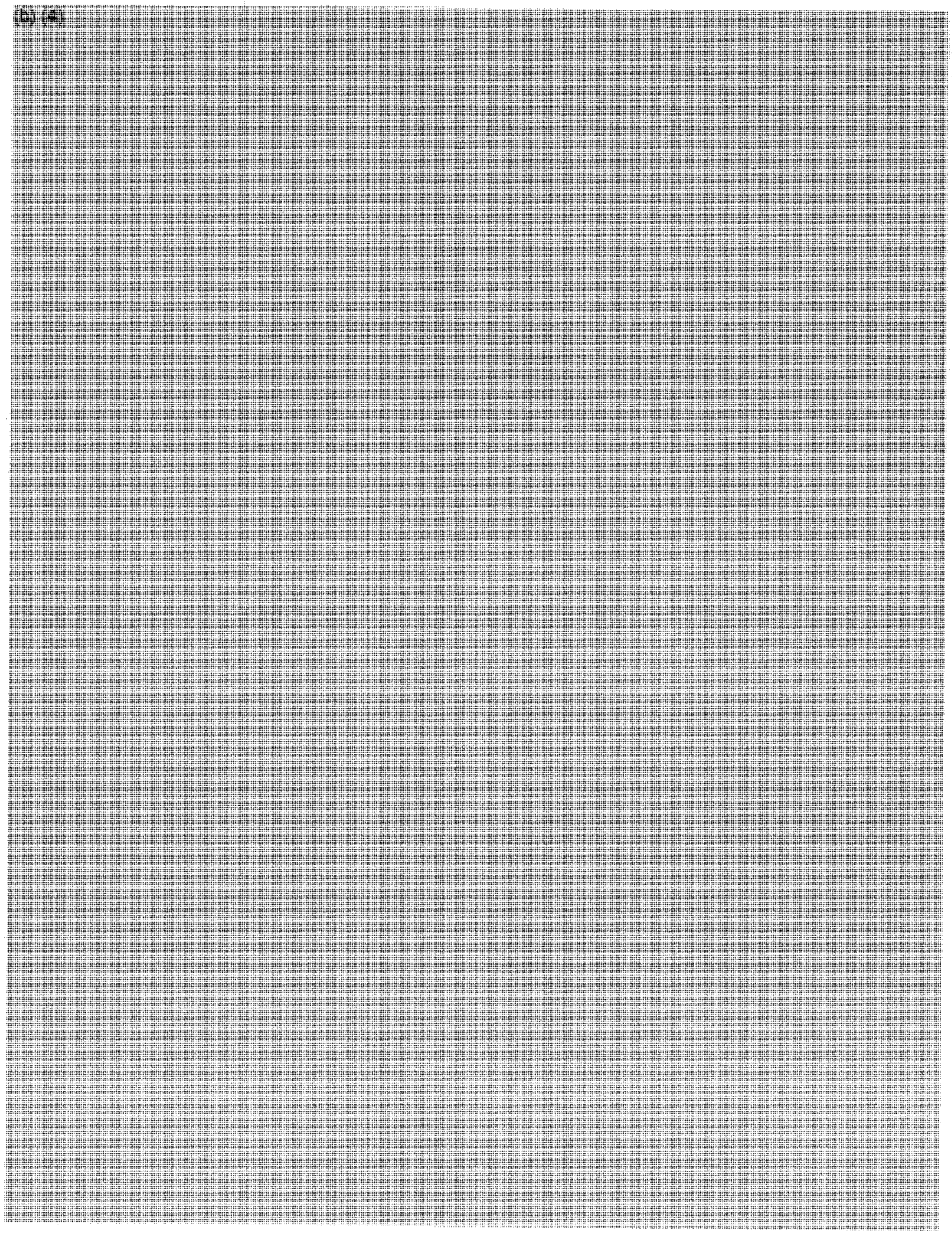
6. Study Drug Administration – Your child will receive a 35 to 60-minute infusion of eteplirsen. A topical anesthetic (numbing) cream (e.g., lidocaine 2.5%, prilocaine 2.5%, or LMX4 cream) may be applied to your child's skin prior to the infusion, if needed. After the infusion ends, your child will be observed for at least 30 to 60 minutes to make sure that he is doing okay. As long as he is okay and all other tests and procedures have been completed, the study doctor will then let you and your child go home.

Please Note: Your child's doctor may recommend the insertion of a port as an option for the IV infusion of eteplirsen, if it is becoming difficult to use an IV to access their veins. A port is a small device inserted under the skin, which makes it easier to give infusions and collect blood.

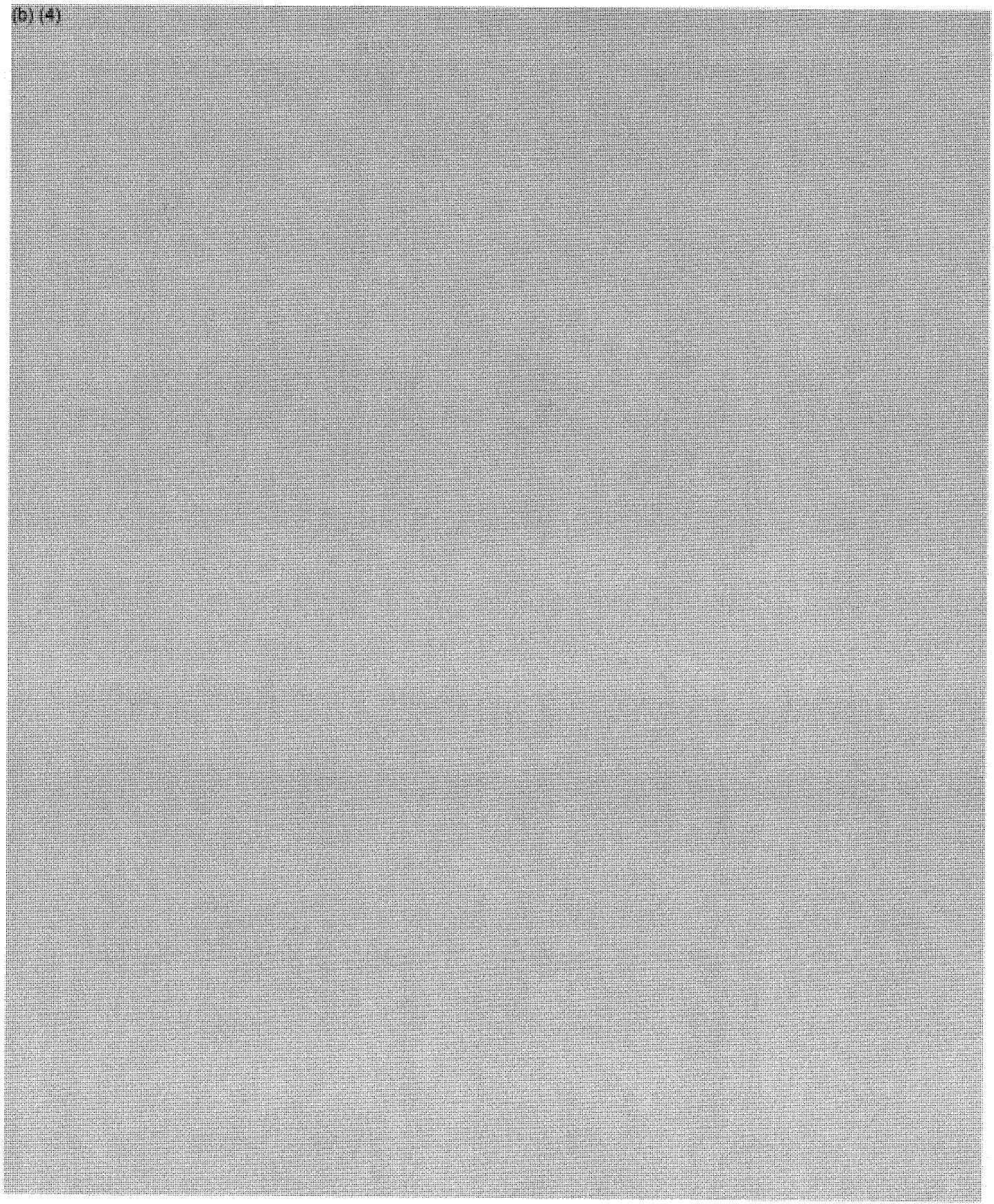
(b) (4)



(b) (4)



(b) (4)



(b) (4)

WHAT ARE THE RISKS OF BEING IN THIS STUDY?
There are risks to taking part in this research study. One risk is that your child may have side effects while in the study from eteplirsen or from participating in the other research procedures.

Some research studies involving eteplirsen have already been done. Some studies involved eteplirsen at lower doses than your child will receive in this research study.

Common health issues that occurred in studies that used lower doses of Eteplirsen than those used in this study were:

Headache, upper respiratory tract infection, back pain, rhinitis (inflammation of the mucous membrane of the nose that may cause nasal congestion and itching, and sneezing), falling, and myalgia (pain in the muscle). There was also an isolated occurrence of decreased heart function without symptoms.

Common health issues that occurred with the same or a higher dose of Eteplirsen over two years were:

Procedural pain, contusion, arthropode (tick or spider) bite, excoriation (scratch), fall, pain in extremity (arm or leg), back pain, arthralgia (joint pain), muscle spasms (cramps), oropharyngeal pain (pain in mouth or throat), nasal congestion, cough, catheter site pain, pyrexia (fever), nasopharyngitis (inflammation of the nose and throat), upper respiratory tract infection, headache, balance disorder, vomiting, diarrhea, nausea, contact dermatitis (skin inflammation), rash, hypokalemia (low blood potassium levels), proteinuria (protein detectable in urine) and hematoma.

Blood Draw/IV Risk
Drawing blood and starting IVs by placing a needle in a vein may cause pain, lightheadedness and fainting, bleeding, bruising, or swelling at the puncture site. Infection is a rare possibility. Topical anesthetic or numbing cream may be used on the skin to decrease the discomfort, if needed. Although there are no known side effects from the numbing cream, skin irritation or an allergic reaction is possible.

Insertion of Port Risk
- An infection that may require the removal of the device
- Thrombosis (a blood clot) that can form in the catheter that may block the device from being accessed.

- Failure of the device - although unlikely, it is possible the device could break
- Pneumothorax (air or gas between the lungs and the chest wall), causing the lungs to collapse
- Injury to an artery

Muscle Biopsy Risk
The common side effects of the muscle biopsies may include discomfort, a scar, infection, bruise, numbness near the biopsy site, and delayed wound healing.

Sedation Risk
Risks from local anesthetic may include pain with infection, and (very rarely) allergic reactions. Minor discomfort during surgery is common, but the likelihood of other risks is extremely small (less than 1%). After use of conscious sedation, your child may get a headache or feel nauseous or dizzy. It is possible that your child will have a reaction to the sedative medication used.

If any of the symptoms listed above are severe, your child must get medical help right away. If you are worried about anything while in this study, please call the study doctor or study nurse at the telephone number on page 1.

Unforeseen Risks
There may be other risks of being in this research study that are not known at this time.

ARE THERE BENEFITS TO TAKING PART IN THIS STUDY?
The potential benefits of eteplirsen in subjects with DMD are unknown. Your child may have some benefits from taking part in this study, but even if your child does not benefit from being in this study, we might learn something that could help others.

WHAT WILL HAPPEN IF NEW INFORMATION IS FOUND OUT ABOUT THE DRUG OR TREATMENT?
If new information is found out during this study that might change your mind about your child taking part or might affect your child's health, your study doctor will discuss it with you and your child as soon as possible.

WHAT OTHER TREATMENTS OR OPTIONS ARE THERE?
Your child's participation in this study is voluntary. It is not necessary to be in this study to get care for this condition. If you decide not to allow your child to be in this study, the study doctor will talk to you and your child about other possible treatments or refer you to your child's regular doctor for care.

WILL THERE BE ANY COSTS TO ME?
It will not cost you or your child anything to be in this study and you or your child will not be paid to be in this study. Travel expenses including airfare (with supporting receipts) for up to two adults and one child for all required visits to Nationwide Children's Hospital will be covered.

INTERNAL NOTE - PI Specific Comp – delete template wording as appropriate

CONFIDENTIALITY OF STUDY INFORMATION

The data collected as part of this study will be kept confidential, but may be shared with the individuals and entities and for the purposes described in this Parental Permission Form and the attached HIPAA Authorization form. In all study-related records, a number and initials will identify your child, unless otherwise described in this Parental Permission Form or the attached HIPAA Authorization form. Data collected and recorded on study forms are the property of the sponsor if information about this study is published, your child's identity will remain confidential. However, the U.S. Food and Drug Administration (FDA), Copernicus Group Independent Review Board (IRB), local IRB and the study sponsor, Sarepta Therapeutics, Inc. and its representatives may be granted direct access to your child's original medical records for verification of clinical trial procedures or data. By signing this Parental Permission Form, you are authorizing such access. A court of law could order medical records shown to other people, but that is unlikely.

WHAT HAPPENS IF BEING IN THIS STUDY CAUSES INJURIES?

If your child is hurt by the study drug, eteplirsen, or the procedures that are part of the study, you should seek medical treatment for your child's injuries and tell the study doctor as soon as possible at the number on the first page of this form. If it is an emergency, call 911 or go to the nearest emergency department.

If your child is injured as a direct result of the proper administration of the study drug, eteplirsen, or the proper performance of procedures that are required solely for the study, and your child has followed the directions of the study team, (b) (4)

(b) (4)

If the care is provided at Nationwide Children's Hospital and/or the satellite site, (b) (4)

(b) (4)

(b) (4) This does not mean that you give up any of your or your child's legal rights to seek compensation for your child's injuries.

LEGAL RIGHTS

The above section does not restrict your right to seek legal assistance. By signing this Parental Permission Form you will not waive any of your child's legal rights as a research subject.

WHAT HAPPENS IF MY CHILD DOES NOT FINISH THIS STUDY?
It is your choice to allow your child to be in this study or to stop at any time. If you decide to stop your child from being in this study, it is okay, but you must call the study doctor or the study nurse. If you stop your child from being in the study, there will not be a penalty or loss of benefits to which your child is otherwise entitled.

If at any time the study doctor believes participating in this study is not the best choice of care for your child, the study may be stopped and other care prescribed. If the study instructions are not followed, your child's participation in the study may also be stopped. If unexpected medical problems come up, the study doctor or the sponsor, Sarepta Therapeutics, Inc., may decide to stop your child's participation in the study.

If your child's participation in the study is stopped before completing all of the study activities, your child will be asked to visit the study doctor, **PI's name to populate** (unless you have withdrawn consent), or you may be asked to return to Nationwide Children's Hospital so that the following information can be collected and assessments can be completed:

(b) (4)

In addition, subjects who have not already had their (b) (4)

If your child withdraws from the study because he is not feeling well, your child will be encouraged to have follow-up assessments when he feels better.

Use of samples and data for research purposes:
1. In this study, **left over blood will be stored for research at a later time**, perhaps even years from now. This research may include DNA (gene) testing. This future research may be for purposes other than your child's medical problem. You will not be told the results of any future research. If you decide at any time that you do not want your child's blood stored for future research, you may contact the Study Doctor or Study Nurse.

Please initial next to "yes" or "no" whether you give permission for the following testing/research:

___ **Yes**, I agree to allow my child's leftover blood or DNA to be stored and used for future research. I understand that the samples may be used for testing/research unrelated to this study and that I will not be told the results.

___ **No**, I do not want my child's leftover blood or DNA to be stored or used for future research.

You may decide later that you would like to withdraw your samples from the research. If so, inform your study doctor and the samples will not be saved for future research, and will instead be destroyed.

The study sponsor and its affiliates and agents who perform evaluation of your child's genes have an economic interest in developing new consumer service and potential diagnostic products. Your child's genes or genetic information about your child may be used to develop consumer products and medical therapies and diagnostics, and these which could be distributed and sold for profit. The study sponsor and its affiliates and agents may patent or sell discoveries based on their evaluation. Some of the scientists or companies may receive money from these activities. You and your child will not receive payment or have a personal economic interest in any services or products that may be developed in this evaluation or that might be developed from your child's DNA or other information you provide, and you should have no expectation of obtaining or acquiring any financial interest in this evaluation.

OTHER IMPORTANT INFORMATION

It is considered a conflict of interest where the parents of a potential subject hold stock of Sarepta Therapeutics, Inc. By signing this consent form, you agree that neither you nor any of your family have stock of or an interest with the potential for financial gain in the sponsor, Sarepta Therapeutics, Inc.

It is important that healthcare providers know about all medicines your child is taking. This includes the study drug being tested in this research study. Because of this, we plan to tell your child's primary care doctor that he is in this research study. This is done so extra care can be taken in prescribing other medicines and looking at any unexplained symptoms that may occur. Your child cannot take part in this study if you do not want us to tell your child's primary care doctor.

The study doctor is being paid by Sarepta Therapeutics, Inc. for the time and knowledge needed to do this study.

Being in more than one research study at the same time may cause injury. Please tell the study doctor if your child is in any other research study so a decision can be made about being in more than one study at the same time.

Keep in mind that your permission for your child's participation in the study will remain valid until such time as you choose to withdraw it. This withdrawal should be in writing and sent to the following address:

Any information collected prior to this withdrawal may be used but no new information would be collected after the time the withdrawal is received.

WHOM SHOULD I CALL IF I HAVE QUESTIONS OR PROBLEMS?
If you have any questions about your child's participation in this research study or if you feel that your child has experienced a research-related injury or reaction to the study drug, contact:

Investigator Name:

Daytime telephone number(s): ; you can reach the study nurse during business hours at

24-hour contact number(s): (7 days a week)

If you have any questions or concerns about your child's rights as a research subject or want to discuss a problem, get information or offer input, you may contact Copernicus Group Independent Review Board (IRB) at 1-888-303-2224 (toll free). An IRB is a group of scientific and non-scientific individuals who perform the initial and ongoing ethical review of the research study with the study subject's rights and welfare in mind. Copernicus Group IRB has reviewed and approved the research study described in this Parental Permission Form. If you have study-related comments, complaints or concerns, you should first contact the study doctor. Please call the IRB if you want to talk to someone other than the study doctor or have difficulty reaching the study doctor. For further information regarding the clinical trials process and your child's role as a research subject, you may visit the Copernicus Group IRB website at www.cgirb.com.

PARENTAL STATEMENT OF PERMISSION

Open-Label, Multiple-Dose, Efficacy, Safety, and Tolerability Study of Eteplirsen in Subjects with Duchenne Muscular Dystrophy who Participated in Study 4658-us-201

I have read this Parental Permission Form and have had a chance to ask questions about this research study, which have been answered to my satisfaction. If I have more questions about participation in this study or a research-related injury, I may contact the study doctor. By signing this Parental Permission Form, I certify that all health information I have given regarding my child is true and correct to the best of my knowledge.

I have been given a copy of the **Site's company name to populate** Notice of Privacy Practices. I have been told that my right to my child's patient information that is created or collected in the course of this research can be temporarily suspended for as long as the research is in progress. I also have been told that my right to access will be reinstated upon completion of this research.

I give permission for my child to take part in this study. I will be given a copy of this Parental Permission Form with all the signatures for my own records as well as a copy of the Experimental Subjects Bill of Rights. ***For CA Sites Only***.

_____
PRINTED NAME OF SUBJECT

_____
PRINTED NAME OF PARENT/LEGAL GUARDIAN

_____ _____
SIGNATURE OF PARENT/LEGAL GUARDIAN | DATE & TIME AM/PM

_____
PRINTED NAME OF SECOND PARENT/ LEGAL GUARDIAN

_____ _____
SIGNATURE OF SECOND PARENT/ LEGAL GUARDIAN | DATE & TIME AM/PM

Permission of the second parent not obtained because (select all that apply):

_____ Other parent is deceased.
_____ Other parent is unknown.
_____ Other parent is not reasonably available.
_____ Only one parent has legal responsibility for the care and custody of subject.

I certify that I have explained the research, its purposes, and the procedures to the patient or subject's parent(s) or legal guardian(s) and have answered all of their questions, before requesting their signature. I believe that he/she understands the information described in this Parental Permission Form and freely consents to have his/her child participate in the study.

_____
PRINTED NAME OF PERSON
OBTAINING CONSENT

_____ _____
SIGNATURE OF PERSON DATE & TIME AM/PM
OBTAINING CONSENT

_____
PRINTED NAME OF INVESTIGATOR

_____ _____
SIGNATURE OF INVESTIGATOR DATE & TIME AM/PM

_____
PRINTED NAME OF WITNESS

_____ _____
SIGNATURE OF WITNESS DATE & TIME AM/PM
FOR VA SITES ONLY

HIPAA AUTHORIZATION

The United States government has issued a privacy rule to protect the privacy rights of patients. This rule was issued under a law called the Health Insurance Portability and Accountability Act of 1996 (HIPAA). The Privacy Rule is designed to protect the confidentiality of your child's personal health information. The document you are reading, called an "Authorization," describes your child's rights and explains how your child's health information will be used and disclosed (shared).

HOW WILL MY CHILD'S STUDY INFORMATION BE KEPT PRIVATE?
Information collected for this study will be kept confidential to the extent provided by law. Health information means the information in your child's medical or other healthcare records, which also may include information that can identify your child. Information that can identify your child is called "protected health information" or PHI. By agreeing to allow your child to be in this study, you are giving permission and authorizing **PI's name to populate** and his study staff to collect, use, and disclose your child's PHI for this research study. The results of the study may be published in scientific journals or presented at medical meetings. In the event of any publication regarding this study, your child's identity will not be revealed.

Your child's PHI collected or created under this research study will be used/disclosed as needed during and even after the end of the study. We will need to use it for research purposes and will release it to other people involved in the research or your child's routine healthcare. We will also generate new healthcare information about your child during the course of the study. This information will come from the tests and procedures and any interviews of your child conducted in connection with the study. The records of this study will be kept for an indefinite period of time, and by signing this Authorization you are authorizing the use of your child's PHI in accordance with this Authorization during that entire period. If you decide to withdraw your child from the study, or if your child is removed from the study by the study doctor or Sponsor (Sarepta Therapeutics, Inc.) you may withdraw, on your child's behalf, your permission for others to use and disclose your child's PHI, except that PHI that has already been collected may still be used by and disclosed to the individuals and entities as described in this Authorization. If you withdraw your permission for the use and disclosure of your child's PHI, your child can no longer take part in this research study.

If you decide to withdraw your permission for the use and disclosure of your child's PHI, this must be in writing. Please send a letter to your study doctor:

Your child's PHI that may be used or disclosed:
Your child's PHI that may be used and disclosed for this study includes: review of your child's past, current or future health records, procedures such as physical examinations, blood or urine tests or other tests, your child's response to any study drug your child receives, your child's study visits, phone calls, study tests and procedures and any other study related health information, may be collected, used and disclosed to others.

Your child's PHI also includes:

- ✓ Name and Date of Birth
- ✓ All medical records, including genetic testing and study tests and procedures
- ✓ Contact information (Addresses, Email addresses, Telephone/fax numbers)
- ✓ Family medical history
- ✓ Photos and videos

Efforts will be made to keep your child's study-related information confidential; however confidentiality cannot be guaranteed. Once disclosed, the PHI may no longer be protected by federal law and may be re-disclosed by those receiving the information.

People or Companies authorized to use, disclose, and receive your child's health information and PHI collected or created by this research study for purposes related to this study:

- **PI's name to populate** and study staff
- The Copernicus Group Independent Review Board (the committee that reviews all human subject research)
- Nationwide Children's Hospital internal auditors
- The Office for Human Research Protections (OHRP) (the federal government office that oversees human patient research)

- Sarepta Therapeutics, Inc., the study sponsor and its designees, representatives and agents (including third parties who are providing services to the sponsor related to the study)
- An independent committee of physicians and experts that will review safety information from this study periodically
- The Food and Drug Administration (FDA) and other governmental health agencies, both within and outside the United States
- Your child's insurance company (if charges are billed to insurance).

Your child's health information and/or PHI also may be used and shared for treatment, payment and healthcare operations. Medical information from this study will become part of your child's hospital medical record.

In order to provide your child with routine care, other people at the hospital may need to review the health information we put into your record. This would include such people as your regular doctors and nurses and the hospital's billing department.

Your personal health information may be further shared by the groups above. If shared by them, the information will no longer be covered by the Privacy Rule. However, these groups are committed to keeping your personal health information confidential.

May I have access to my child's health information and PHI?
You will always have access to your child's medical record. A summary may be made available to you at the completion of the study. You will not have access to your child's research file because all information contained in the research file is either information obtained directly from your child, or was gathered from your child's medical records, to which you do have access. In some cases your child's research file may contain some information not known to you or the researchers that if known, would affect the scientific importance of the study.

AUTHORIZATION

I authorize the release of my child's medical records and personal health information related to this study to the Sponsor, including its affiliates, successors and assigns, both in the U.S. and other countries, and/or any third party working with Sponsor to conduct the study or to analyze or review study-related documents or data, the Copernicus Group Independent Review Board, the FDA and other regulatory agencies, and to the other individuals and entities as described above. I have been told that I will receive a signed and dated copy of this Authorization for my records.

_____

Printed First and Last Name of Subject

_____

Printed First and Last Name of Parent/Legal Guardian

_____ _____

Signature of Parent/Legal Guardian Date

_____

Printed First and Last Name of Parent/Legal Guardian

_____ _____

Signature of Parent/Legal Guardian Date

_____

Printed Name of Person Obtaining Authorization

_____ _____

Signature of Person Obtaining Authorization Date

_____

Printed Name of Investigator

_____ _____

Signature of Investigator Date

APPROVED: Apr 23, 2014
COPERNICUS GROUP IRB

copernicus group independent review board
Approved:

PARENTAL PERMISSION FORM AND HIPAA AUTHORIZATION

STUDY TITLE: Open-Label, Multiple-Dose, Efficacy, Safety, and Tolerability Study of Eteplirsen in Subjects with Duchenne Muscular Dystrophy who Participated in Study 4658-us-201

PROTOCOL NUMBER: 4658-us-202

PROTOCOL AMENDMENT: 05 Dated 13 Feb 2014

STUDY SPONSOR: Sarepta Therapeutics, Inc.

STUDY DOCTOR:

RESEARCH SITE ADDRESS(ES):

DAYTIME TELEPHONE NUMBER(S):

24-HOUR TELEPHONE NUMBER(S):

SUBJECT'S NAME: _____

INTRODUCTION

The purpose of this Parental Permission Form is to give you the information you will need to help you decide whether or not to allow your child to be in this study. Please read this form carefully. You should ask questions about what your child will be asked to do, the risks, the benefits, your child's rights as a subject, or anything else about the research or this form that is not clear to you. When all of your questions have been answered to your satisfaction, you can decide if you want your child to take part in this study or not. If you agree to allow your child to take part in this study and you sign this permission form, you will be given a copy for your records. If your child is 10 years of age or older, he will sign a separate informed consent form called an "Assent." You and your child will be given a copy for your records.

You are being asked to allow your child to be in this research study because your child has a muscle disorder called Duchenne muscular dystrophy (DMD). DMD is caused by a mutation (a change) in the gene that makes dystrophin protein. Dystrophin is important for protecting your child's muscles from stress and damage during activity. Because of the mutation in your child's gene, your child's body is not able to make enough working dystrophin to protect your child's muscles.

This study is investigating a study drug called eteplirsen, which is designed to skip a certain fragment of the dystrophin gene called exon 51. In people with changes, called deletions, in certain parts of the dystrophin gene (including exons 45-50, 47-50, 48-50, 50, 52, or 52-63), skipping exon 51 is believed to allow the body to produce a shortened, but still working, form of dystrophin protein. This may result in improved muscle function for people with DMD.

In this study, all subjects will receive eteplirsen once a week and take part in study-specific tests for 164 weeks.

Participation in this study is voluntary. Please learn enough about this research study, its risks and benefits, to decide whether you should agree to allow your child to take part. The study team will explain the study to you, and give you a chance to ask questions about anything you do not understand. This process is called "informed consent." It is up to you to choose if you want your child to be in this study. You may refuse to allow your child to be in this study or your child may quit this study at any time, and standard medical care will still be available here or at a doctor of your choice without a penalty or loss of benefits to your child. If your child is between 10 and 17 years of age and agrees to take part in the study, he will be asked to sign an Assent Form. You will be given a signed and dated copy of this Parental Permission Form and the Assent Form.

Note: A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you or your child. At most, the Web site will include a summary of the results. You can search this Web site at any time.

WHY ARE WE DOING THIS RESEARCH STUDY?

This study will examine the effects of continued treatment with eteplirsen in children with DMD who have successfully completed the 28-week eteplirsen study, Study 4658-us-201. To better understand how eteplirsen works over a long period of time; the sponsor will use data from both studies (4658-us-201 and 4658-us-202) to compare how your child does in this study to how he was doing before he started eteplirsen in Study 4658-us-201.

Sarepta Therapeutics, Inc. is developing eteplirsen for the treatment of DMD by intravenous (IV, meaning through a vein) administration. Eteplirsen is designed to skip exon 51, which is believed to allow for the production of a shortened, but still working, form of the dystrophin protein and therefore result in improved muscle function for people with DMD.

Eteplirsen is considered to be an experimental drug. Experimental means that this study drug is currently being tested. Eteplirsen has not been approved for marketing by the Food and Drug Administration (FDA) for use in the United States.

WHERE WILL THE STUDY BE DONE AND HOW MANY PARTICIPANTS WILL TAKE PART?

This study will only be open to the 12 subjects who took part in the previous eteplirsen study, Study 4658-us-201. This study will be done at Nationwide Children's Hospital (the central site) and at up to 12 sites closer to the homes of participating subjects (satellite sites).

To take part in the study your child will need to meet all of the inclusion criteria and none of the exclusion criteria that your child's study doctor will discuss with you. The study doctor will also speak with you about some medicines that should not be taken by your child while participating in this study.

To be enrolled in the study, your child must:

1. Have completed 28 weeks of treatment in Study 4658-us-201
2. Have a parent(s) or legal guardian(s) who is able to understand and comply with all of the study requirements
3. Have a parent(s) or legal guardian(s) who is willing to provide written informed consent for the subject to take part in the study
4. Be willing, if at least age 10, to provide informed assent (agreement)

If your child has a prior or ongoing medical condition that the study doctor believes might affect his safety, or make it difficult for him to attend all of the required study visits and receive all of the study drug, or might affect the results of this study, your child will not be able to take part in this study.

WHAT WILL HAPPEN DURING THE STUDY AND HOW LONG WILL IT LAST?

During this study, your child will receive IV infusions of either 30 or 50 mg/kg eteplirsen once a week for 164 weeks (approximately 3 years). Your child will receive the same dose of eteplirsen in this study that he received in Study 4658-us-201. That means if your child received the high dose (50 mg/kg) of eteplirsen in 4658-us-201, then he will receive the high dose in this study, and if he received the low dose of eteplirsen in 4658-us-201 (30 mg/kg), then he will receive the low dose in this study. Remember that the dose of eteplirsen that your child receives (high or low) was randomly assigned to him (picked by chance like tossing a coin in the air) during Study 4658-us-201. There was an even chance (50/50) that he would be assigned to the high or low dose.

This study is open-label. Open-label means that the study doctor, the study nurse, the study sponsor (Sarepta Therapeutics, Inc.), you, your child, and everyone else who might work with your child in this study will know your child is receiving eteplirsen.

Your child will receive all weekly infusions at the identified satellite site that is closer to your home. The personnel there are trained, and the site is approved to take part in this study. You and your child will be asked to sign new Parental Permission and Assent Forms when you transfer to the satellite site.

Option for Home infusions:
After your Week 124 visit, you may be given the option to have a home infusion visiting nurse come to your house to give your child their weekly infusions. If you are interested in this option, you will need to discuss this with your study doctor. Your study doctor can provide more information about the home infusion option and help you to decide whether or not this is a good option for your child. If you and your study doctor agree to have your child infused at home, you and your child will still need to return to the study site about once every month for study assessments and an infusion. You will also be responsible for continuing to communicate with the study doctor about how your child is doing.

You and your child will still need to travel to Nationwide Children's Hospital approximately once every 24 weeks so your child can complete certain study-specific tests.

The procedures and tests that will take place at each of the weekly study visits are presented below.

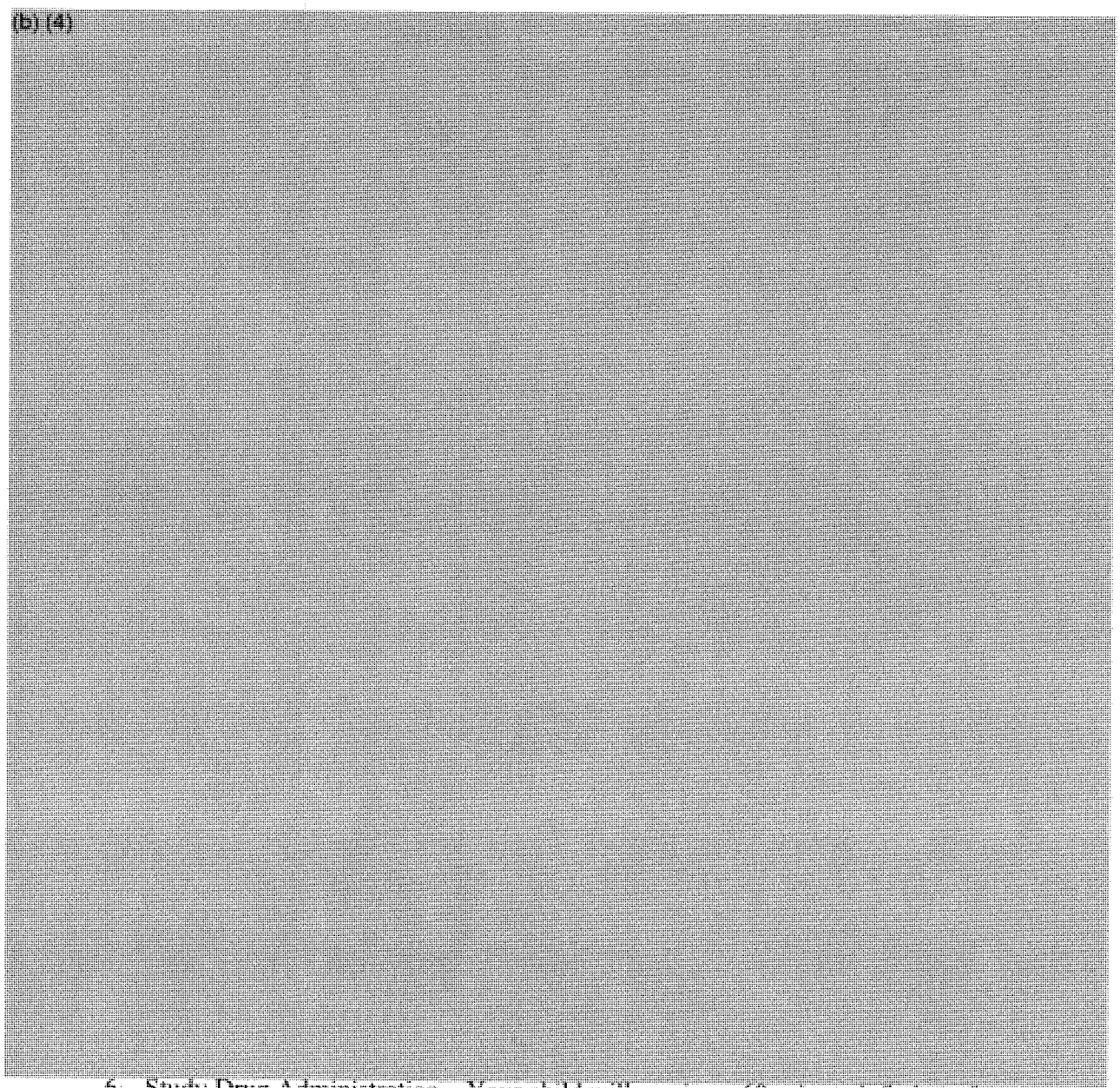
If a situation occurs that your child is unable to attend a scheduled visit and your child is at risk of missing a weekly dose, you must immediately notify the study doctor. It is very important that no more than 2 doses are missed in a 6-month period. If your child misses more than 8 doses during the 164 week study, he may be withdrawn from the study.

Screening/Baseline Period
Because this is an extension study for children who successfully completed Study 4658-us-201, there will be no formal screening period for this study. Instead, the study doctor will review the details of this study with you, obtain your consent and your child's agreement (assent) to take part in this study, and make sure this study is right for your child at the last visit (Week 28) of Study 4658-us-201.

In addition to procedures and tests specific to Study 4658-us-201, the following procedures will be performed at (b) (4) of Study 4658-us-201:

(b) (4)

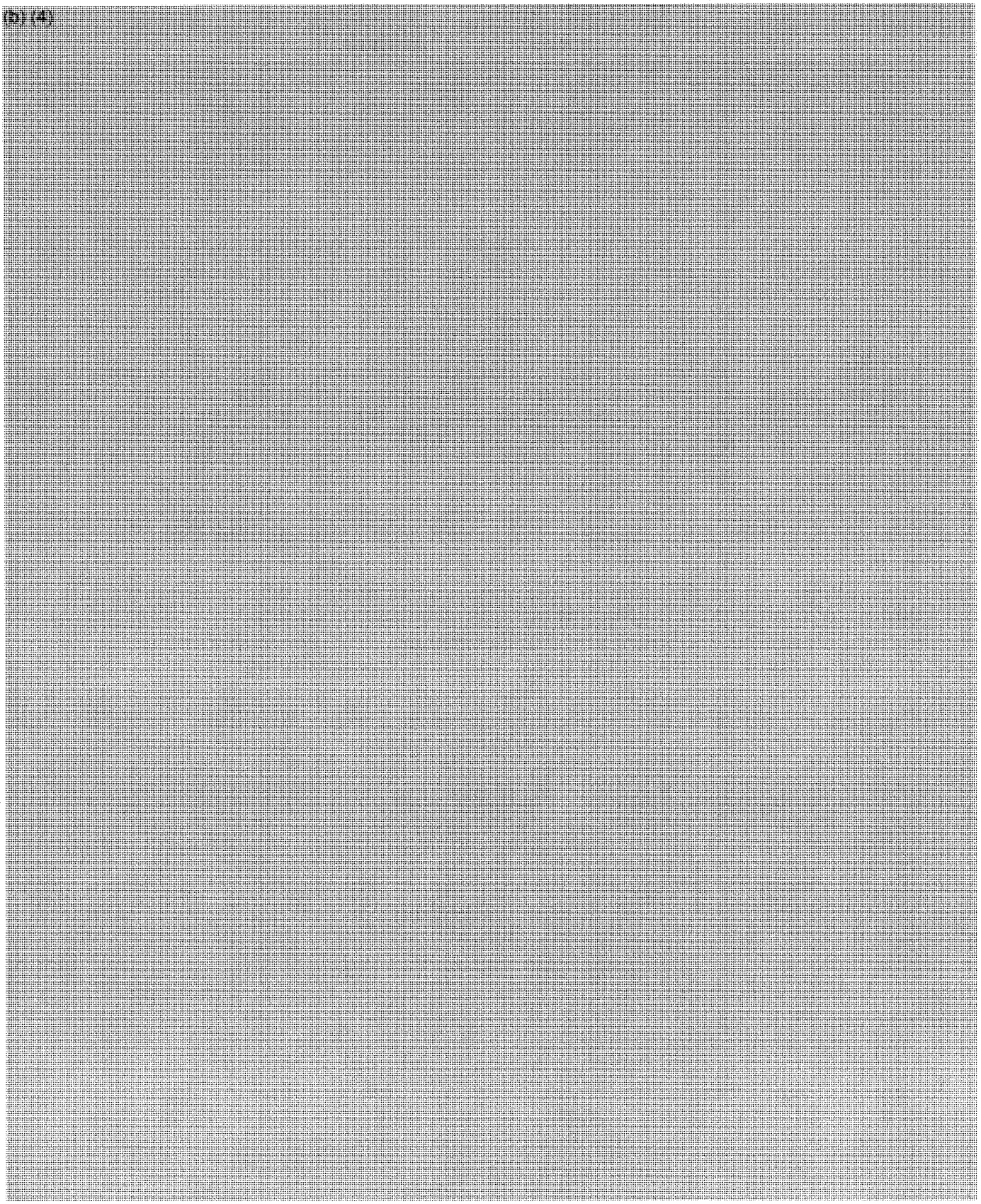
(b) (4)



6. Study Drug Administration – Your child will receive a 60-minute infusion of eteplirsen. A topical anesthetic (numbing) cream (e.g., lidocaine 2.5%, prilocaine 2.5%, or LMX4 cream) may be applied to your child's skin prior to the infusion, if needed. After the infusion ends, your child will be observed for at least 1 hour to make sure that he is doing okay. As long as he is okay and all other tests and procedures have been completed, the study doctor will then let you and your child go home.

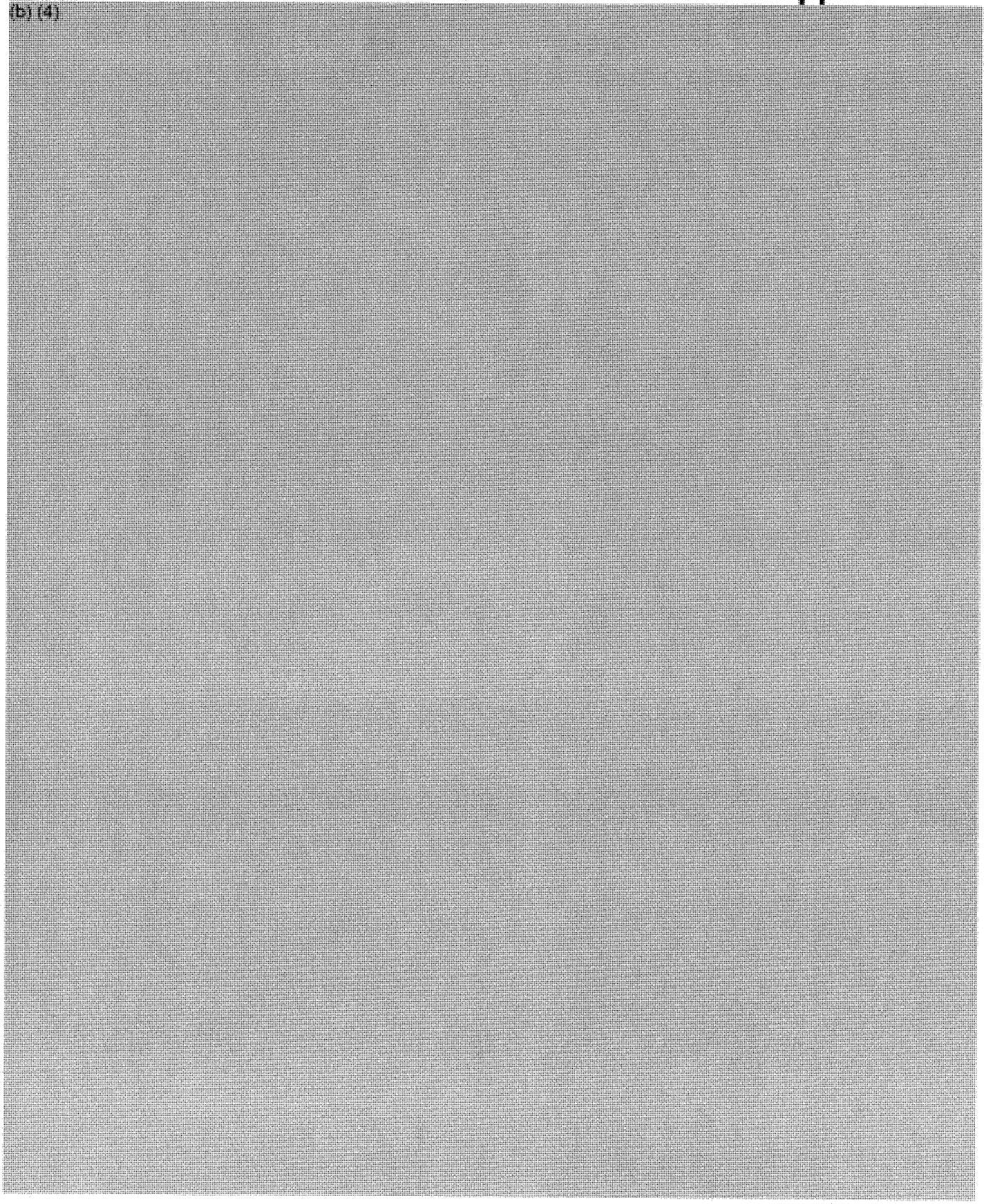
Please Note: Your child's doctor may recommend the insertion of a port as an option for the IV infusion of eteplirsen, if it is becoming difficult to use an IV to access their veins. A port is a small device inserted under the skin, which makes it easier to give infusions and collect blood.

(b) (4)



Parental/Legal Guardian Initials _____

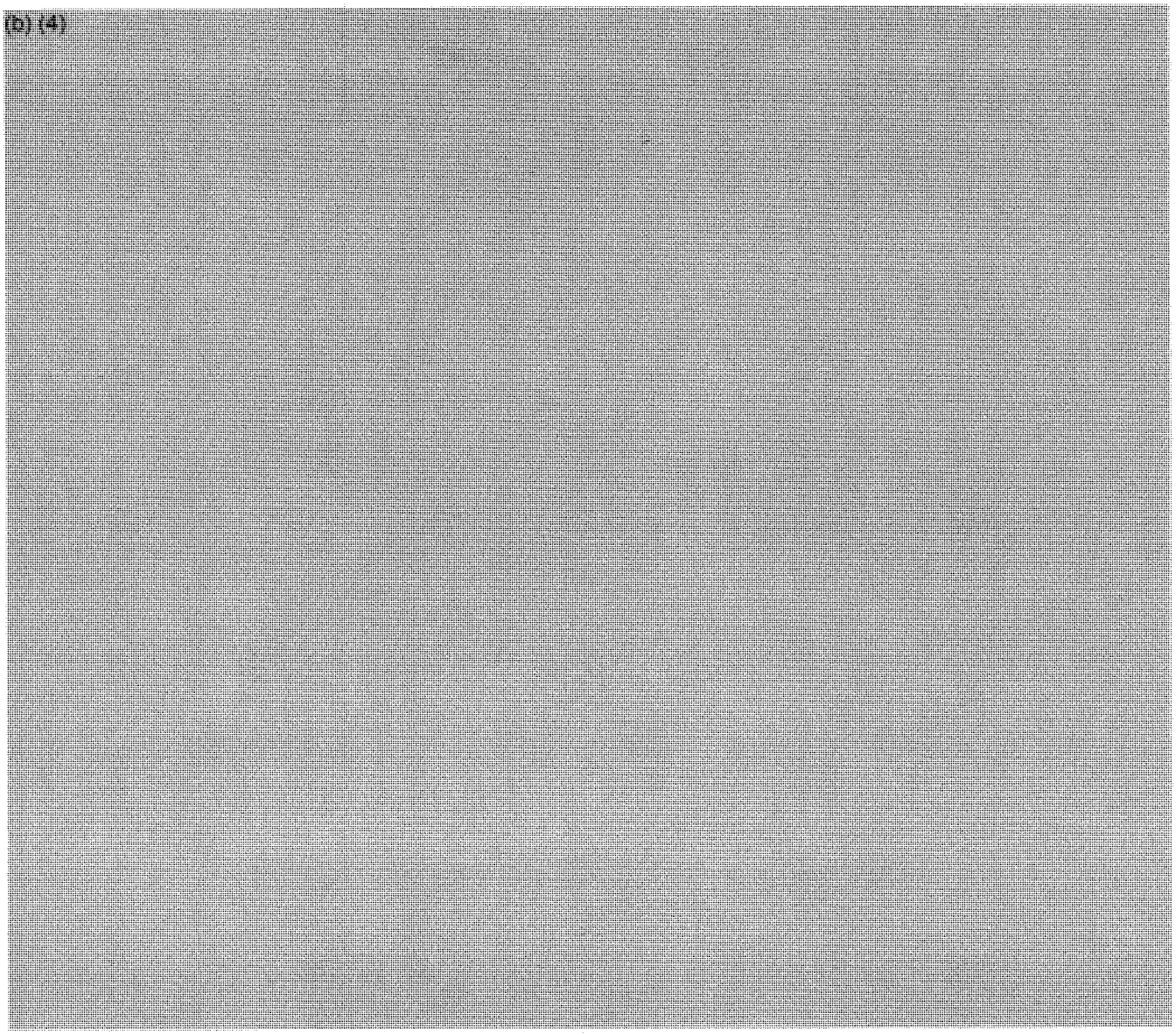
(b) (4)



Parental/Legal Guardian Initials _____

V6.0

(b) (4)



WHAT ARE THE RISKS OF BEING IN THIS STUDY?

Two clinical studies have been done with eteplirsen in children with DMD in the United Kingdom and study 4658-us-201 has been completed in the US. The first study was a placebo-controlled study of several doses of eteplirsen in 7 boys with DMD aged 10 to 17 years. Doses ranged from 0.09 mg to 0.9 mg/kg and were given by a single injection into a small muscle on the foot (this is called an intramuscular or IM injection). Several of the boys showed an increase in dystrophin protein in the muscle of the foot that had been injected with eteplirsen.

The second study was an open-label study of eteplirsen administered into the vein (this is called an intravenous or IV injection or infusion). This study enrolled 19 boys with DMD, who were 5 to 15 years of age, and patients received up to 12 weekly infusions of eteplirsen. Doses ranged from 0.5 to 20.0 mg/kg. In this second study, levels of dystrophin protein were increased at the end of the study in 7 out of the 17 patients that had muscle biopsies taken before starting eteplirsen and at the end of the study.

In both studies, eteplirsen was well-tolerated over the doses given (up to 20.0 mg/kg). Overall, the problems that occurred (called adverse events) were generally mild or moderate in intensity. The common side effects of eteplirsen were:

- headache (42%)
- upper respiratory tract infection (42%)
- back pain (37%)
- rhinitis (inflammation of the mucous membrane of the nose that may cause nasal congestion and itching, and sneezing) (37%)
- falling (26%)
- myalgia (pain in the muscle) (21%)

One subject, who had a pre-existing heart condition due to DMD, had a decrease in his heart function without symptoms while taking 4.0 mg/kg of eteplirsen. This problem was considered possibly related to the eteplirsen and the subject was withdrawn from study drug administration.

Through Week 92 of this study (120 total weeks from the start of Study 4658-us-201), there have been no clinically significant treatment-related adverse events and the treatment appears to be well tolerated. Some patients had mild elevation of urine protein on a laboratory urine dipstick test, which resolved without intervention and resulted in no clinical symptoms. The patients continued treatment without interruption.

One study that was conducted in muscular dystrophy laboratory mice with a drug for mice similar to eteplirsen showed a mild increase in the size of the cerebrospinal fluid space inside the brain that may be a type of hydrocephaly (water in the brain). The importance of this finding from laboratory mice and how it relates to long-term dosing of eteplirsen in humans is unclear. Additional review and analysis is being conducted and reviewed related to this finding. At this time there are no recommendations to change the current eteplirsen trial.

It is important that you give the study staff your child's complete medical history. Not giving them this information or not completely following the directions of the study could harm your child.

All study drugs may cause some side effects or other reactions. There is no way to predict if your child will experience any of these side effects. Side effects that are not yet known may also occur.

Blood Draw/IV Risk

Drawing blood and starting IVs by placing a needle in a vein may cause pain, lightheadedness and fainting, bleeding, bruising, or swelling at the puncture site. Infection is a rare possibility. Topical anesthetic or numbing cream may be used on the skin to decrease the discomfort, if needed. Although there are no known side effects from the numbing cream, skin irritation or an allergic reaction is possible.

Insertion of Port Risk

- An infection that may require the removal of the device
- Thrombosis (a blood clot) that can form in the catheter that may block the device from being accessed.
- Failure of the device - although unlikely, it is possible the device could break
- Pneumothorax (air or gas between the lungs and the chest wall), causing the lungs to collapse
- Injury to an artery

Muscle Biopsy Risk

The common side effects of the muscle biopsies may include discomfort, a scar, infection, bruise, numbness near the biopsy site, and delayed wound healing.

Sedation Risk

Risks from local anesthetic may include pain with infection, and (very rarely) allergic reactions. Minor discomfort during surgery is common, but the likelihood of other risks is extremely small (less than 1%). After use of conscious sedation, your child may get a headache or feel nauseous or dizzy. It is possible that your child will have a reaction to the sedative medication used.

If any of the symptoms listed above are severe, your child must get medical help right away. If you are worried about anything while in this study, please call the study doctor or study nurse at the telephone number on page 1.

Unforeseen Risks

There may be other risks of being in this research study that are not known at this time.

ARE THERE BENEFITS TO TAKING PART IN THIS STUDY?

The potential benefits of eteplirsen in subjects with DMD are unknown. Your child may have some benefits from taking part in this study, but even if your child does not benefit from being in this study, we might learn something that could help others.

WHAT WILL HAPPEN IF NEW INFORMATION IS FOUND OUT ABOUT THE DRUG OR TREATMENT?

If new information is found out during this study that might change your mind about your child taking part or might affect your child's health, your study doctor will discuss it with you and your child as soon as possible.

WHAT OTHER TREATMENTS OR OPTIONS ARE THERE?

Your child's participation in this study is voluntary. It is not necessary to be in this study to get care for this condition. If you decide not to allow your child to be in this study, the study doctor will talk to you and your child about other possible treatments or refer you to your child's regular doctor for care.

WILL THERE BE ANY COSTS TO ME?

It will not cost you or your child anything to be in this study and you or your child will not be paid to be in this study. Travel expenses including airfare (with supporting receipts) for up to two adults and one child for all required visits to Nationwide Children's Hospital will be covered.

CONFIDENTIALITY OF STUDY INFORMATION

The data collected as part of this study will be kept confidential, but may be shared with the individuals and entities and for the purposes described in this Parental Permission Form and the attached HIPAA Authorization form. In all study-related records, a number and initials will identify your child, unless otherwise described in this Parental Permission Form or the attached HIPAA Authorization form. Data collected and recorded on study forms are the property of the sponsor if information about this study is published, your child's identity will remain confidential. However, the U.S. Food and Drug Administration (FDA), Copernicus Group Independent Review Board (IRB), local IRB and the study sponsor, Sarepta Therapeutics, Inc. and its representatives may be granted direct access to your child's original medical records for verification of clinical trial procedures or data. By signing this Parental Permission Form, you are authorizing such access. A court of law could order medical records shown to other people, but that is unlikely.

WHAT HAPPENS IF BEING IN THIS STUDY CAUSES INJURIES?

If your child is hurt by the study drug, eteplirsen, or the procedures that are part of the study, you should seek medical treatment for your child's injuries and tell the study doctor as soon as possible at the number on the first page of this form. If it is an emergency, call 911 or go to the nearest emergency department.

If your child is injured as a direct result of the proper administration of the study drug, eteplirsen, or the proper performance of procedures that are required solely for the study, and your child has followed the directions of the study team, (b) (4)

(b) (4)

If the care is provided at Nationwide Children's Hospital and/or the satellite site, (b) (4)

(b) (4)

(b) (4) This does not mean that you give up any of your or your child's legal rights to seek compensation for your child's injuries.

LEGAL RIGHTS

The above section does not restrict your right to seek legal assistance. By signing this Parental Permission Form you will not waive any of your child's legal rights as a research subject.

WHAT HAPPENS IF MY CHILD DOES NOT FINISH THIS STUDY?

It is your choice to allow your child to be in this study or to stop at any time. If you decide to stop your child from being in this study, it is okay, but you must call the study doctor or the study nurse. If you stop your child from being in the study, there will not be a penalty or loss of benefits to which your child is otherwise entitled.

If at any time the study doctor believes participating in this study is not the best choice of care for your child, the study may be stopped and other care prescribed. If the study instructions are not followed, your child's participation in the study may also be stopped. If unexpected medical problems come up, the study doctor or the sponsor, Sarepta Therapeutics, Inc., may decide to stop your child's participation in the study.

If your child's participation in the study is stopped before completing all of the study activities, your child will be asked to visit the study doctor, (unless you have withdrawn consent), or you may be asked to return to Nationwide Children's Hospital so that the following information can be collected and assessments can be completed:

(b) (4)

In addition, subjects who have not already had their (b) (4)

If your child withdraws from the study because he is not feeling well, your child will be encouraged to have follow-up assessments when he feels better.

Use of samples and data for research purposes:
1. In this study, **left over blood or tissue will be stored for research at a later time**, perhaps even years from now. This research may include DNA (gene) testing. This future research may be for purposes other than your child's medical problem. You will not be told the results of any future research. If you decide at any time that you do not want your child's blood or tissue stored for future research, you may contact the Study Doctor or Study Nurse.

Please initial next to "yes" or "no" whether you give permission for the following testing/research:

___ **Yes**, I agree to allow my child's leftover blood, DNA or tissue to be stored and used for future research. I understand that the samples may be used for testing/research unrelated to this study and that I will not be told the results.

___ **No**, I do not want my child's leftover blood, DNA or tissue to be stored or used for future research.

If you agree, may Nationwide Children's Hospital or its research partners **keep your child's name and other identifying information with your child's sample(s)**?

Please initial:

___ **Yes**, my child's personal identifiers and medical information can be kept with my child's sample(s). All information will be kept secure and confidential.

___ **No**, my child's name and identifier(s) must be removed from my sample(s). My child's sample(s) cannot be linked back to me.

Your child may have had a muscle or skin biopsy done at an institution other than Nationwide Children's Hospital. The researchers at this institution may have kept your child's sample(s) and/or developed cell lines.

2. May Nationwide Children's Hospital grow cell lines from your child's muscle or skin specimens? These cell lines may be "immortalized" by turning on genes that make them grow without stopping in test tubes.

Please initial:

___ **Yes**, Nationwide Children's Hospital may grow cell lines from my child's muscle and skin. These may be immortalized in the laboratory.

___ **No**, Nationwide Children's Hospital may not grow cell lines from my child's muscle and skin.

---

3. May Nationwide Children's Hospital share your child's cell lines or tissue with other researchers working on muscle or neurological diseases?

Please initial:

___ **Yes**, Nationwide Children's Hospital may share my child's skin or muscle tissue, or the cell lines that grow from it, with other laboratories.

___ **No**, Nationwide Children's Hospital may not share my child's skin or muscle tissue, or the cell lines that grow from it, with other laboratories.

The study sponsor and its affiliates and agents who perform evaluation of your child's genes have an economic interest in developing new consumer service and potential diagnostic products. Your child's genes or genetic information about your child may be used to develop consumer products and medical therapies and diagnostics, and these which could be distributed and sold for profit. The study sponsor and its affiliates and agents may patent or sell discoveries based on their evaluation. Some of the scientists or companies may receive money from these activities. You and your child will not receive payment or have a personal economic interest in any services or products that may be developed in this evaluation or that might be developed from your child's DNA or other information you provide, and you should have no expectation of obtaining or acquiring any financial interest in this evaluation.

You may decide later that you would like to withdraw your child's sample from the research. If you decide to do this, and you have consented to keep your name and other identifying information with your child's sample(s), we will destroy your child's sample. However, if you decide that you would like your child's personal identifiers removed from your child's sample, you will not be able to withdraw it in the future because we will not be able to link your child's sample back to your child.

If an Institutional Review Board decides it is necessary, a letter describing the nature of the proposed research will be mailed to your last known address. You will be asked about your interest in your child's participation and have the opportunity to participate in the proposed research by responding to the letter. Change of address may be sent to Dr. Jerry Mendell, Center for Gene Therapy, The Research Institute at Nationwide Children's Hospital, 700 Children's Dr., Columbus, OH 43205 and the satellite site . Should you decide not to allow further use or storage of the specimen(s), you may have the specimen destroyed by writing to the same address and the satellite site . Dr. Mendell retains the right to cease storage of the specimen(s) without sending notice to you or obtaining your consent.

OTHER IMPORTANT INFORMATION

It is considered a conflict of interest where the parents of a potential subject hold stock of Sarepta Therapeutics, Inc. By signing this consent form, you agree that neither you nor any of your family have stock of or an interest with the potential for financial gain in the sponsor, Sarepta Therapeutics, Inc.

It is important that healthcare providers know about all medicines your child is taking. This includes the study drug being tested in this research study. Because of this, we plan to tell your child's primary care doctor that he is in this research study. This is done so extra care can be taken in prescribing other medicines and looking at any unexplained symptoms that may occur. Your child cannot take part in this study if you do not want us to tell your child's primary care doctor.

The study doctor is being paid by Sarepta Therapeutics, Inc. for the time and knowledge needed to do this study.

Being in more than one research study at the same time may cause injury. Please tell the study doctor if your child is in any other research study so a decision can be made about being in more than one study at the same time.

Keep in mind that your permission for your child's participation in the study will remain valid until such time as you choose to withdraw it. This withdrawal should be in writing and sent to the following address:
***

***
Any information collected prior to this withdrawal may be used but no new information would be collected after the time the withdrawal is received.

WHOM SHOULD I CALL IF I HAVE QUESTIONS OR PROBLEMS?
If you have any questions about your child's participation in this research study or if you feel that your child has experienced a research-related injury or reaction to the study drug, contact:

Investigator Name:

Daytime telephone number(s): ; you can reach the study nurse during business hours at

24-hour contact number(s): (7 days a week)

If you have any questions or concerns about your child's rights as a research subject or want to discuss a problem, get information or offer input, you may contact Copernicus Group Independent Review Board (IRB) at 1-888-303-2224 (toll free). An IRB is a group of scientific and non-scientific individuals who perform the initial and ongoing ethical review of the research study with the study subject's rights and welfare in mind. Copernicus Group IRB has reviewed and approved the research study described in this Parental Permission Form. If you have study-related comments, complaints or concerns, you should first contact the study doctor. Please call the IRB if you want to talk to someone other than the study doctor or have difficulty reaching the study doctor. For further information regarding the clinical trials process and your child's role as a research subject, you may visit the Copernicus Group IRB website at www.cgirb.com.

PARENTAL STATEMENT OF PERMISSION

Open-Label, Multiple-Dose, Efficacy, Safety, and Tolerability Study of Eteplirsen in Subjects with Duchenne Muscular Dystrophy who Participated in Study 4658-us-201

I have read this Parental Permission Form and have had a chance to ask questions about this research study, which have been answered to my satisfaction. If I have more questions about participation in this study or a research-related injury, I may contact the study doctor. By signing this Parental Permission Form, I certify that all health information I have given regarding my child is true and correct to the best of my knowledge.

I have been given a copy of the Notice of Privacy Practices. I have been told that my right to my child's patient information that is created or collected in the course of this research can be temporarily suspended for as long as the research is in progress. I also have been told that my right to access will be reinstated upon completion of this research.

I give permission for my child to take part in this study. I will be given a copy of this Parental Permission Form with all the signatures for my own records.

_____
PRINTED NAME OF SUBJECT

_____
PRINTED NAME OF PARENT/LEGAL GUARDIAN

_____ _____
SIGNATURE OF PARENT/LEGAL GUARDIAN DATE & TIME AM/PM

_____
PRINTED NAME OF SECOND PARENT/ LEGAL GUARDIAN

_____ _____
SIGNATURE OF SECOND PARENT/ LEGAL GUARDIAN DATE & TIME AM/PM

Permission of the second parent not obtained because (select all that apply):

_____ Other parent is deceased.
_____ Other parent is unknown.
_____ Other parent is not reasonably available.
_____ Only one parent has legal responsibility for the care and custody of subject.

I certify that I have explained the research, its purposes, and the procedures to the patient or subject's parent(s) or legal guardian(s) and have answered all of their questions, before requesting their signature. I believe that he/she understands the information described in this Parental Permission Form and freely consents to have his/her child participate in the study.

PRINTED NAME OF PERSON OBTAINING CONSENT

SIGNATURE OF PERSON OBTAINING CONSENT

DATE & TIME AM/PM

PRINTED NAME OF INVESTIGATOR

SIGNATURE OF INVESTIGATOR

DATE & TIME AM/PM

PRINTED NAME OF WITNESS

SIGNATURE OF WITNESS
FOR VA SITES ONLY

DATE & TIME AM/PM

HIPAA AUTHORIZATION

The United States government has issued a privacy rule to protect the privacy rights of patients. This rule was issued under a law called the Health Insurance Portability and Accountability Act of 1996 (HIPAA). The Privacy Rule is designed to protect the confidentiality of your child's personal health information. The document you are reading, called an "Authorization," describes your child's rights and explains how your child's health information will be used and disclosed (shared).

HOW WILL MY CHILD'S STUDY INFORMATION BE KEPT PRIVATE?

Information collected for this study will be kept confidential to the extent provided by law. Health information means the information in your child's medical or other healthcare records, which also may include information that can identify your child. Information that can identify your child is called "protected health information" or PHI. By agreeing to allow your child to be in this study, you are giving permission and authorizing and his study staff to collect, use, and disclose your child's PHI for this research study. The results of the study may be published in scientific journals or presented at medical meetings. In the event of any publication regarding this study, your child's identity will not be revealed.

Your child's PHI collected or created under this research study will be used/disclosed as needed during and even after the end of the study. We will need to use it for research purposes and will release it to other people involved in the research or your child's routine healthcare. We will also generate new healthcare information about your child during the course of the study. This information will come from the tests and procedures and any interviews of your child conducted in connection with the study. The records of this study will be kept for an indefinite period of time, and by signing this Authorization you are authorizing the use of your child's PHI in accordance with this Authorization during that entire period. If you decide to withdraw your child from the study, or if your child is removed from the study by the study doctor or Sponsor (Sarepta Therapeutics, Inc.) you may withdraw, on your child's behalf, your permission for others to use and disclose your child's PHI, except that PHI that has already been collected may still be used by and disclosed to the individuals and entities as described in this Authorization. If you withdraw your permission for the use and disclosure of your child's PHI, your child can no longer take part in this research study.

If you decide to withdraw your permission for the use and disclosure of your child's PHI, this must be in writing. Please send a letter to your study doctor:

Your child's PHI that may be used or disclosed:

Your child's PHI that may be used and disclosed for this study includes: review of your child's past, current or future health records, procedures such as physical examinations, blood or urine tests or other tests, your child's response to any study drug your child receives, your child's study visits, phone calls, study tests and procedures and any other study related health information, may be collected, used and disclosed to others. Your child's PHI also includes:

- ✓ Name and Date of Birth
- ✓ All medical records, including genetic testing and study tests and procedures
- ✓ Contact information (Addresses, Email addresses, Telephone/fax numbers)
- ✓ Family medical history
- ✓ Photos and videos

Efforts will be made to keep your child's study-related information confidential; however confidentiality cannot be guaranteed. Once disclosed, the PHI may no longer be protected by federal law and may be re-disclosed by those receiving the information.

People or Companies authorized to use, disclose, and receive your child's health information and PHI collected or created by this research study for purposes related to this study:

- and study staff
- The Copernicus Group Independent Review Board (the committee that reviews all human subject research)
- Nationwide Children's Hospital internal auditors
- The Office for Human Research Protections (OHRP) (the federal government office that oversees human patient research)
- Sarepta Therapeutics, Inc., the study sponsor and its designees, representatives and agents (including third parties who are providing services to the sponsor related to the study)
- An independent committee of physicians and experts that will review safety information from this study periodically
- The Food and Drug Administration (FDA) and other governmental health agencies, both within and outside the United States
- Your child's insurance company (if charges are billed to insurance).

Your child's health information and/or PHI also may be used and shared for treatment, payment and healthcare operations. Medical information from this study will become part of your child's hospital medical record.

In order to provide your child with routine care, other people at the hospital may need to review the health information we put into your record. This would include such people as your regular doctors and nurses and the hospital's billing department.

Your personal health information may be further shared by the groups above. If shared by them, the information will no longer be covered by the Privacy Rule. However, these groups are committed to keeping your personal health information confidential.

May I have access to my child's health information and PHI?

You will always have access to your child's medical record. A summary may be made available to you at the completion of the study. You will not have access to your child's research file because all information contained in the research file is either information obtained directly from your child, or was gathered from your child's medical records, to which you do have access. In some cases your child's research file may contain some information not known to you or the researchers that if known, would affect the scientific importance of the study.

AUTHORIZATION

I authorize the release of my child's medical records and personal health information related to this study to the Sponsor, including its affiliates, successors and assigns, both in the U.S. and other countries, and/or any third party working with Sponsor to conduct the study or to analyze or review study-related documents or data, the Copernicus Group Independent Review Board, the FDA and other regulatory agencies, and to the other individuals and entities as described above. I have been told that I will receive a signed and dated copy of this Authorization for my records.

_____
Printed First and Last Name of Subject

_____
Printed First and Last Name of Parent/Legal Guardian

_____ _____
Signature of Parent/Legal Guardian Date

_____
Printed First and Last Name of Parent/Legal Guardian

_____ _____
Signature of Parent/Legal Guardian Date

_____
Printed Name of Person Obtaining Authorization

_____ _____
Signature of Person Obtaining Authorization Date

_____
Printed Name of Investigator

_____ _____
Signature of Investigator Date

APPROVED: Jul 12, 2013
COPERNICUS GROUP IRB

copernicus group independent review board

Approved: «Approved»

PARENTAL PERMISSION FORM AND HIPAA AUTHORIZATION

STUDY TITLE: Open-Label, Multiple-Dose, Efficacy, Safety, and Tolerability Study of Eteplirsen in Subjects with Duchenne Muscular Dystrophy who Participated in Study 4658-us-201

PROTOCOL NUMBER: 4658-us-202

PROTOCOL AMENDMENT: 04 Dated 16 May 2013

STUDY SPONSOR: Sarepta Therapeutics, Inc.

STUDY DOCTOR:

RESEARCH SITE ADDRESS(ES):

DAYTIME TELEPHONE NUMBER(S):

24-HOUR TELEPHONE NUMBER(S): (*24 hours a day, 7 days a week*)

SUBJECT'S NAME: _____

INTRODUCTION

The purpose of this Parental Permission Form is to give you the information you will need to help you decide whether or not to allow your child to be in this study. Please read this form carefully. You should ask questions about what your child will be asked to do, the risks, the benefits, your child's rights as a subject, or anything else about the research or this form that is not clear to you. When all of your questions have been answered to your satisfaction, you can decide if you want your child to take part in this study or not. If you agree to allow your child to take part in this study and you sign this permission form, you will be given a copy for your records. If your child is 10 years of age or older, he will sign a separate informed consent form called an "Assent." You and your child will be given a copy for your records.

You are being asked to allow your child to be in this research study because your child has a muscle disorder called Duchenne muscular dystrophy (DMD). DMD is caused by a mutation (a change) in the gene that makes dystrophin protein. Dystrophin is important for protecting your child's muscles from stress and damage during activity. Because of the mutation in your child's gene, your child's body is not able to make enough working dystrophin to protect your child's muscles.

This study is investigating a study drug called eteplirsen, which is designed to skip a certain fragment of the dystrophin gene called exon 51. In people with changes, called deletions, in certain parts of the dystrophin gene (including exons 45-50, 47-50, 48-50, 50, 52, or 52-63), skipping exon 51 is believed to allow the body to produce a shortened, but still working, form of dystrophin protein. This may result in improved muscle function for people with DMD.

In this study, all subjects will receive eteplirsen once a week and take part in study-specific tests for 164 weeks.

Participation in this study is voluntary. Please learn enough about this research study, its risks and benefits, to decide whether you should agree to allow your child to take part. The study team will explain the study to you, and give you a chance to ask questions about anything you do not understand. This process is called "informed consent." It is up to you to choose if you want your child to be in this study. You may refuse to allow your child to be in this study or your child may quit this study at any time, and standard medical care will still be available here or at a doctor of your choice without a penalty or loss of benefits to your child. If your child is between 10 and 13 years of age and agrees to take part in the study, he will be asked to sign an Assent Form. You will be given a signed and dated copy of this Parental Permission Form and the Assent Form.

Note: A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you or your child. At most, the Web site will include a summary of the results. You can search this Web site at any time.

WHY ARE WE DOING THIS RESEARCH STUDY?

This study will examine the effects of continued treatment with eteplirsen in children with DMD who have successfully completed the 28-week eteplirsen study, Study 4658-us-201. To better understand how eteplirsen works over a long period of time; the sponsor will use data from both studies (4658-us-201 and 4658-us-202) to compare how your child does in this study to how he was doing before he started eteplirsen in Study 4658-us-201.

Sarepta Therapeutics, Inc. is developing eteplirsen for the treatment of DMD by intravenous (IV, meaning through a vein) administration. Eteplirsen is designed to skip exon 51, which is believed to allow for the production of a shortened, but still working, form of the dystrophin protein and therefore result in improved muscle function for people with DMD.

Eteplirsen is considered to be an experimental drug. Experimental means that this study drug is currently being tested. Eteplirsen has not been approved for marketing by the Food and Drug Administration (FDA) for use in the United States.

WHERE WILL THE STUDY BE DONE AND HOW MANY PARTICIPANTS WILL TAKE PART?

This study will only be open to the 12 subjects who took part in the previous eteplirsen study, Study 4658-us-201. This study will be done at Nationwide Children's Hospital (the central site) and at up to 12 sites closer to the homes of participating subjects (satellite sites).

To take part in the study your child will need to meet all of the inclusion criteria and none of the exclusion criteria that your child's study doctor will discuss with you. The study doctor will also speak with you about some medicines that should not be taken by your child while participating in this study.

To be enrolled in the study, your child must:

1. Have completed 28 weeks of treatment in Study 4658-us-201
2. Have a parent(s) or legal guardian(s) who is able to understand and comply with all of the study requirements
3. Have a parent(s) or legal guardian(s) who is willing to provide written informed consent for the subject to take part in the study
4. Be willing, if at least age 10, to provide informed assent (agreement)

If your child has a prior or ongoing medical condition that the study doctor believes might affect his safety, or make it difficult for him to attend all of the required study visits and receive all of the study drug, or might affect the results of this study, your child will not be able to take part in this study.

WHAT WILL HAPPEN DURING THE STUDY AND HOW LONG WILL IT LAST?

During this study, your child will receive IV infusions of either 30 or 50 mg/kg eteplirsen once a week for 164 weeks (approximately 3 years). Your child will receive the same dose of eteplirsen in this study that he received in Study 4658-us-201. That means if your child received the high dose (50 mg/kg) of eteplirsen in 4658-us-201, then he will receive the high dose in this study, and if he received the low dose of eteplirsen in 4658-us-201 (30 mg/kg), then he will receive the low dose in this study. Remember that the dose of eteplirsen that your child receives (high or low) was randomly assigned to him (picked by chance like tossing a coin in the air) during Study 4658-us-201. There was an even chance (50/50) that he would be assigned to the high or low dose.

This study is open-label. Open-label means that the study doctor, the study nurse, the study sponsor (Sarepta Therapeutics, Inc.), you, your child, and everyone else who might work with your child in this study will know your child is receiving eteplirsen.

Your child will receive all weekly infusions at the identified satellite site that is closer to your home. The personnel there are trained, and the site is approved to take part in this study. You and your child will be asked to sign new Parental Permission and Assent Forms when you transfer to the satellite site. However, you and your child will still need to travel to Nationwide Children's Hospital approximately once every 24 weeks so your child can complete certain study-specific tests.

The procedures and tests that will take place at each of the weekly study visits are presented below.

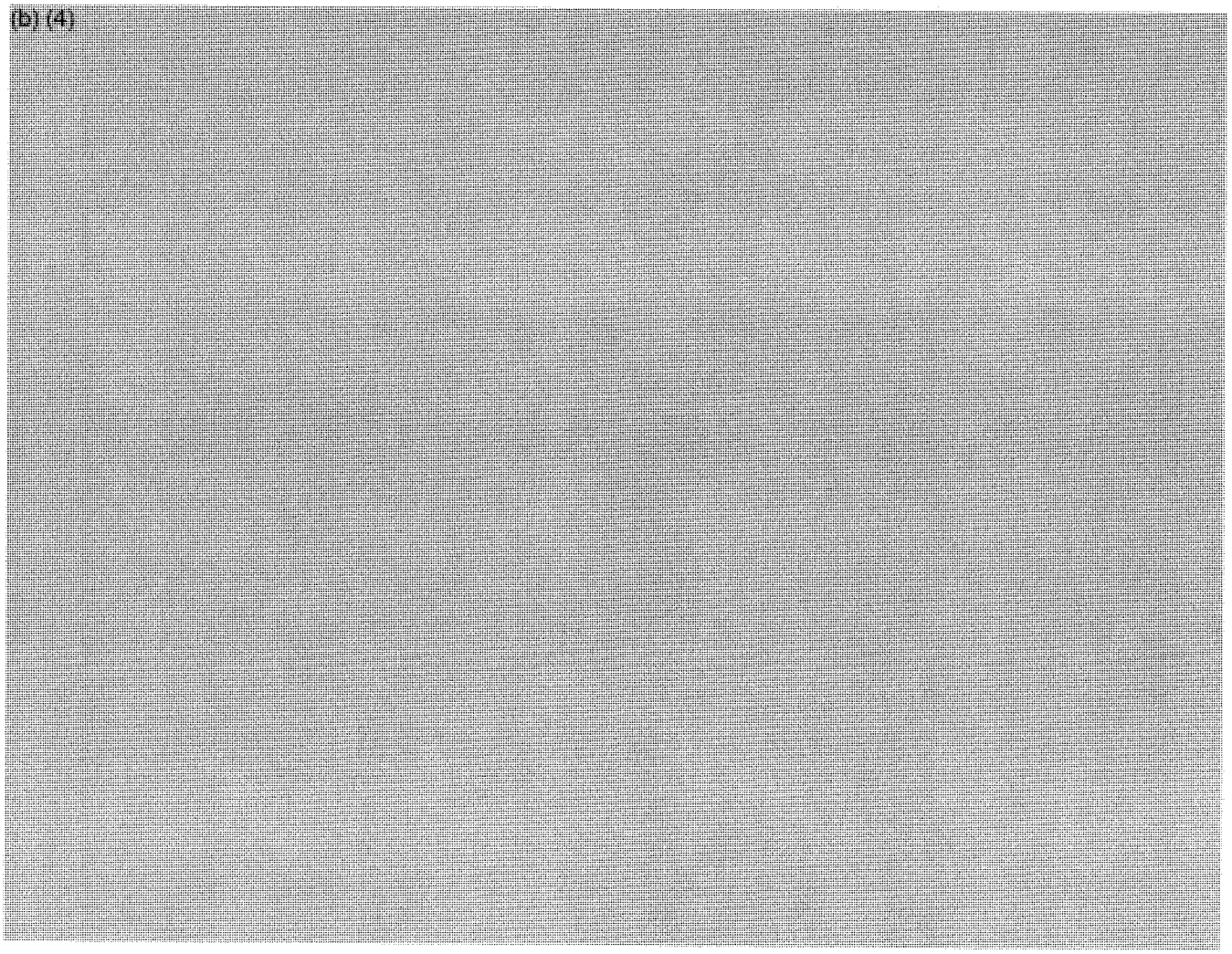
If a situation occurs that your child is unable to attend a scheduled visit and your child is at risk of missing a weekly dose, you must immediately notify the study doctor. It is very important that no more than 2 doses are missed in a 6-month period. If your child misses more than 8 doses during the 164 week study, he may be withdrawn from the study.

Screening/Baseline Period

Because this is an extension study for children who successfully completed Study 4658-us-201, there will be no formal screening period for this study. Instead, the study doctor will review the details of this study with you, obtain your consent and your child's agreement (assent) to take part in this study, and make sure this study is right for your child at the last visit (Week 28) of Study 4658-us-201.

In addition to procedures and tests specific to Study 4658-us-201, the following procedures will be performed at (b) (4) of Study 4658-us-201:

(b) (4)



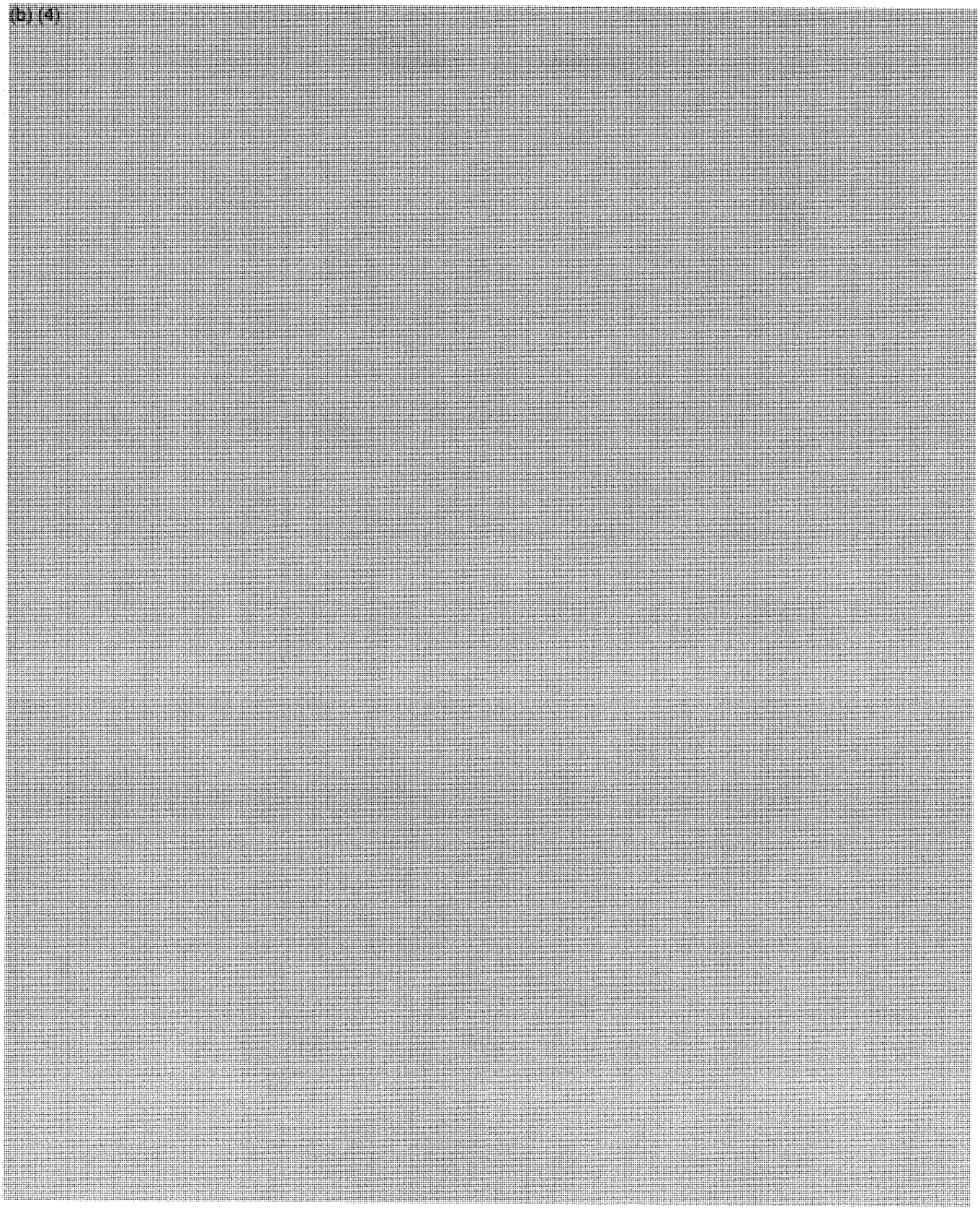
(b) (4)

6. Study Drug Administration – Your child will receive a 60-minute infusion of eteplirsen. A topical anesthetic (numbing) cream (e.g., lidocaine 2.5%, prilocaine 2.5%, or LMX4 cream) may be applied to your child's skin prior to the infusion, if needed. After the infusion ends, your child will be observed for at least 1 hour to make sure that he is doing okay. As long as he is okay and all other tests and procedures have been completed, the study doctor will then let you and your child go home.

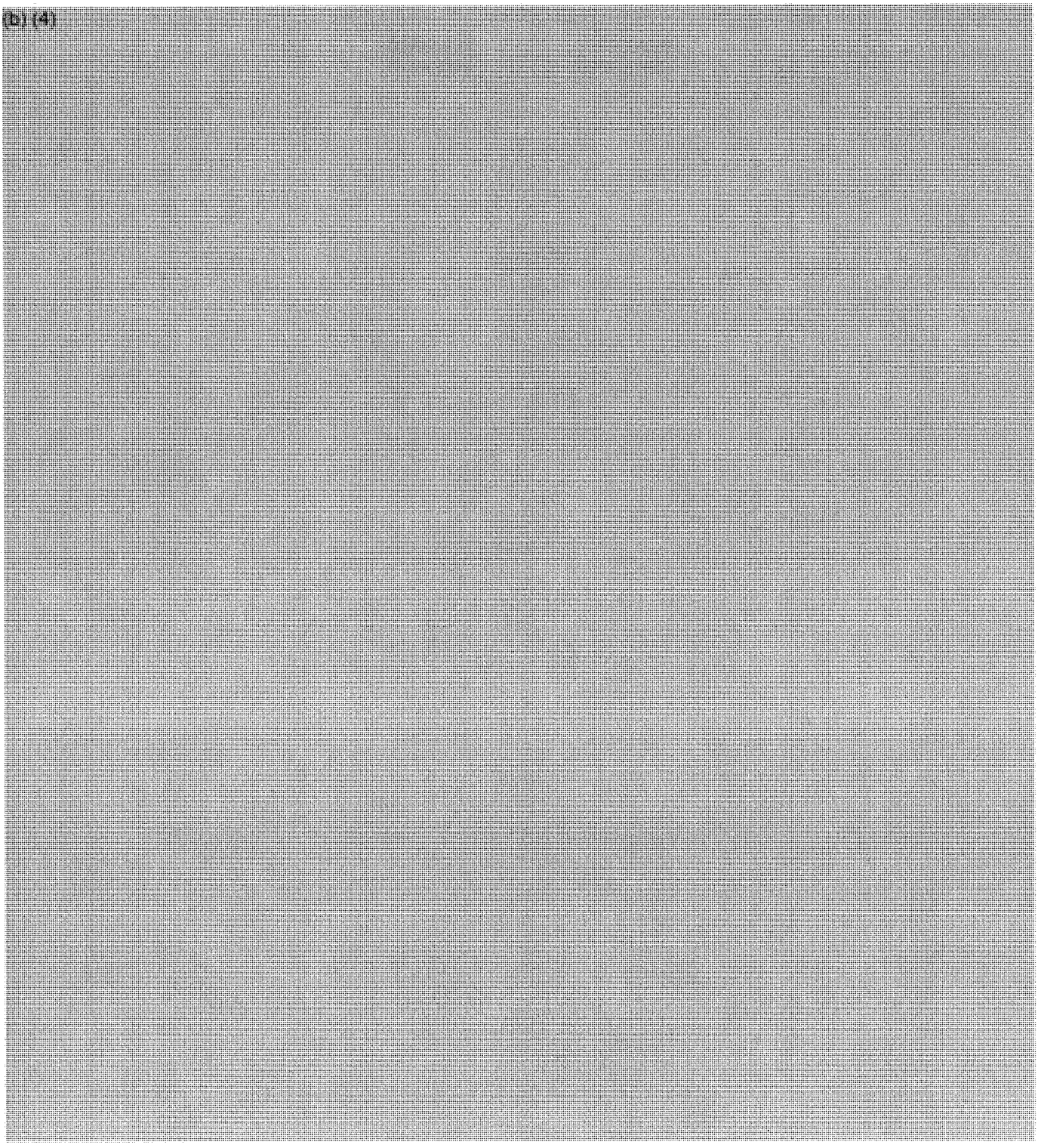
Please Note: Your child's doctor may recommend the insertion of a port as an option for the IV infusion of eteplirsen, if it is becoming difficult to use an IV to access their veins. A port is a small device inserted under the skin, which makes it easier to give infusions and collect blood.

(b) (4)

(b) (4)



(b) (4)



WHAT ARE THE RISKS OF BEING IN THIS STUDY?

Two clinical studies have been done with eteplirsen in children with DMD in the United Kingdom and study 4658-us-201 has been completed in the US. The first study was a placebo-controlled study of several doses of eteplirsen in 7 boys with DMD aged 10 to 17 years. Doses

ranged from 0.09 mg to 0.9 mg/kg and were given by a single injection into a small muscle on the foot (this is called an intramuscular or IM injection). Several of the boys showed an increase in dystrophin protein in the muscle of the foot that had been injected with eteplirsen.

The second study was an open-label study of eteplirsen administered into the vein (this is called an intravenous or IV injection or infusion). This study enrolled 19 boys with DMD, who were 5 to 15 years of age, and patients received up to 12 weekly infusions of eteplirsen. Doses ranged from 0.5 to 20.0 mg/kg. In this second study, levels of dystrophin protein were increased at the end of the study in 7 out of the 17 patients that had muscle biopsies taken before starting eteplirsen and at the end of the study.

In both studies, eteplirsen was well-tolerated over the doses given (up to 20.0 mg/kg). Overall, the problems that occurred (called adverse events) were generally mild or moderate in intensity. The common side effects of eteplirsen were:

- headache (42%)
- upper respiratory tract infection (42%)
- back pain (37%)
- rhinitis (inflammation of the mucous membrane of the nose that may cause nasal congestion and itching, and sneezing) (37%)
- falling (26%)
- myalgia (pain in the muscle) (21%)

One subject, who had a pre-existing heart condition due to DMD, had a decrease in his heart function without symptoms while taking 4.0 mg/kg of eteplirsen. This problem was considered possibly related to the eteplirsen and the subject was withdrawn from study drug administration.

Through Week 46 of this study (74 total weeks from the start of Study 4658-us-201), there have been no clinically significant treatment-related adverse events, serious adverse events, or discontinuations. At Week 16 of this study, 1 patient had an elevation of urine protein on a laboratory urine dipstick test, which resolved without intervention and resulted in no clinical symptoms. The patient continued treatment without interruption and remained free of proteinuria through Week 46.

One recent study that is being conducted in laboratory mice with a drug for mice similar to eteplirsen showed a mild increase in the size of the cerebrospinal fluid space inside the brain that may be a type of hydrocephaly (water in the brain). The importance of this finding from laboratory mice and how it relates to long-term dosing of eteplirsen in humans is unclear. Additional review and analysis is being conducted and reviewed related to this finding. At this time there are no recommendations to change the current eteplirsen trial.

It is important that you give the study staff your child's complete medical history. Not giving them this information or not completely following the directions of the study could harm your child.

All study drugs may cause some side effects or other reactions. There is no way to predict if your child will experience any of these side effects. Side effects that are not yet known may also occur.

Blood Draw/IV Risk
Drawing blood and starting IVs by placing a needle in a vein may cause pain, lightheadedness and fainting, bleeding, bruising, or swelling at the puncture site. Infection is a rare possibility. Topical anesthetic or numbing cream may be used on the skin to decrease the discomfort, if needed. Although there are no known side effects from the numbing cream, skin irritation or an allergic reaction is possible.

Insertion of Port Risk

- An infection that may require the removal of the device
- Thrombosis (a blood clot) that can form in the catheter that may block the device from being accessed.
- Failure of the device - although unlikely, it is possible the device could break
- Pneumothorax (air or gas between the lungs and the chest wall), causing the lungs to collapse
- Injury to an artery

Muscle Biopsy Risk
The common side effects of the muscle biopsies may include discomfort, a scar, infection, bruise, numbness near the biopsy site, and delayed wound healing.

Sedation Risk
Risks from local anesthetic may include pain with infection, and (very rarely) allergic reactions. Minor discomfort during surgery is common, but the likelihood of other risks is extremely small (less than 1%). After use of conscious sedation, your child may get a headache or feel nauseous or dizzy. It is possible that your child will have a reaction to the sedative medication used.

If any of the symptoms listed above are severe, your child must get medical help right away. If you are worried about anything while in this study, please call the study doctor or study nurse at the telephone number on page 1.

Unforeseen Risks
There may be other risks of being in this research study that are not known at this time.

ARE THERE BENEFITS TO TAKING PART IN THIS STUDY?

The potential benefits of eteplirsen in subjects with DMD are unknown. Your child may have some benefits from taking part in this study, but even if your child does not benefit from being in this study, we might learn something that could help others.

WHAT WILL HAPPEN IF NEW INFORMATION IS FOUND OUT ABOUT THE DRUG OR TREATMENT?

If new information is found out during this study that might change your mind about your child taking part or might affect your child's health, your study doctor will discuss it with you and your child as soon as possible.

WHAT OTHER TREATMENTS OR OPTIONS ARE THERE?

Your child's participation in this study is voluntary. It is not necessary to be in this study to get care for this condition. If you decide not to allow your child to be in this study, the study doctor will talk to you and your child about other possible treatments or refer you to your child's regular doctor for care.

WILL THERE BE ANY COSTS TO ME?

It will not cost you or your child anything to be in this study and you or your child will not be paid to be in this study. Travel expenses including airfare (with supporting receipts) for up to two adults and one child for all required visits to Nationwide Children's Hospital will be covered.

CONFIDENTIALITY OF STUDY INFORMATION

The data collected as part of this study will be kept confidential, but may be shared with the individuals and entities and for the purposes described in this Parental Permission Form and the attached HIPAA Authorization form. In all study-related records, a number and initials will identify your child, unless otherwise described in this Parental Permission Form or the attached HIPAA Authorization form. Data collected and recorded on study forms are the property of the sponsor if information about this study is published, your child's identity will remain confidential. However, the U.S. Food and Drug Administration (FDA), Copernicus Group Independent Review Board (IRB), local IRB and the study sponsor, Sarepta Therapeutics, Inc. and its representatives may be granted direct access to your child's original medical records for verification of clinical trial procedures or data. By signing this Parental Permission Form, you are authorizing such access. A court of law could order medical records shown to other people, but that is unlikely.

WHAT HAPPENS IF BEING IN THIS STUDY CAUSES INJURIES?

If your child is hurt by the study drug, eteplirsen, or the procedures that are part of the study, you should seek medical treatment for your child's injuries and tell the study doctor as soon as possible at the number on the first page of this form. If it is an emergency, call 911 or go to the nearest emergency department.

If your child is injured as a direct result of the proper administration of the study drug, eteplirsen, or the proper performance of procedures that are required solely for the study, and your child has followed the directions of the study team, (b) (4)

(b) (4)

If the care is provided at Nationwide Children's Hospital and/or the satellite site, (b) (4)

(b) (4)

(b) (4) This does not mean that you give up any of your or your child's legal rights to seek compensation for your child's injuries.

LEGAL RIGHTS

The above section does not restrict your right to seek legal assistance. By signing this Parental Permission Form you will not waive any of your child's legal rights as a research subject.

WHAT HAPPENS IF MY CHILD DOES NOT FINISH THIS STUDY?

It is your choice to allow your child to be in this study or to stop at any time. If you decide to stop your child from being in this study, it is okay, but you must call the study doctor or the study nurse. If you stop your child from being in the study, there will not be a penalty or loss of benefits to which your child is otherwise entitled.

If at any time the study doctor believes participating in this study is not the best choice of care for your child, the study may be stopped and other care prescribed. If the study instructions are not followed, your child's participation in the study may also be stopped. If unexpected medical problems come up, the study doctor or the sponsor, Sarepta Therapeutics, Inc., may decide to stop your child's participation in the study.

If your child's participation in the study is stopped before completing all of the study activities, your child will be asked to visit the study doctor, «FirstName» «MiddleName» «LastName» «Suffix» (unless you have withdrawn consent), or you may be asked to return to Nationwide Children's Hospital so that the following information can be collected and assessments can be completed:

(b) (4)

In addition, subjects who have not already had their (b) (4)

If your child withdraws from the study because he is not feeling well, your child will be encouraged to have follow-up assessments when he feels better.

Use of samples and data for research purposes:
1. In this study, **left over blood or tissue will be stored for research at a later time**, perhaps even years from now. This research may include DNA (gene) testing. This future research may be for purposes other than your child's medical problem. You will not be told the results of any future research. If you decide at any time that you do not want your child's blood or tissue stored for future research, you may contact the Study Doctor or Study Nurse.

Please initial next to "yes" or "no" whether you give permission for the following testing/research:

___ **Yes**, I agree to allow my child's leftover blood, DNA or tissue to be stored and used for future research.

I understand that the samples may be used for testing/research unrelated to this study and that I will not be told the results.

___ **No**, I do not want my child's leftover blood, DNA or tissue to be stored or used for future research.

If you agree, may Nationwide Children's Hospital or its research partners **keep your child's name and other identifying information with your child's sample(s)**?

Please initial:

___ **Yes**, my child's personal identifiers and medical information can be kept with my child's sample(s). All information will be kept secure and confidential.

___ **No**, my child's name and identifier(s) must be removed from my sample(s). My child's sample(s) cannot be linked back to me.

Your child may have had a muscle or skin biopsy done at an institution other than Nationwide Children's Hospital. The researchers at this institution may have kept your child's sample(s) and/or developed cell lines.

2. May Nationwide Children's Hospital grow cell lines from your child's muscle or skin specimens?

These cell lines may be "immortalized" by turning on genes that make them grow without stopping in test tubes.

Please initial:

___ **Yes**, Nationwide Children's Hospital may grow cell lines from my child's muscle and skin. These may be immortalized in the laboratory.

___ **No**, Nationwide Children's Hospital may not grow cell lines from my child's muscle and skin.

---

3. May Nationwide Children's Hospital share your child's cell lines or tissue with other researchers working on muscle or neurological diseases?

Please initial:

___ **Yes**, Nationwide Children's Hospital may share my child's skin or muscle tissue, or the cell lines that grow from it, with other laboratories.

___ **No**, Nationwide Children's Hospital may not share my child's skin or muscle tissue, or the cell lines that grow from it, with other laboratories.

The study sponsor and its affiliates and agents who perform evaluation of your child's genes have an economic interest in developing new consumer service and potential diagnostic products. Your child's genes or genetic information about your child may be used to develop consumer products and medical therapies and diagnostics, and these which could be distributed and sold for profit. The study sponsor and its affiliates and agents may patent or sell discoveries based on their evaluation. Some of the scientists or companies may receive money from these activities. You and your child will not receive payment or have a personal economic interest in any services or products that may be developed in this evaluation or that might be developed from your child's DNA or other information you provide, and you should have no expectation of obtaining or acquiring any financial interest in this evaluation.

You may decide later that you would like to withdraw your child's sample from the research. If you decide to do this, and you have consented to keep your name and other identifying information with your child's sample(s), we will destroy your child's sample. However, if you decide that you would like your child's personal identifiers removed from your child's sample, you will not be able to withdraw it in the future because we will not be able to link your child's sample back to your child.

If an Institutional Review Board decides it is necessary, a letter describing the nature of the proposed research will be mailed to your last known address. You will be asked about your interest in your child's participation and have the opportunity to participate in the proposed research by responding to the letter. Change of address may be sent to Dr. Jerry Mendell, Center

for Gene Therapy, The Research Institute at Nationwide Children's Hospital, 700 Children's Dr, Columbus, OH 43205 and the satellite site «Company». Should you decide not to allow further use or storage of the specimen(s), you may have the specimen destroyed by writing to the same address and the satellite site «Company». Dr. Mendell retains the right to cease storage of the specimen(s) without sending notice to you or obtaining your consent.

OTHER IMPORTANT INFORMATION

It is considered a conflict of interest where the parents of a potential subject hold stock of Sarepta Therapeutics, Inc. By signing this consent form, you agree that neither you nor any of your family have stock of or an interest with the potential for financial gain in the sponsor, Sarepta Therapeutics, Inc.

It is important that healthcare providers know about all medicines your child is taking. This includes the study drug being tested in this research study. Because of this, we plan to tell your child's primary care doctor that he is in this research study. This is done so extra care can be taken in prescribing other medicines and looking at any unexplained symptoms that may occur. Your child cannot take part in this study if you do not want us to tell your child's primary care doctor.

The study doctor is being paid by Sarepta Therapeutics, Inc. for the time and knowledge needed to do this study.

Being in more than one research study at the same time may cause injury. Please tell the study doctor if your child is in any other research study so a decision can be made about being in more than one study at the same time.

Keep in mind that your permission for your child's participation in the study will remain valid until such time as you choose to withdraw it. This withdrawal should be in writing and sent to the following address:

«FirstName» «MiddleName» «LastName» «Suffix»
«Company»
«Address» «SuiteDept»
«City» «State» «Zip»

Any information collected prior to this withdrawal may be used but no new information would be collected after the time the withdrawal is received.

WHOM SHOULD I CALL IF I HAVE QUESTIONS OR PROBLEMS?

If you have any questions about your child's participation in this research study or if you feel that your child has experienced a research-related injury or reaction to the study drug, contact:

Investigator Name: **«FirstName» «MiddleName» «LastName» «Suffix»**

Daytime telephone number(s): «Phone»; you can reach the study nurse during business hours at [Study Nurse Phone]

24-hour contact number(s): «Phone2» (7 days a week)

If you have any questions or concerns about your child's rights as a research subject or want to discuss a problem, get information or offer input, you may contact Copernicus Group Independent Review Board (IRB) at 1-888-303-2224 (toll free). An IRB is a group of scientific and non-scientific individuals who perform the initial and ongoing ethical review of the research study with the study subject's rights and welfare in mind. Copernicus Group IRB has reviewed and approved the research study described in this Parental Permission Form. If you have study-related comments, complaints or concerns, you should first contact the study doctor. Please call the IRB if you want to talk to someone other than the study doctor or have difficulty reaching the study doctor. For further information regarding the clinical trials process and your child's role as a research subject, you may visit the Copernicus Group IRB website at www.cgirb.com.

PARENTAL STATEMENT OF PERMISSION

Open-Label, Multiple-Dose, Efficacy, Safety, and Tolerability Study of Eteplirsen in Subjects with Duchenne Muscular Dystrophy who Participated in Study 4658-us-201

I have read this Parental Permission Form and have had a chance to ask questions about this research study, which have been answered to my satisfaction. If I have more questions about participation in this study or a research-related injury, I may contact the study doctor. By signing this Parental Permission Form, I certify that all health information I have given regarding my child is true and correct to the best of my knowledge.

I have been given a copy of the «Company» Notice of Privacy Practices. I have been told that my right to my child's patient information that is created or collected in the course of this research can be temporarily suspended for as long as the research is in progress. I also have been told that my right to access will be reinstated upon completion of this research.

I give permission for my child to take part in this study. I will be given a copy of this Parental Permission Form with all the signatures for my own records.

_____
PRINTED NAME OF SUBJECT

_____
PRINTED NAME OF PARENT/LEGAL GUARDIAN

_____ _____
SIGNATURE OF PARENT/LEGAL GUARDIAN DATE & TIME AM/PM

_____
PRINTED NAME OF SECOND PARENT/ LEGAL GUARDIAN

_____ _____
SIGNATURE OF SECOND PARENT/ LEGAL GUARDIAN DATE & TIME AM/PM

Permission of the second parent not obtained because (select all that apply):

_____ Other parent is deceased.
_____ Other parent is unknown.
_____ Other parent is not reasonably available.
_____ Only one parent has legal responsibility for the care and custody of subject.

I certify that I have explained the research, its purposes, and the procedures to the patient or subject's parent(s) or legal guardian(s) and have answered all of their questions, before requesting their signature. I believe that he/she understands the information described in this Parental Permission Form and freely consents to have his/her child participate in the study.

PRINTED NAME OF PERSON OBTAINING CONSENT

SIGNATURE OF PERSON OBTAINING CONSENT

DATE & TIME AM/PM

PRINTED NAME OF INVESTIGATOR

SIGNATURE OF INVESTIGATOR

DATE & TIME AM/PM

PRINTED NAME OF WITNESS

SIGNATURE OF WITNESS
FOR VA SITES ONLY

DATE & TIME AM/PM

HIPAA AUTHORIZATION

The United States government has issued a privacy rule to protect the privacy rights of patients. This rule was issued under a law called the Health Insurance Portability and Accountability Act of 1996 (HIPAA). The Privacy Rule is designed to protect the confidentiality of your child's personal health information. The document you are reading, called an "Authorization," describes your child's rights and explains how your child's health information will be used and disclosed (shared).

HOW WILL MY CHILD'S STUDY INFORMATION BE KEPT PRIVATE?

Information collected for this study will be kept confidential to the extent provided by law. Health information means the information in your child's medical or other healthcare records, which also may include information that can identify your child. Information that can identify your child is called "protected health information" or PHI. By agreeing to allow your child to be in this study, you are giving permission and authorizing «FirstName» «MiddleName» «LastName» «Suffix» and his study staff to collect, use, and disclose your child's PHI for this research study. The results of the study may be published in scientific journals or presented at medical meetings. In the event of any publication regarding this study, your child's identity will not be revealed.

Your child's PHI collected or created under this research study will be used/disclosed as needed during and even after the end of the study. We will need to use it for research purposes and will release it to other people involved in the research or your child's routine healthcare. We will also generate new healthcare information about your child during the course of the study. This information will come from the tests and procedures and any interviews of your child conducted in connection with the study. The records of this study will be kept for an indefinite period of time, and by signing this Authorization you are authorizing the use of your child's PHI in accordance with this Authorization during that entire period. If you decide to withdraw your child from the study, or if your child is removed from the study by the study doctor or Sponsor (Sarepta Therapeutics, Inc.) you may withdraw, on your child's behalf, your permission for others to use and disclose your child's PHI, except that PHI that has already been collected may still be used by and disclosed to the individuals and entities as described in this Authorization. If you withdraw your permission for the use and disclosure of your child's PHI, your child can no longer take part in this research study.

If you decide to withdraw your permission for the use and disclosure of your child's PHI, this must be in writing. Please send a letter to your study doctor:

«FirstName» «MiddleName» «LastName» «Suffix»
«Company»
«Address» «SuiteDept»
«City» «State» «Zip»

Your child's PHI that may be used or disclosed:
Your child's PHI that may be used and disclosed for this study includes: review of your child's past, current or future health records, procedures such as physical examinations, blood or urine tests or other tests, your child's response to any study drug your child receives, your child's study visits, phone calls, study tests and procedures and any other study related health information, may be collected, used and disclosed to others. Your child's PHI also includes:

- ✓ Name and Date of Birth
- ✓ All medical records, including genetic testing and study tests and procedures
- ✓ Contact information (Addresses, Email addresses, Telephone/fax numbers)
- ✓ Family medical history
- ✓ Photos and videos

Efforts will be made to keep your child's study-related information confidential; however confidentiality cannot be guaranteed. Once disclosed, the PHI may no longer be protected by federal law and may be re-disclosed by those receiving the information.

People or Companies authorized to use, disclose, and receive your child's health information and PHI collected or created by this research study for purposes related to this study:

- «FirstName» «MiddleName» «LastName» «Suffix» and study staff
- The Copernicus Group Independent Review Board (the committee that reviews all human subject research)
- Nationwide Children's Hospital internal auditors
- The Office for Human Research Protections (OHRP) (the federal government office that oversees human patient research)
- Sarepta Therapeutics, Inc., the study sponsor and its designees, representatives and agents (including third parties who are providing services to the sponsor related to the study)
- An independent committee of physicians and experts that will review safety information from this study periodically
- The Food and Drug Administration (FDA) and other governmental health agencies, both within and outside the United States
- Your child's insurance company (if charges are billed to insurance).

Your child's health information and/or PHI also may be used and shared for treatment, payment and healthcare operations. Medical information from this study will become part of your child's hospital medical record.

In order to provide your child with routine care, other people at the hospital may need to review the health information we put into your record. This would include such people as your regular doctors and nurses and the hospital's billing department.

Your personal health information may be further shared by the groups above. If shared by them, the information will no longer be covered by the Privacy Rule. However, these groups are committed to keeping your personal health information confidential.

May I have access to my child's health information and PHI?

You will always have access to your child's medical record. A summary may be made available to you at the completion of the study. You will not have access to your child's research file because all information contained in the research file is either information obtained directly from your child, or was gathered from your child's medical records, to which you do have access. In some cases your child's research file may contain some information not known to you or the researchers that if known, would affect the scientific importance of the study.

AUTHORIZATION

I authorize the release of my child's medical records and personal health information related to this study to the Sponsor, including its affiliates, successors and assigns, both in the U.S. and other countries, and/or any third party working with Sponsor to conduct the study or to analyze or review study-related documents or data, the Copernicus Group Independent Review Board, the FDA and other regulatory agencies, and to the other individuals and entities as described above. I have been told that I will receive a signed and dated copy of this Authorization for my records.

_____

Printed First and Last Name of Subject

_____

Printed First and Last Name of Parent/Legal Guardian

_____ _____

Signature of Parent/Legal Guardian Date

_____

Printed First and Last Name of Parent/Legal Guardian

_____ _____

Signature of Parent/Legal Guardian Date

_____

Printed Name of Person Obtaining Authorization

_____ _____

Signature of Person Obtaining Authorization Date

_____

Printed Name of Investigator

_____ _____

Signature of Investigator Date

APPROVED: Oct 18, 2012
COPERNICUS GROUP IRB

copernicus group independent review board

Approved: «Approved»

PARENTAL PERMISSION FORM AND HIPAA AUTHORIZATION

STUDY TITLE: Open-Label, Multiple-Dose, Efficacy, Safety, and Tolerability Study of Eteplirsen in Subjects with Duchenne Muscular Dystrophy who Participated in Study 4658-us-201

PROTOCOL NUMBER: 4658-us-202

PROTOCOL AMENDMENT: 02 Dated 04 October 2012

STUDY SPONSOR: Sarepta Therapeutics, Inc.

STUDY DOCTOR:

RESEARCH SITE ADDRESS(ES):

DAYTIME TELEPHONE NUMBER(S):

24-HOUR TELEPHONE NUMBER(S): (*24 hours a day, 7 days a week*)

SUBJECT'S NAME: _____

INTRODUCTION

The purpose of this Parental Permission Form is to give you the information you will need to help you decide whether or not to allow your child to be in this study. Please read this form carefully. You should ask questions about what your child will be asked to do, the risks, the benefits, your child's rights as a subject, or anything else about the research or this form that is not clear to you. When all of your questions have been answered to your satisfaction, you can decide if you want your child to take part in this study or not. If you agree to allow your child to take part in this study and you sign this permission form, you will be given a copy for your records. If your child is 10 years of age or older, he will sign a separate informed consent form called an "Assent." You and your child will be given a copy for your records.

You are being asked to allow your child to be in this research study because your child has a muscle disorder called Duchenne muscular dystrophy (DMD). DMD is caused by a mutation (a change) in the gene that makes dystrophin protein. Dystrophin is important for protecting your child's muscles from stress and activity. Because of the mutation in your child's gene, your child's body is not able to make enough working dystrophin to protect your child's muscles.

This study is investigating a study drug called eteplirsen, which is designed to skip a certain fragment of the dystrophin gene called exon 51. In people with changes, called deletions, in certain parts of the dystrophin gene (including exons 45-50, 47-50, 48-50, 50, 52, or 52-63), skipping exon 51 is believed to allow the body to produce a shortened, but still working, form of dystrophin protein. This may result in improved muscle function for people with DMD.

In this study, all subjects will receive eteplirsen once a week and take part in study-specific tests for 80 weeks.

Participation in this study is voluntary. Please learn enough about this research study, its risks and benefits, to decide whether you should agree to allow your child to take part. The study team will explain the study to you, and give you a chance to ask questions about anything you do not understand. This process is called "informed consent." It is up to you to choose if you want your child to be in this study. You may refuse to allow your child to be in this study or your child may quit this study at any time, and standard medical care will still be available here or at a doctor of your choice without a penalty or loss of benefits to your child. If your child is between 10 and 13 years of age and agrees to take part in the study, he will be asked to sign an Assent Form. You will be given a signed and dated copy of this Parental Permission Form and the Assent Form.

Note: A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you or your child. At most, the Web site will include a summary of the results. You can search this Web site at any time.

WHY ARE WE DOING THIS RESEARCH STUDY?

This study will examine the effects of continued treatment with eteplirsen in children with DMD who have successfully completed the 28-week eteplirsen study, Study 4658-us-201. To better understand how eteplirsen works over a long period of time; the sponsor will use data from both studies (4658-us-201 and 4658-us-202) to compare how your child does in this study to how he was doing before he started eteplirsen in Study 4658-us-201.

Sarepta Therapeutics, Inc. is developing eteplirsen for the treatment of DMD by intravenous (IV, meaning through a vein) administration. Eteplirsen is designed to skip exon 51, which is believed to allow for the production of a shortened, but still working, form of the dystrophin protein and therefore result in improved muscle function for people with DMD.

Eteplirsen is considered experimental. Experimental means that this study drug is currently being tested. Eteplirsen has not been approved by the Food and Drug Administration (FDA) for use in the United States.

WHERE WILL THE STUDY BE DONE AND HOW MANY PARTICIPANTS WILL TAKE PART?

This study will be open to the 12 subjects who took part in the previous eteplirsen study, Study 4658-us-201. This study will be done at Nationwide Children's Hospital (the central site) and at up to 12 sites closer to the homes of participating subjects (satellite sites).

To take part in the study your child will need to meet all of the inclusion criteria and none of the exclusion criteria that your child's study doctor will discuss with you. The study doctor will also speak with you about some medicines that should not be taken by your child while participating in this study.

To be enrolled in the study, your child must:

1. Have completed 28 weeks of treatment in Study 4658-us-201
2. Have a parent(s) or legal guardian(s) who is able to understand and comply with all of the study requirements
3. Have a parent(s) or legal guardian(s) who is willing to provide written informed consent for the subject to take part in the study
4. Be willing, if at least age 10, to provide informed assent (agreement)

If your child has a prior or ongoing medical condition that the study doctor believes might affect his safety, or make it difficult for him to attend all of the required study visits and receive all of the study drug, or might affect the results of this study, your child will not be able to take part in this study.

WHAT WILL HAPPEN DURING THE STUDY AND HOW LONG WILL IT LAST?

During this study, your child will receive IV infusions of either 30 or 50 mg/kg eteplirsen once a week for 80 weeks (about a year and a half). Your child will receive the same dose of eteplirsen in this study that he received in Study 4658-us-201. That means if your child received the high dose (50 mg/kg) of eteplirsen in 4658-us-201, then he will receive the high dose in this study, and if he received the low dose of eteplirsen in 4658-us-201 (30 mg/kg), then he will receive the low dose in this study. Remember that the dose of eteplirsen that your child receives (high or low) was randomly assigned to him (picked by chance like tossing a coin in the air) during Study 4658-us-201. There was an even chance (50/50) that he would be assigned to the high or low dose.

This study is open-label. Open-label means that the study doctor, the study nurse, the study sponsor (Sarepta Therapeutics, Inc.), you, your child, and everyone else who might work with your child in this study will know your child is receiving eteplirsen.

All infusions of eteplirsen and all study tests will be performed at the central site, Nationwide Children's Hospital, until a suitable satellite site closer to your child's home is identified, the personnel there are trained, and the site is approved to take part in this study. Once the satellite is approved and ready, your child will receive all of his weekly infusions of eteplirsen at that site. You and your child will be asked to sign new Parental Permission and Assent Forms when you transfer to the satellite site. However, you and your child will still need to travel to Nationwide Children's Hospital approximately once every 12 weeks so your child can complete certain study-specific tests.

The procedures and tests that will take place at each of the weekly study visits are presented below.

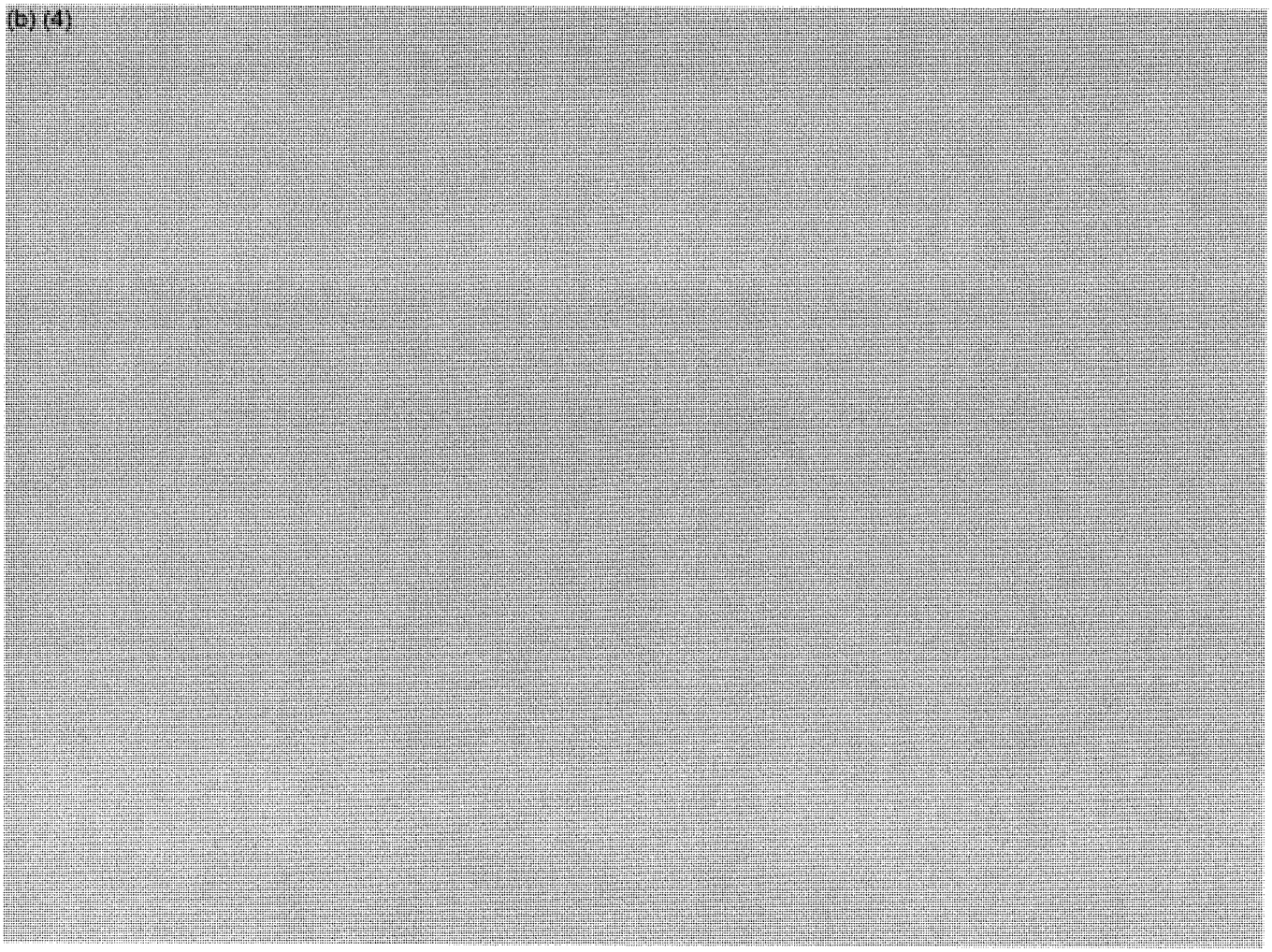
If a situation occurs that your child is unable to attend a scheduled visit and your child is at risk of missing a weekly dose, you must immediately notify the study doctor. It is very important that no more than 2 doses are missed in a 6-month period. If your child misses more than 6 doses during the 80 week study, he may be withdrawn from the study.

Screening/Baseline Period

Because this is an extension study for children who successfully completed Study 4658-us-201, there will be no formal screening period for this study. Instead, the study doctor will review the details of this study with you, obtain your consent and your child's agreement (assent) to take part in this study, and make sure this study is right for your child at the last visit (Week 28) of Study 4658-us-201.

In addition to procedures and tests specific to Study 4658-us-201, the following procedures will be performed at (b) (4) of Study 4658-us-201:

(b) (4)



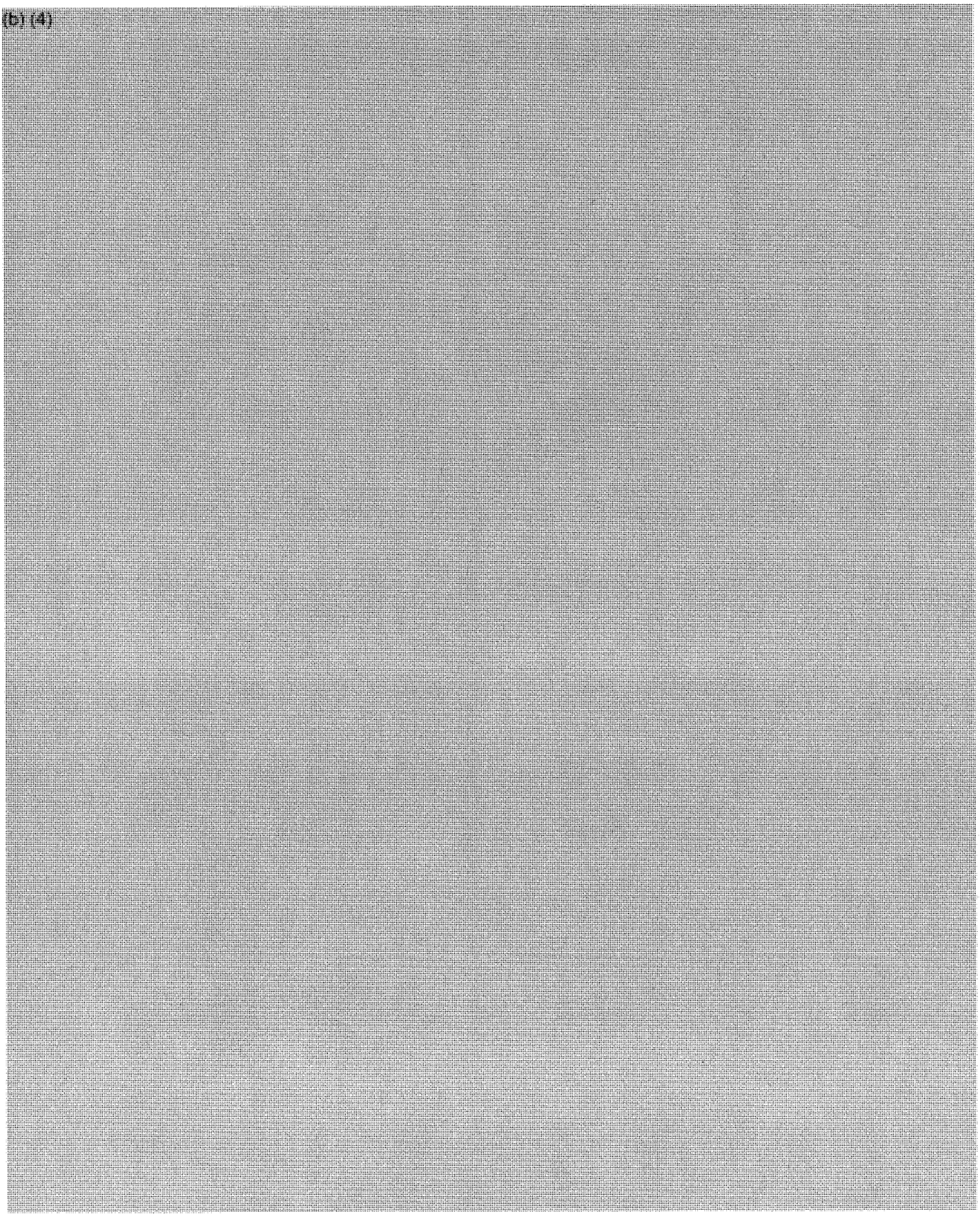
(b) (4)

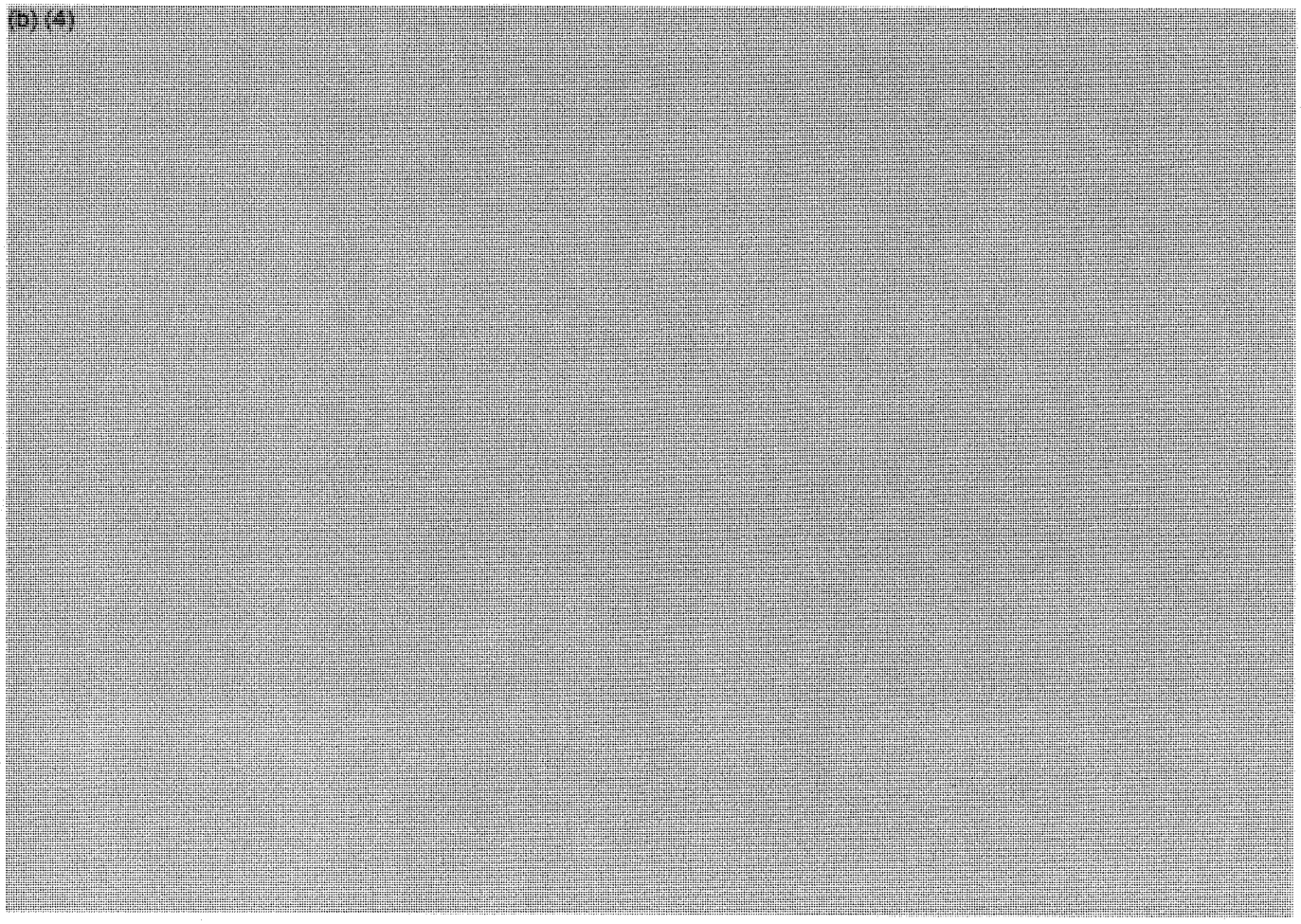
6. Study Drug Administration – Your child will receive a 60-minute infusion of eteplirsen. A topical anesthetic (numbing) cream (e.g., lidocaine 2.5%, prilocaine 2.5%, or LMX4 cream) may be applied to your child's skin prior to the infusion, if needed. After the infusion ends, your child will be observed for at least 1 hour to make sure that he is doing okay. As long as he is okay and all other tests and procedures have been completed, the study doctor will then let you and your child go home.

Please Note: Your child's doctor may recommend the insertion of a port as an option for the IV infusion of eteplirsen, if it is becoming difficult to use an IV to access their veins. A port is a small device inserted under the skin, which makes it easier to give infusions and collect blood.

(b) (4)

(b) (4)





WHAT ARE THE RISKS OF BEING IN THIS STUDY?

Two clinical studies have been done with eteplirsen in children with DMD in the United Kingdom and study 4658-us-201 has been completed in the US. The first study was a placebo-controlled study of several doses of eteplirsen in 7 boys with DMD aged 10 to 17 years. Doses ranged from 0.09 mg to 0.9 mg/kg and were given by a single injection into a small muscle on the foot (this is called an intramuscular or IM injection). Several of the boys showed an increase in dystrophin protein in the muscle of the foot that had been injected with eteplirsen.

The second study was an open-label study of eteplirsen administered into the vein (this is called an intravenous or IV injection or infusion). This study enrolled 19 boys with DMD, who were 5 to 15 years of age, and patients received up to 12 weekly infusions of eteplirsen. Doses ranged from 0.5 to 20.0 mg/kg. In this second study, levels of dystrophin protein were increased at the end of the study in 7 out of the 17 patients that had muscle biopsies taken before starting eteplirsen and at the end of the study.

In both studies, eteplirsen was well-tolerated over the doses given (up to 20.0 mg/kg). Overall, the problems that occurred (called adverse events) were generally mild or moderate in intensity. The common side effects of eteplirsen were:

- headache (42%)
- upper respiratory tract infection (42%)
- back pain (37%)
- rhinitis (inflammation of the mucous membrane of the nose that may cause nasal congestion and itching, and sneezing) (37%)
- falling (26%)
- myalgia (pain in the muscle) (21%)

One subject, who had a pre-existing heart condition due to DMD, had a decrease in his heart function without symptoms while taking 4.0 mg/kg of eteplirsen. This problem was considered possibly related to the eteplirsen and the subject was withdrawn from study drug administration.

The final safety information for study 4658-us-201 is not yet available, but early findings from the results showed that no adverse events were experienced by any subject that were related to the study medication and no subject stopped early in the study. In addition, there were no changes in vital signs, physical examination findings, ECGs, safety laboratory results or several blood markers that test for kidney problems that were related to the study medication.

One recent study that is being conducted in laboratory mice with a drug for mice similar to eteplirsen showed a mild increase in the size of the cerebrospinal fluid space inside the brain that may be a type of hydrocephaly (water in the brain). The importance of this finding from laboratory mice and how it relates to long-term dosing of eteplirsen in humans is unclear. Additional review and analysis is being conducted and reviewed related to this finding. At this time there are no recommendations to change the current eteplirsen trial.

It is important that you give the study staff your child's complete medical history. Not giving them this information or not completely following the directions of the study could harm your child.

All study drugs may cause some side effects or other reactions. There is no way to predict if your child will experience any of these side effects. Side effects that are not yet known may also occur.

Blood Draw/IV Risk
Drawing blood and starting IVs by placing a needle in a vein may cause pain, lightheadedness and fainting, bleeding, bruising, or swelling at the puncture site. Infection is a rare possibility. Topical anesthetic or numbing cream may be used on the skin to decrease the discomfort, if needed. Although there are no known side effects from the numbing cream, skin irritation or an allergic reaction is possible.

Insertion of Port Risk

- An infection that may require the removal of the device
- Thrombosis (a blood clot) that can form in the catheter that may block the device from being accessed.
- Failure of the device - although unlikely, it is possible the device could break

- Pneumothorax (air or gas between the lungs and the chest wall), causing the lungs to collapse
- Injury to an artery

Muscle Biopsy Risk
The common side effects of the muscle biopsies may include discomfort, a scar, infection, bruise, numbness near the biopsy site, and delayed wound healing.

Sedation Risk
Risks from local anesthetic may include pain with infection, and (very rarely) allergic reactions. Minor discomfort during surgery is common, but the likelihood of other risks is extremely small (less than 1%). After use of conscious sedation, your child may get a headache or feel nauseous or dizzy. It is possible that your child will have a reaction to the sedative medication used.

If any of the symptoms listed above are severe, your child must get medical help right away. If you are worried about anything while in this study, please call the study doctor or study nurse at the telephone number on page 1.

Unforeseen Risks
There may be other risks of being in this research study that are not known at this time.

ARE THERE BENEFITS TO TAKING PART IN THIS STUDY?
The potential benefits of eteplirsen in subjects with DMD are unknown. Your child may have some benefits from taking part in this study, but even if your child does not benefit from being in this study, we might learn something that could help others.

WHAT WILL HAPPEN IF NEW INFORMATION IS FOUND OUT ABOUT THE DRUG OR TREATMENT?
If new information is found out during this study that might change your mind about your child taking part or might affect your child's health, your study doctor will discuss it with you and your child as soon as possible.

WHAT OTHER TREATMENTS OR OPTIONS ARE THERE?
Your child's participation in this study is voluntary. It is not necessary to be in this study to get care for this condition. If you decide not to allow your child to be in this study, the study doctor will talk to you and your child about other possible treatments or refer you to your child's regular doctor for care.

WILL THERE BE ANY COSTS TO ME?
It will not cost you or your child anything to be in this study and you or your child will not be paid to be in this study. Travel expenses including airfare (with supporting receipts) for up to two adults and one child for all required visits to Nationwide Children's Hospital will be covered.

CONFIDENTIALITY OF STUDY INFORMATION
The data collected as part of this study will be kept confidential, but may be shared with the individuals and entities and for the purposes described in this Parental Permission Form and the attached HIPAA Authorization form. In all study-related records, a number and initials will identify your child, unless otherwise described in this Parental Permission Form or the attached

HIPAA Authorization form. Data collected and recorded on study forms are the property of the sponsor if information about this study is published, your child's identity will remain confidential. However, the U.S. Food and Drug Administration (FDA), Copernicus Group Independent Review Board (IRB), and the study sponsor, Sarepta Therapeutics, Inc. and its representatives may be granted direct access to your child's original medical records for verification of clinical trial procedures or data. By signing this Parental Permission Form, you are authorizing such access. A court of law could order medical records shown to other people, but that is unlikely.

WHAT HAPPENS IF BEING IN THIS STUDY CAUSES INJURIES?

If your child is hurt by the study drug, eteplirsen, or the procedures that are part of the study, you should seek medical treatment for your child's injuries and tell the study doctor as soon as possible at the number on the first page of this form. If it is an emergency, call 911 or go to the nearest emergency department.

If your child is injured as a direct result of the proper administration of the study drug, eteplirsen, or the proper performance of procedures that are required solely for the study, and your child has followed the directions of the study team, (b) (4)

(b) (4)

If the care is provided at Nationwide Children's Hospital, (b) (4)

(b) (4)

(b) (4) This does not mean that you give up any of your or your child's legal rights to seek compensation for your child's injuries.

LEGAL RIGHTS

The above section does not restrict your right to seek legal assistance. By signing this Parental Permission Form you will not waive any of your child's legal rights as a research subject.

WHAT HAPPENS IF MY CHILD DOES NOT FINISH THIS STUDY?

It is your choice to allow your child to be in this study or to stop at any time. If you decide to stop your child from being in this study, it is okay, but you must call the study doctor or the study nurse. If you stop your child from being in the study, there will not be a penalty or loss of benefits to which your child is otherwise entitled.

If at any time the study doctor believes participating in this study is not the best choice of care for your child, the study may be stopped and other care prescribed. If the study instructions are not followed, your child's participation in the study may also be stopped. If unexpected medical problems come up, the study doctor or the sponsor, Sarepta Therapeutics, Inc., may decide to stop your child's participation in the study.

If your child's participation in the study is stopped before completing all of the study activities, your child will be asked to visit the study doctor, «FirstName» «MiddleName» «LastName» «Suffix» (unless you have withdrawn consent), or you may be asked to return to Nationwide Children's Hospital so that the following information can be collected and assessments can be completed:

(b) (4)

In addition, subjects who have not already had their (b) (4) .

If your child withdraws from the study because he is not feeling well, your child will be encouraged to have follow-up assessments when he feels better.

OTHER IMPORTANT INFORMATION

It is considered a conflict of interest where the parents of a potential subject hold stock of Sarepta Therapeutics, Inc. By signing this consent form, you agree that neither you nor any of your family have stock of or an interest with the potential for financial gain in the sponsor, Sarepta Therapeutics, Inc.

It is important that healthcare providers know about all medicines your child is taking. This includes the study drug being tested in this research study. Because of this, we plan to tell your child's primary care doctor that he is in this research study. This is done so extra care can be taken in prescribing other medicines and looking at any unexplained symptoms that may occur. Your child cannot take part in this study if you do not want us to tell your child's primary care doctor.

The study doctor is being paid by Sarepta Therapeutics, Inc. for the time and knowledge needed to do this study.

Being in more than one research study at the same time may cause injury. Please tell the study doctor if your child is in any other research study so a decision can be made about being in more than one study at the same time.

Keep in mind that your permission for your child's participation in the study will remain valid until such time as you choose to withdraw it. This withdrawal should be in writing and sent to the following address:

«FirstName» «MiddleName» «LastName» «Suffix»
«Company»
«Address» «SuiteDept»
«City» «State» «Zip»

Any information collected prior to this withdrawal may be used but no new information would be collected after the time the withdrawal is received.

WHOM SHOULD I CALL IF I HAVE QUESTIONS OR PROBLEMS?

If you have any questions about your child's participation in this research study or if you feel that your child has experienced a research-related injury or reaction to the study drug, contact:

Investigator Name: **«FirstName» «MiddleName» «LastName» «Suffix»**

Daytime telephone number(s): «Phone»; you can reach the study nurse during business hours at [Study Nurse Phone]

24-hour contact number(s): «Phone2» (7 days a week)

If you have any questions or concerns about your child's rights as a research subject or want to discuss a problem, get information or offer input, you may contact Copernicus Group Independent Review Board (IRB) at 1-888-303-2224 (toll free). An IRB is a group of scientific and non-scientific individuals who perform the initial and ongoing ethical review of the research study with the study subject's rights and welfare in mind. Copernicus Group IRB has reviewed and approved the research study described in this Parental Permission Form. If you have study-related comments, complaints or concerns, you should first contact the study doctor. Please call the IRB if you want to talk to someone other than the study doctor or have difficulty reaching the study doctor. For further information regarding the clinical trials process and your child's role as a research subject, you may visit the Copernicus Group IRB website at www.cgirb.com.

PARENTAL STATEMENT OF PERMISSION

Open-Label, Multiple-Dose, Efficacy, Safety, and Tolerability Study of Eteplirsen in Subjects with Duchenne Muscular Dystrophy who Participated in Study 4658-us-201

I have read this Parental Permission Form and have had a chance to ask questions about this research study, which have been answered to my satisfaction. If I have more questions about participation in this study or a research-related injury, I may contact the study doctor. By signing this Parental Permission Form, I certify that all health information I have given regarding my child is true and correct to the best of my knowledge.

I have been given a copy of the Nationwide Children's Hospital Notice of Privacy Practices. I have been told that my right to my child's patient information that is created or collected in the course of this research can be temporarily suspended for as long as the research is in progress. I also have been told that my right to access will be reinstated upon completion of this research.

I give permission for my child to take part in this study. I will be given a copy of this Parental Permission Form with all the signatures for my own records.

_____
PRINTED NAME OF SUBJECT

_____
PRINTED NAME OF PARENT/LEGAL GUARDIAN

_____ _____
SIGNATURE OF PARENT/LEGAL GUARDIAN | DATE & TIME AM/PM

_____
PRINTED NAME OF SECOND PARENT/ LEGAL GUARDIAN

_____ _____
SIGNATURE OF SECOND PARENT/ LEGAL GUARDIAN | DATE & TIME AM/PM

Permission of the second parent not obtained because (select all that apply):

_____ Other parent is deceased.
_____ Other parent is unknown.
_____ Other parent is not reasonably available.
_____ Only one parent has legal responsibility for the care and custody of subject.

I certify that I have explained the research, its purposes, and the procedures to the patient or subject's parent(s) or legal guardian(s) and have answered all of their questions, before requesting their signature. I believe that he/she understands the information described in this Parental Permission Form and freely consents to have his/her child participate in the study.

PRINTED NAME OF PERSON OBTAINING CONSENT

SIGNATURE OF PERSON OBTAINING CONSENT

DATE & TIME AM/PM

PRINTED NAME OF INVESTIGATOR

SIGNATURE OF INVESTIGATOR

DATE & TIME AM/PM

PRINTED NAME OF WITNESS

SIGNATURE OF WITNESS
FOR VA SITES ONLY

DATE & TIME AM/PM

HIPAA AUTHORIZATION

The United States government has issued a privacy rule to protect the privacy rights of patients. This rule was issued under a law called the Health Insurance Portability and Accountability Act of 1996 (HIPAA). The Privacy Rule is designed to protect the confidentiality of your child's personal health information. The document you are reading, called an "Authorization," describes your child's rights and explains how your child's health information will be used and disclosed (shared).

HOW WILL MY CHILD'S STUDY INFORMATION BE KEPT PRIVATE?

Information collected for this study will be kept confidential to the extent provided by law. Health information means the information in your child's medical or other healthcare records, which also may include information that can identify your child. Information that can identify your child is called "protected health information" or PHI. By agreeing to allow your child to be in this study, you are giving permission and authorizing «FirstName» «MiddleName» «LastName» «Suffix» and his study staff to collect, use, and disclose your child's PHI for this research study. The results of the study may be published in scientific journals or presented at medical meetings. In the event of any publication regarding this study, your child's identity will not be revealed.

Your child's PHI collected or created under this research study will be used/disclosed as needed during and even after the end of the study. We will need to use it for research purposes and will release it to other people involved in the research or your child's routine healthcare. We will also generate new healthcare information about your child during the course of the study. This information will come from the tests and procedures and any interviews of your child conducted in connection with the study. The records of this study will be kept for an indefinite period of time, and by signing this Authorization you are authorizing the use of your child's PHI in accordance with this Authorization during that entire period. If you decide to withdraw your child from the study, or if your child is removed from the study by the study doctor or Sponsor (Sarepta Therapeutics, Inc.) you may withdraw, on your child's behalf, your permission for others to use and disclose your child's PHI, except that PHI that has already been collected may still be used by and disclosed to the individuals and entities as described in this Authorization. If you withdraw your permission for the use and disclosure of your child's PHI, your child can no longer take part in this research study.

If you decide to withdraw your permission for the use and disclosure of your child's PHI, this must be in writing. Please send a letter to your study doctor:

«FirstName» «MiddleName» «LastName» «Suffix»
«Company»
«Address» «SuiteDept»
«City» «State» «Zip»

Your child's PHI that may be used or disclosed:
Your child's PHI that may be used and disclosed for this study includes: review of your child's past, current or future health records, procedures such as physical examinations, blood or urine tests or other tests, your child's response to any study drug your child receives, your child's study visits, phone calls, study tests and procedures and any other study related health information, may be collected, used and disclosed to others. Your child's PHI also includes:

- ✓ Name and Date of Birth
- ✓ All medical records, including genetic testing and study tests and procedures
- ✓ Contact information (Addresses, Email addresses, Telephone/fax numbers)
- ✓ Family medical history
- ✓ Photos and videos

Efforts will be made to keep your child's study-related information confidential; however confidentiality cannot be guaranteed. Once disclosed, the PHI may no longer be protected by federal law and may be re-disclosed by those receiving the information.

People or Companies authorized to use, disclose, and receive your child's health information and PHI collected or created by this research study for purposes related to this study:

- «FirstName» «MiddleName» «LastName» «Suffix» and study staff
- The Copernicus Group Independent Review Board (the committee that reviews all human subject research)
- Nationwide Children's Hospital internal auditors
- The Office for Human Research Protections (OHRP) (the federal government office that oversees human patient research)
- Sarepta Therapeutics, Inc., the study sponsor and its designees, representatives and agents (including third parties who are providing services to the sponsor related to the study)
- An independent committee of physicians and experts that will review safety information from this study periodically
- The Food and Drug Administration (FDA) and other governmental health agencies, both within and outside the United States
- Your child's insurance company (if charges are billed to insurance).

Your child's health information and/or PHI also may be used and shared for treatment, payment and healthcare operations. Medical information from this study will become part of your child's hospital medical record.

In order to provide your child with routine care, other people at the hospital may need to review the health information we put into your record. This would include such people as your regular doctors and nurses and the hospital's billing department.

Your personal health information may be further shared by the groups above. If shared by them, the information will no longer be covered by the Privacy Rule. However, these groups are committed to keeping your personal health information confidential.

May I have access to my child's health information and PHI?

You will always have access to your child's medical record. A summary may be made available to you at the completion of the study. You will not have access to your child's research file because all information contained in the research file is either information obtained directly from your child, or was gathered from your child's medical records, to which you do have access. In some cases your child's research file may contain some information not known to you or the researchers that if known, would affect the scientific importance of the study.

AUTHORIZATION

I authorize the release of my child's medical records and personal health information related to this study to the Sponsor, including its affiliates, successors and assigns, both in the U.S. and other countries, and/or any third party working with Sponsor to conduct the study or to analyze or review study-related documents or data, the Copernicus Group Independent Review Board, the FDA and other regulatory agencies, and to the other individuals and entities as described above. I have been told that I will receive a signed and dated copy of this Authorization for my records.

_____

Printed First and Last Name of Subject

_____

Printed First and Last Name of Parent/Legal Guardian

_____ _____

Signature of Parent/Legal Guardian Date

_____

Printed First and Last Name of Parent/Legal Guardian

_____ _____

Signature of Parent/Legal Guardian Date

_____

Printed Name of Person Obtaining Authorization

_____ _____

Signature of Person Obtaining Authorization Date

_____

Printed Name of Investigator

_____ _____

Signature of Investigator Date

APPROVED: May 16, 2012
COPERNICUS GROUP IRB

copernicus group independent review board

Approved:

PARENTAL PERMISSION FORM AND HIPAA AUTHORIZATION

STUDY TITLE: Open-Label, Multiple-Dose, Efficacy, Safety, and Tolerability Study of Eteplirsen in Subjects with Duchenne Muscular Dystrophy who Participated in Study 4658-us-201

PROTOCOL NUMBER: 4658-us-202

PROTOCOL AMENDMENT: 01 Dated 20 April 2012

STUDY SPONSOR: AVI BioPharma, Inc.

STUDY DOCTOR:

RESEARCH SITE ADDRESS(ES):

DAYTIME TELEPHONE NUMBER(S):

24-HOUR TELEPHONE NUMBER(S): (*24 hours a day, 7 days a week*)

SUBJECT'S NAME: _____

INTRODUCTION

The purpose of this Parental Permission Form is to give you the information you will need to help you decide whether or not to allow your child to be in this study. Please read this form carefully. You should ask questions about what your child will be asked to do, the risks, the benefits, your child's rights as a subject, or anything else about the research or this form that is not clear to you. When all of your questions have been answered to your satisfaction, you can decide if you want your child to take part in this study or not. If you agree to allow your child to take part in this study and you sign this permission form, you will be given a copy for your records. If your child is 10 years of age or older, he will sign a separate informed consent form called an "Assent." You and your child will be given a copy for your records.

You are being asked to allow your child to be in this research study because your child has a muscle disorder called Duchenne muscular dystrophy (DMD). DMD is caused by a mutation (a change) in the gene that makes dystrophin protein. Dystrophin is important for protecting your child's muscles from stress and activity. Because of the mutation in your child's gene, your child's body is not able to make enough working dystrophin to protect your child's muscles.

This study is investigating a study drug called eteplirsen, which is designed to skip a certain fragment of the dystrophin gene called exon 51. In people with changes, called deletions, in certain parts of the dystrophin gene (including exons 45-50, 47-50, 48-50, 50, 52, or 52-63), skipping exon 51 is believed to allow the body to produce a shortened, but still working, form of dystrophin protein. This may result in improved muscle function for people with DMD.

In this study, all subjects will receive eteplirsen once a week and take part in study-specific tests for 80 weeks.

Participation in this study is voluntary. Please learn enough about this research study, its risks and benefits, to decide whether you should agree to allow your child to take part. The study team will explain the study to you, and give you a chance to ask questions about anything you do not understand. This process is called "informed consent." It is up to you to choose if you want your child to be in this study. You may refuse to allow your child to be in this study or your child may quit this study at any time, and standard medical care will still be available here or at a doctor of your choice without a penalty or loss of benefits to your child. If your child is between 10 and 13 years of age and agrees to take part in the study, he will be asked to sign an Assent Form. You will be given a signed and dated copy of this Parental Permission Form and the Assent Form.

Note: A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you or your child. At most, the Web site will include a summary of the results. You can search this Web site at any time.

WHY ARE WE DOING THIS RESEARCH STUDY?

This study will examine the effects of continued treatment with eteplirsen in children with DMD who have successfully completed the 28-week eteplirsen study, Study 4658-us-201. To better understand how eteplirsen works over a long period of time; the sponsor will use data from both studies (4658-us-201 and 4658-us-202) to compare how your child does in this study to how he was doing before he started eteplirsen in Study 4658-us-201.

AVI BioPharma, Inc. is developing eteplirsen for the treatment of DMD by intravenous (IV, meaning through a vein) administration. Eteplirsen is designed to skip exon 51, which is believed to allow for the production of a shortened, but still working, form of the dystrophin protein and therefore result in improved muscle function for people with DMD.

Eteplirsen is considered experimental. Experimental means that this study drug is currently being tested. Eteplirsen has not been approved by the Food and Drug Administration (FDA) for use in the United States.

WHERE WILL THE STUDY BE DONE AND HOW MANY PARTICIPANTS WILL TAKE PART?

This study will be open to the 12 subjects who took part in the previous eteplirsen study, Study 4658-us-201. This study will be done at Nationwide Children's Hospital (the central site) and at up to 12 sites closer to the homes of participating subjects (satellite sites).

To take part in the study your child will need to meet all of the inclusion criteria and none of the exclusion criteria that your child's study doctor will discuss with you. The study doctor will also speak with you about some medicines that should not be taken by your child while participating in this study.

To be enrolled in the study, your child must:

1. Have completed 28 weeks of treatment in Study 4658-us-201
2. Have a parent(s) or legal guardian(s) who is able to understand and comply with all of the study requirements
3. Have a parent(s) or legal guardian(s) who is willing to provide written informed consent for the subject to take part in the study
4. Be willing, if at least age 10, to provide informed assent (agreement)

If your child has a prior or ongoing medical condition that the study doctor believes might affect his safety, or make it difficult for him to attend all of the required study visits and receive all of the study drug, or might affect the results of this study, your child will not be able to take part in this study.

WHAT WILL HAPPEN DURING THE STUDY AND HOW LONG WILL IT LAST?

During this study, your child will receive IV infusions of either 30 or 50 mg/kg eteplirsen once a week for 80 weeks (about a year and a half). Your child will receive the same dose of eteplirsen in this study that he received in Study 4658-us-201. That means if your child received the high dose (50 mg/kg) of eteplirsen in 4658-us-201, then he will receive the high dose in this study, and if he received the low dose of eteplirsen in 4658-us-201 (30 mg/kg), then he will receive the low dose in this study. Remember that the dose of eteplirsen that your child receives (high or low) was randomly assigned to him (picked by chance like tossing a coin in the air) during Study 4658-us-201. There was an even chance (50/50) that he would be assigned to the high or low dose.

This study is open-label. Open-label means that the study doctor, the study nurse, the study sponsor (AVI BioPharma, Inc.), you, your child, and everyone else who might work with your child in this study will know your child is receiving eteplirsen.

All infusions of eteplirsen and all study tests will be performed at the central site, Nationwide Children's Hospital, until a suitable satellite site closer to your child's home is identified, the personnel there are trained, and the site is approved to take part in this study. Once the satellite is approved and ready, your child will receive all of his weekly infusions of eteplirsen at that site. You and your child will be asked to sign new Parental Permission and Assent Forms when you transfer to the satellite site. However, you and your child will still need to travel to Nationwide Children's Hospital approximately once every 12 weeks so your child can complete certain study-specific tests.

The procedures and tests that will take place at each of the weekly study visits are presented below.

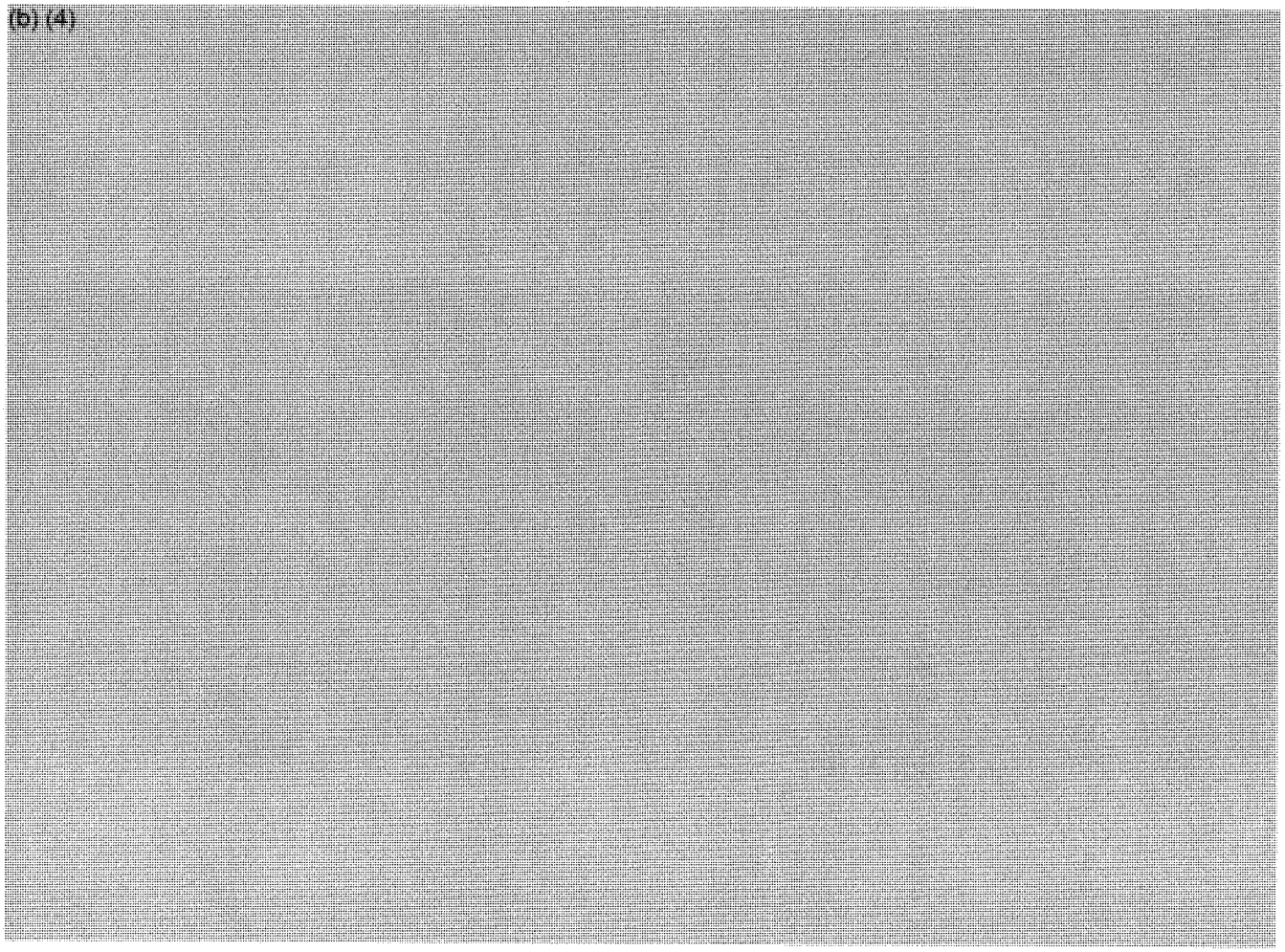
If a situation occurs that your child is unable to attend a scheduled visit and your child is at risk of missing a weekly dose, you must immediately notify the study doctor. It is very important that no more than 2 doses are missed in a 6-month period. If your child misses more than 6 doses during the 80 week study, he may be withdrawn from the study.

Screening/Baseline Period

Because this is an extension study for children who successfully completed Study 4658-us-201, there will be no formal screening period for this study. Instead, the study doctor will review the details of this study with you, obtain your consent and your child's agreement (assent) to take part in this study, and make sure this study is right for your child at the last visit (Week 28) of Study 4658-us-201.

In addition to procedures and tests specific to Study 4658-us-201, the following procedures will be performed at (b) (4) of Study 4658-us-201:

(b) (4)

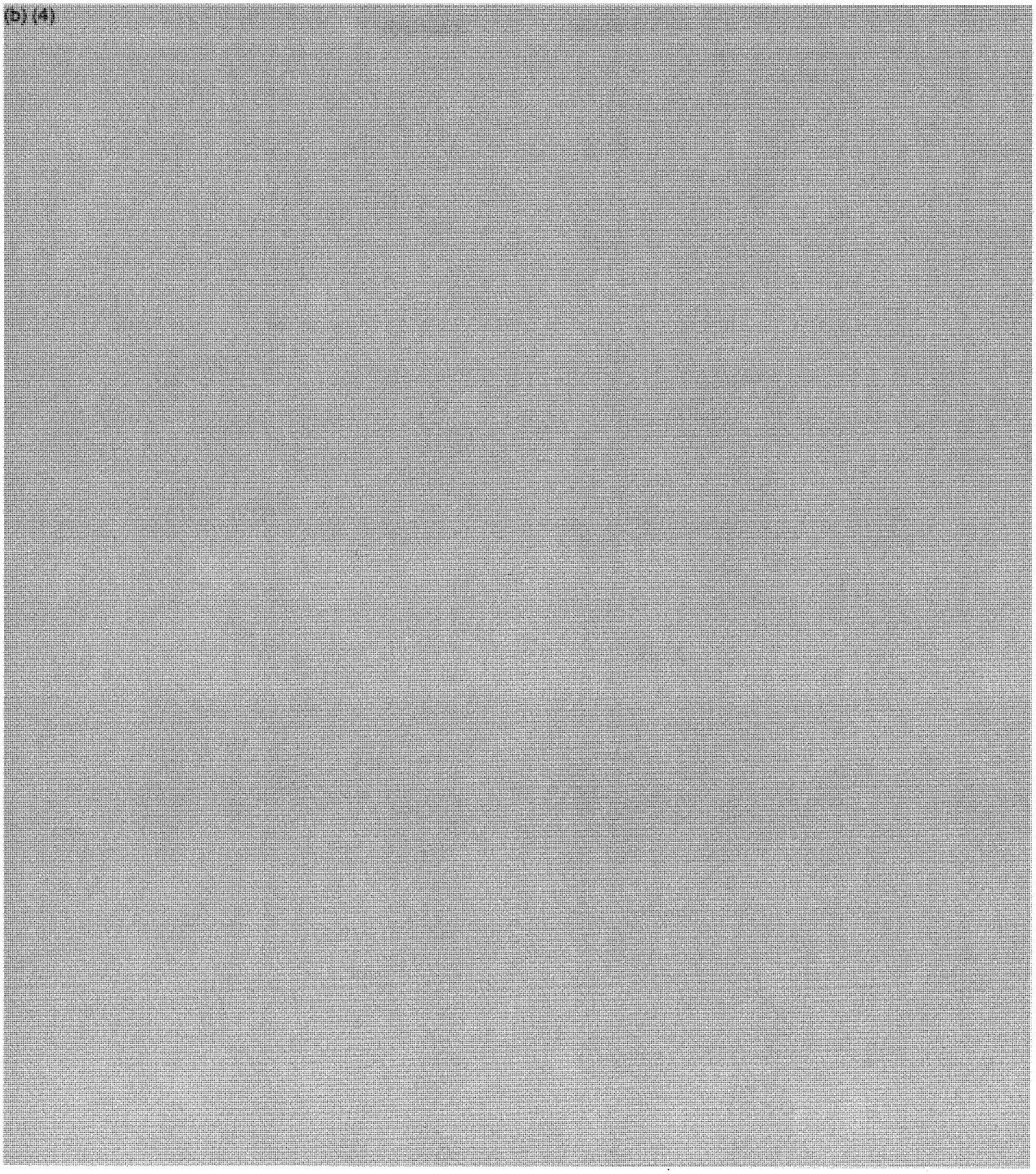


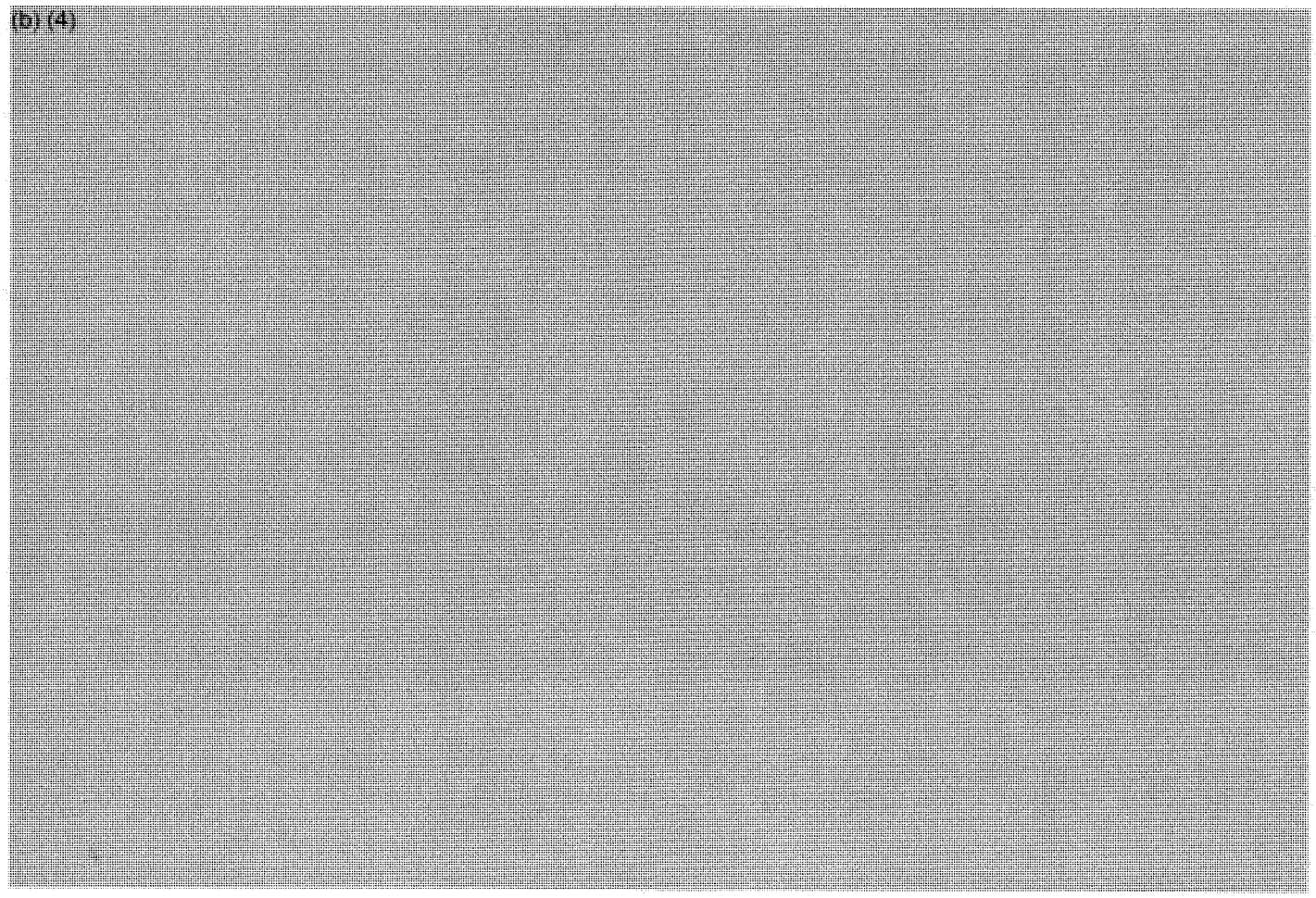
(b) (4)

6. Study Drug Administration – Your child will receive a 60-minute infusion of eteplirsen. A topical anesthetic (numbing) cream (e.g., lidocaine 2.5%, prilocaine 2.5%, or LMX4 cream) may be applied to your child's skin prior to the infusion, if needed. After the infusion ends, your child will be observed for at least 1 hour to make sure that he is doing okay. As long as he is okay and all other tests and procedures have been completed, the study doctor will then let you and your child go home.

(b) (4)

(b) (4)





WHAT ARE THE RISKS OF BEING IN THIS STUDY?

Two clinical studies have been done with eteplirsen in children with DMD in the United Kingdom and study 4658-us-201 has been completed in the US. The first study was a placebo-controlled study of several doses of eteplirsen in 7 boys with DMD aged 10 to 17 years. Doses ranged from 0.09 mg to 0.9 mg/kg and were given by a single injection into a small muscle on the foot (this is called an intramuscular or IM injection). Several of the boys showed an increase in dystrophin protein in the muscle of the foot that had been injected with eteplirsen.

The second study was an open-label study of eteplirsen administered into the vein (this is called an intravenous or IV injection or infusion). This study enrolled 19 boys with DMD, who were 5 to 15 years of age, and patients received up to 12 weekly infusions of eteplirsen. Doses ranged from 0.5 to 20.0 mg/kg. In this second study, levels of dystrophin protein were increased at the end of the study in 7 out of the 17 patients that had muscle biopsies taken before starting eteplirsen and at the end of the study.

In both studies, eteplirsen was well-tolerated over the doses given (up to 20.0 mg/kg). Overall, the problems that occurred (called adverse events) were generally mild or moderate in intensity. The common side effects of eteplirsen were:

- headache (42%)
- upper respiratory tract infection (42%)
- back pain (37%)
- rhinitis (inflammation of the mucous membrane of the nose that may cause nasal congestion and itching, and sneezing) (37%)
- falling (26%)
- myalgia (pain in the muscle) (21%)

One subject, who had a pre-existing heart condition due to DMD, had a decrease in his heart function without symptoms while taking 4.0 mg/kg of eteplirsen. This problem was considered possibly related to the eteplirsen and the subject was withdrawn from study drug administration.

The final safety information for study 4658-us-201 is not yet available, but early findings from the results showed that no adverse events were experienced by any subject that were related to the study medication and no subject stopped early in the study. In addition, there were no changes in vital signs, physical examination findings, ECGs, safety laboratory results or several blood markers that test for kidney problems that were related to the study medication.

One recent study that is being conducted in laboratory mice with a drug for mice similar to eteplirsen showed a mild increase in the size of the cerebrospinal fluid space inside the brain that may be a type of hydrocephaly (water in the brain). The importance of this finding from laboratory mice and how it relates to long-term dosing of eteplirsen in humans is unclear. Additional review and analysis is being conducted and reviewed related to this finding. At this time there are no recommendations to change the current eteplirsen trial.

It is important that you give the study staff your child's complete medical history. Not giving them this information or not completely following the directions of the study could harm your child.

All study drugs may cause some side effects or other reactions. There is no way to predict if your child will experience any of these side effects. Side effects that are not yet known may also occur.

Blood Draw/IV Risk
Drawing blood and starting IVs by placing a needle in a vein may cause pain, lightheadedness and fainting, bleeding, bruising, or swelling at the puncture site. Infection is a rare possibility. Topical anesthetic or numbing cream may be used on the skin to decrease the discomfort, if needed. Although there are no known side effects from the numbing cream, skin irritation or an allergic reaction is possible.

Muscle Biopsy Risk
The common side effects of the muscle biopsies may include discomfort, a scar, infection, bruise, numbness near the biopsy site, and delayed wound healing.

Sedation Risk
Risks from local anesthetic may include pain with infection, and (very rarely) allergic reactions. Minor discomfort during surgery is common, but the likelihood of other risks is extremely small (less than 1%). After use of conscious sedation, your child may get a headache or feel nauseous or dizzy. It is possible that your child will have a reaction to the sedative medication used.

If any of the symptoms listed above are severe, your child must get medical help right away. If you are worried about anything while in this study, please call the study doctor or study nurse at the telephone number on page 1.

Unforeseen Risks
There may be other risks of being in this research study that are not known at this time.

ARE THERE BENEFITS TO TAKING PART IN THIS STUDY?
The potential benefits of eteplirsen in subjects with DMD are unknown. Your child may have some benefits from taking part in this study, but even if your child does not benefit from being in this study, we might learn something that could help others.

WHAT WILL HAPPEN IF NEW INFORMATION IS FOUND OUT ABOUT THE DRUG OR TREATMENT?
If new information is found out during this study that might change your mind about your child taking part or might affect your child's health, your study doctor will discuss it with you and your child as soon as possible.

WHAT OTHER TREATMENTS OR OPTIONS ARE THERE?
Your child's participation in this study is voluntary. It is not necessary to be in this study to get care for this condition. If you decide not to allow your child to be in this study, the study doctor will talk to you and your child about other possible treatments or refer you to your child's regular doctor for care.

WILL THERE BE ANY COSTS TO ME?
It will not cost you or your child anything to be in this study and you or your child will not be paid to be in this study. Travel expenses including airfare (with supporting receipts) for up to two adults and one child for all required visits to Nationwide Children's Hospital will be covered.

CONFIDENTIALITY OF STUDY INFORMATION
The data collected as part of this study will be kept confidential, but may be shared with the individuals and entities and for the purposes described in this Parental Permission Form and the attached HIPAA Authorization form. In all study-related records, a number and initials will identify your child, unless otherwise described in this Parental Permission Form or the attached HIPAA Authorization form. Data collected and recorded on study forms are the property of the sponsor if information about this study is published, your child's identity will remain confidential. However, the U.S. Food and Drug Administration (FDA), Copernicus Group Independent Review Board (IRB), and the study sponsor, AVI BioPharma, Inc. and its representatives may be granted direct access to your child's original medical records for verification of clinical trial procedures or data. By signing this Parental Permission Form, you are authorizing such access. A court of law could order medical records shown to other people, but that is unlikely.

WHAT HAPPENS IF BEING IN THIS STUDY CAUSES INJURIES?

If your child is hurt by the study drug, eteplirsen, or the procedures that are part of the study, you should seek medical treatment for your child's injuries and tell the study doctor as soon as possible at the number on the first page of this form. If it is an emergency, call 911 or go to the nearest emergency department.

If your child is injured as a direct result of the proper administration of the study drug, eteplirsen, or the proper performance of procedures that are required solely for the study, and your child has followed the directions of the study team, (b) (4)

(b) (4)

If the care is provided at Nationwide Children's Hospital, (b) (4)

(b) (4)

(b) (4) This does not mean that you give up any of your or your child's legal rights to seek compensation for your child's injuries.

LEGAL RIGHTS

The above section does not restrict your right to seek legal assistance. By signing this Parental Permission Form you will not waive any of your child's legal rights as a research subject.

WHAT HAPPENS IF MY CHILD DOES NOT FINISH THIS STUDY?

It is your choice to allow your child to be in this study or to stop at any time. If you decide to stop your child from being in this study, it is okay, but you must call the study doctor or the study nurse. If you stop your child from being in the study, there will not be a penalty or loss of benefits to which your child is otherwise entitled.

If at any time the study doctor believes participating in this study is not the best choice of care for your child, the study may be stopped and other care prescribed. If the study instructions are not followed, your child's participation in the study may also be stopped. If unexpected medical problems come up, the study doctor or the sponsor, AVI BioPharma, Inc., may decide to stop your child's participation in the study.

If your child's participation in the study is stopped before completing all of the study activities, your child will be asked to visit the study doctor, «FirstName» «MiddleName» «LastName» «Suffix» (unless you have withdrawn consent), or you may be asked to return to Nationwide Children's Hospital so that the following information can be collected and assessments can be completed:

(b) (4)

(b) (4)

In addition, subjects who have not already had their (b) (4)

If your child withdraws from the study because he is not feeling well, your child will be encouraged to have follow-up assessments when he feels better.

OTHER IMPORTANT INFORMATION

It is considered a conflict of interest where the parents of a potential subject hold stock of AVI BioPharma, Inc. By signing this consent form, you agree that neither you nor any of your family have stock of or an interest with the potential for financial gain in the sponsor, AVI BioPharma, Inc.

It is important that healthcare providers know about all medicines your child is taking. This includes the study drug being tested in this research study. Because of this, we plan to tell your child's primary care doctor that he is in this research study. This is done so extra care can be taken in prescribing other medicines and looking at any unexplained symptoms that may occur. Your child cannot take part in this study if you do not want us to tell your child's primary care doctor.

The study doctor is being paid by AVI BioPharma, Inc. for the time and knowledge needed to do this study.

Being in more than one research study at the same time may cause injury. Please tell the study doctor if your child is in any other research study so a decision can be made about being in more than one study at the same time.

Keep in mind that your permission for your child's participation in the study will remain valid until such time as you choose to withdraw it. This withdrawal should be in writing and sent to the following address:

«FirstName» «MiddleName» «LastName» «Suffix»
«Company»
«Address» «SuiteDept»
«City» «State» «Zip»

Any information collected prior to this withdrawal may be used but no new information would be collected after the time the withdrawal is received.

WHOM SHOULD I CALL IF I HAVE QUESTIONS OR PROBLEMS?

If you have any questions about your child's participation in this research study or if you feel that your child has experienced a research-related injury or reaction to the study drug, contact:

Investigator Name: «FirstName» «MiddleName» «LastName» «Suffix»

Daytime telephone number(s): «Phone»; you can reach the study nurse during business hours at [Study Nurse Phone]

24-hour contact number(s): «Phone2» (7 days a week)

If you have any questions or concerns about your child's rights as a research subject or want to discuss a problem, get information or offer input, you may contact Copernicus Group Independent Review Board (IRB) at 1-888-303-2224 (toll free). An IRB is a group of scientific and non-scientific individuals who perform the initial and ongoing ethical review of the research study with the study subject's rights and welfare in mind. Copernicus Group IRB has reviewed and approved the research study described in this Parental Permission Form. If you have study-related comments, complaints or concerns, you should first contact the study doctor. Please call the IRB if you want to talk to someone other than the study doctor or have difficulty reaching the study doctor. For further information regarding the clinical trials process and your child's role as a research subject, you may visit the Copernicus Group IRB website at www.cgirb.com.

PARENTAL STATEMENT OF PERMISSION

Open-Label, Multiple-Dose, Efficacy, Safety, and Tolerability Study of Eteplirsen in Subjects with Duchenne Muscular Dystrophy who Participated in Study 4658-us-201

I have read this Parental Permission Form and have had a chance to ask questions about this research study, which have been answered to my satisfaction. If I have more questions about participation in this study or a research-related injury, I may contact the study doctor. By signing this Parental Permission Form, I certify that all health information I have given regarding my child is true and correct to the best of my knowledge.

I have been given a copy of the Nationwide Children's Hospital Notice of Privacy Practices. I have been told that my right to my child's patient information that is created or collected in the course of this research can be temporarily suspended for as long as the research is in progress. I also have been told that my right to access will be reinstated upon completion of this research.

I give permission for my child to take part in this study. I will be given a copy of this Parental Permission Form with all the signatures for my own records.

_____
PRINTED NAME OF SUBJECT

_____
PRINTED NAME OF PARENT/LEGAL GUARDIAN

_____ _____
SIGNATURE OF PARENT/LEGAL GUARDIAN | DATE & TIME AM/PM

_____
PRINTED NAME OF SECOND PARENT/ LEGAL GUARDIAN

_____ _____
SIGNATURE OF SECOND PARENT/ LEGAL GUARDIAN | DATE & TIME AM/PM

Permission of the second parent not obtained because (select all that apply):

_____ Other parent is deceased.
_____ Other parent is unknown.
_____ Other parent is not reasonably available.
_____ Only one parent has legal responsibility for the care and custody of subject.

I certify that I have explained the research, its purposes, and the procedures to the patient or subject's parent(s) or legal guardian(s) and have answered all of their questions, before requesting their signature. I believe that he/she understands the information described in this Parental Permission Form and freely consents to have his/her child participate in the study.

PRINTED NAME OF PERSON OBTAINING CONSENT

SIGNATURE OF PERSON OBTAINING CONSENT

DATE & TIME AM/PM

PRINTED NAME OF INVESTIGATOR

SIGNATURE OF INVESTIGATOR

DATE & TIME AM/PM

PRINTED NAME OF WITNESS

SIGNATURE OF WITNESS
FOR VA SITES ONLY

DATE & TIME AM/PM

HIPAA AUTHORIZATION

The United States government has issued a privacy rule to protect the privacy rights of patients. This rule was issued under a law called the Health Insurance Portability and Accountability Act of 1996 (HIPAA). The Privacy Rule is designed to protect the confidentiality of your child's personal health information. The document you are reading, called an "Authorization," describes your child's rights and explains how your child's health information will be used and disclosed (shared).

HOW WILL MY CHILD'S STUDY INFORMATION BE KEPT PRIVATE?

Information collected for this study will be kept confidential to the extent provided by law. Health information means the information in your child's medical or other healthcare records, which also may include information that can identify your child. Information that can identify your child is called "protected health information" or PHI. By agreeing to allow your child to be in this study, you are giving permission and authorizing «FirstName» «MiddleName» «LastName» «Suffix» and his study staff to collect, use, and disclose your child's PHI for this research study. The results of the study may be published in scientific journals or presented at medical meetings. In the event of any publication regarding this study, your child's identity will not be revealed.

Your child's PHI collected or created under this research study will be used/disclosed as needed during and even after the end of the study. We will need to use it for research purposes and will release it to other people involved in the research or your child's routine healthcare. We will also generate new healthcare information about your child during the course of the study. This information will come from the tests and procedures and any interviews of your child conducted in connection with the study. The records of this study will be kept for an indefinite period of time, and by signing this Authorization you are authorizing the use of your child's PHI in accordance with this Authorization during that entire period. If you decide to withdraw your child from the study, or if your child is removed from the study by the study doctor or Sponsor (AVI BioPharma, Inc.) you may withdraw, on your child's behalf, your permission for others to use and disclose your child's PHI, except that PHI that has already been collected may still be used by and disclosed to the individuals and entities as described in this Authorization. If you withdraw your permission for the use and disclosure of your child's PHI, your child can no longer take part in this research study.

If you decide to withdraw your permission for the use and disclosure of your child's PHI, this must be in writing. Please send a letter to your study doctor:

«FirstName» «MiddleName» «LastName» «Suffix»
«Company»
«Address» «SuiteDept»
«City» «State» «Zip»

Your child's PHI that may be used or disclosed:
Your child's PHI that may be used and disclosed for this study includes: review of your child's past, current or future health records, procedures such as physical examinations, blood or urine tests or other tests, your child's response to any study drug your child receives, your child's study visits, phone calls, study tests and procedures and any other study related health information, may be collected, used and disclosed to others. Your child's PHI also includes:

- ✓ Name and Date of Birth
- ✓ All medical records, including genetic testing and study tests and procedures
- ✓ Contact information (Addresses, Email addresses, Telephone/fax numbers)
- ✓ Family medical history
- ✓ Photos and videos

Efforts will be made to keep your child's study-related information confidential; however confidentiality cannot be guaranteed. Once disclosed, the PHI may no longer be protected by federal law and may be re-disclosed by those receiving the information.

People or Companies authorized to use, disclose, and receive your child's health information and PHI collected or created by this research study for purposes related to this study:

- «FirstName» «MiddleName» «LastName» «Suffix» and study staff
- The Copernicus Group Independent Review Board (the committee that reviews all human subject research)
- Nationwide Children's Hospital internal auditors
- The Office for Human Research Protections (OHRP) (the federal government office that oversees human patient research)
- AVI BioPharma, Inc., the study sponsor and its designees, representatives and agents (including third parties who are providing services to the sponsor related to the study)
- An independent committee of physicians and experts that will review safety information from this study periodically
- The Food and Drug Administration (FDA) and other governmental health agencies, both within and outside the United States
- Your child's insurance company (if charges are billed to insurance).

Your child's health information and/or PHI also may be used and shared for treatment, payment and healthcare operations. Medical information from this study will become part of your child's hospital medical record.

In order to provide your child with routine care, other people at the hospital may need to review the health information we put into your record. This would include such people as your regular doctors and nurses and the hospital's billing department.

Your personal health information may be further shared by the groups above. If shared by them, the information will no longer be covered by the Privacy Rule. However, these groups are committed to keeping your personal health information confidential.

May I have access to my child's health information and PHI?

You will always have access to your child's medical record. A summary may be made available to you at the completion of the study. You will not have access to your child's research file because all information contained in the research file is either information obtained directly from your child, or was gathered from your child's medical records, to which you do have access. In some cases your child's research file may contain some information not known to you or the researchers that if known, would affect the scientific importance of the study.

AUTHORIZATION

I authorize the release of my child's medical records and personal health information related to this study to the Sponsor, including its affiliates, successors and assigns, both in the U.S. and other countries, and/or any third party working with Sponsor to conduct the study or to analyze or review study-related documents or data, the Copernicus Group Independent Review Board, the FDA and other regulatory agencies, and to the other individuals and entities as described above. I have been told that I will receive a signed and dated copy of this Authorization for my records.

_____

Printed First and Last Name of Subject

_____

Printed First and Last Name of Parent/Legal Guardian

_____ _____

Signature of Parent/Legal Guardian Date

_____

Printed First and Last Name of Parent/Legal Guardian

_____ _____

Signature of Parent/Legal Guardian Date

_____

Printed Name of Person Obtaining Authorization

_____ _____

Signature of Person Obtaining Authorization Date

_____

Printed Name of Investigator

_____ _____

Signature of Investigator Date

APPROVED: May 03, 2012
COPERNICUS GROUP IRB

copernicus group independent review board

Approved: «Approved»

PARENTAL PERMISSION FORM AND HIPAA AUTHORIZATION

STUDY TITLE: Open-Label, Multiple-Dose, Efficacy, Safety, and Tolerability Study of Eteplirsen in Subjects with Duchenne Muscular Dystrophy who Participated in Study 4658-us-201

PROTOCOL NUMBER: 4658-us-202

PROTOCOL AMENDMENT: 01 Dated 20 April 2012

STUDY SPONSOR: AVI BioPharma, Inc.

STUDY DOCTOR:

RESEARCH SITE ADDRESS(ES):

DAYTIME TELEPHONE NUMBER(S):

24-HOUR TELEPHONE NUMBER(S): (*24 hours a day, 7 days a week*)

SUBJECT'S NAME: _____

INTRODUCTION

The purpose of this Parental Permission Form is to give you the information you will need to help you decide whether or not to allow your child to be in this study. Please read this form carefully. You should ask questions about what your child will be asked to do, the risks, the benefits, your child's rights as a subject, or anything else about the research or this form that is not clear to you. When all of your questions have been answered to your satisfaction, you can decide if you want your child to take part in this study or not. If you agree to allow your child to take part in this study and you sign this permission form, you will be given a copy for your records. If your child is 10 years of age or older, he will sign a separate informed consent form called an "Assent." You and your child will be given a copy for your records.

You are being asked to allow your child to be in this research study because your child has a muscle disorder called Duchenne muscular dystrophy (DMD). DMD is caused by a mutation (a change) in the gene that makes dystrophin protein. Dystrophin is important for protecting your muscles from stress and activity. Because of the mutation in your child's gene, your child's body is not able to make enough working dystrophin to protect your child's muscles

This study is investigating a study drug called eteplirsen, which is designed to skip a certain fragment of the dystrophin gene called exon 51. In people with changes, called deletions, in certain parts of the dystrophin gene (including exons 45-50, 47-50, 48-50, 50, 52, or 52-63), skipping exon 51 is believed to allow the body to produce a shortened, but still working, form of dystrophin protein. This may result in improved muscle function for people with DMD.

In this study, all subjects will receive eteplirsen once a week and take part in study-specific tests for 80 weeks.

Participation in this study is voluntary. Please learn enough about this research study, its risks and benefits, to decide whether you should agree to allow your child to take part. The study team will explain the study to you, and give you a chance to ask questions about anything you do not understand. This process is called "informed consent." It is up to you to choose if you want your child to be in this study. You may refuse to allow your child to be in this study or your child may quit this study at any time, and standard medical care will still be available here or at a doctor of your choice without a penalty or loss of benefits to your child. If your child is between 10 and 13 years of age and agrees to take part in the study, he will be asked to sign an Assent Form. You will be given a signed and dated copy of this Parental Permission Form and the Assent Form.

Note: A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you or your child. At most, the Web site will include a summary of the results. You can search this Web site at any time.

WHY ARE WE DOING THIS RESEARCH STUDY?

This study will examine the effects of continued treatment with eteplirsen in children with DMD who have successfully completed the 28-week eteplirsen study, Study 4658-us-201. To better understand how eteplirsen works over a long period of time, the sponsor will use data from both studies (4658-us-201 and 4658-us-202) to compare how your child does in this study to how he was doing before he started eteplirsen in Study 4658-us-201.

AVI BioPharma, Inc. is developing eteplirsen for the treatment of DMD by intravenous (IV, meaning through a vein) administration. Eteplirsen is designed to skip exon 51, which is believed to allow for the production of a shortened, but still working, form of the dystrophin protein and therefore result in improved muscle function for people with DMD.

Eteplirsen is considered experimental. Experimental means that this study drug is currently being tested. Eteplirsen has not been approved by the Food and Drug Administration (FDA) for use in the United States.

WHERE WILL THE STUDY BE DONE AND HOW MANY PARTICIPANTS WILL TAKE PART?

This study will be open to the 12 subjects who took part in the previous eteplirsen study, Study 4658-us-201. This study will be done at Nationwide Children's Hospital (the central site) and at up to 12 sites closer to the homes of participating subjects (satellite sites).
To take part in the study your child will need to meet all of the inclusion criteria and none of the exclusion criteria that your child's study doctor will discuss with you. The study doctor will also speak with you about some medicines that should not be taken by your child while participating in this study.

To be enrolled in the study, your child must:

1. Have completed 28 weeks of treatment in Study 4658-us-201
2. Have a parent(s) or legal guardian(s) who is able to understand and comply with all of the study requirements
3. Have a parent(s) or legal guardian(s) who is willing to provide written informed consent for the subject to take part in the study
4. Be willing, if at least age 10, to provide informed assent (agreement)

If your child has a prior or ongoing medical condition that the study doctor believes might affect his safety, or make it difficult for him to attend all of the required study visits and receive all of the study drug, or might affect the results of this study, your child will not be able to take part in this study.

WHAT WILL HAPPEN DURING THE STUDY AND HOW LONG WILL IT LAST?

During this study, your child will receive IV infusions of either 30 or 50 mg/kg eteplirsen once a week for 80 weeks (about a year and a half). Your child will receive the same dose of eteplirsen in this study that he received in Study 4658-us-201. That means if your child received the high dose (50 mg/kg) of eteplirsen in 4658-us-201, then he will receive the high dose in this study, and if he received the low dose of eteplirsen in 4658-us-201 (30 mg/kg), then he will receive the low dose in this study. Remember that the dose of eteplirsen that your child receives (high or low) was randomly assigned to him (picked by chance like tossing a coin in the air) during Study 4658-us-201. There was an even chance (50/50) that he would be assigned to the high or low dose.

This study is open-label. Open-label means that the study doctor, the study nurse, the study sponsor (AVI BioPharma, Inc.), you, your child, and everyone else who might work with your child in this study will know your child is receiving eteplirsen.

All infusions of eteplirsen and all study tests will be performed at the central site, Nationwide Children's Hospital, until a suitable satellite site closer to your child's home is identified, the personnel there are trained, and the site is approved to take part in this study. Once the satellite is approved and ready, your child will receive all of his weekly infusions of eteplirsen at that site. You and your child will be asked to sign new Parental Permission and Assent Forms when you transfer to the satellite site. However, you and your child will still need to travel to Nationwide Children's Hospital approximately once every 12 weeks so your child can complete certain study-specific tests.

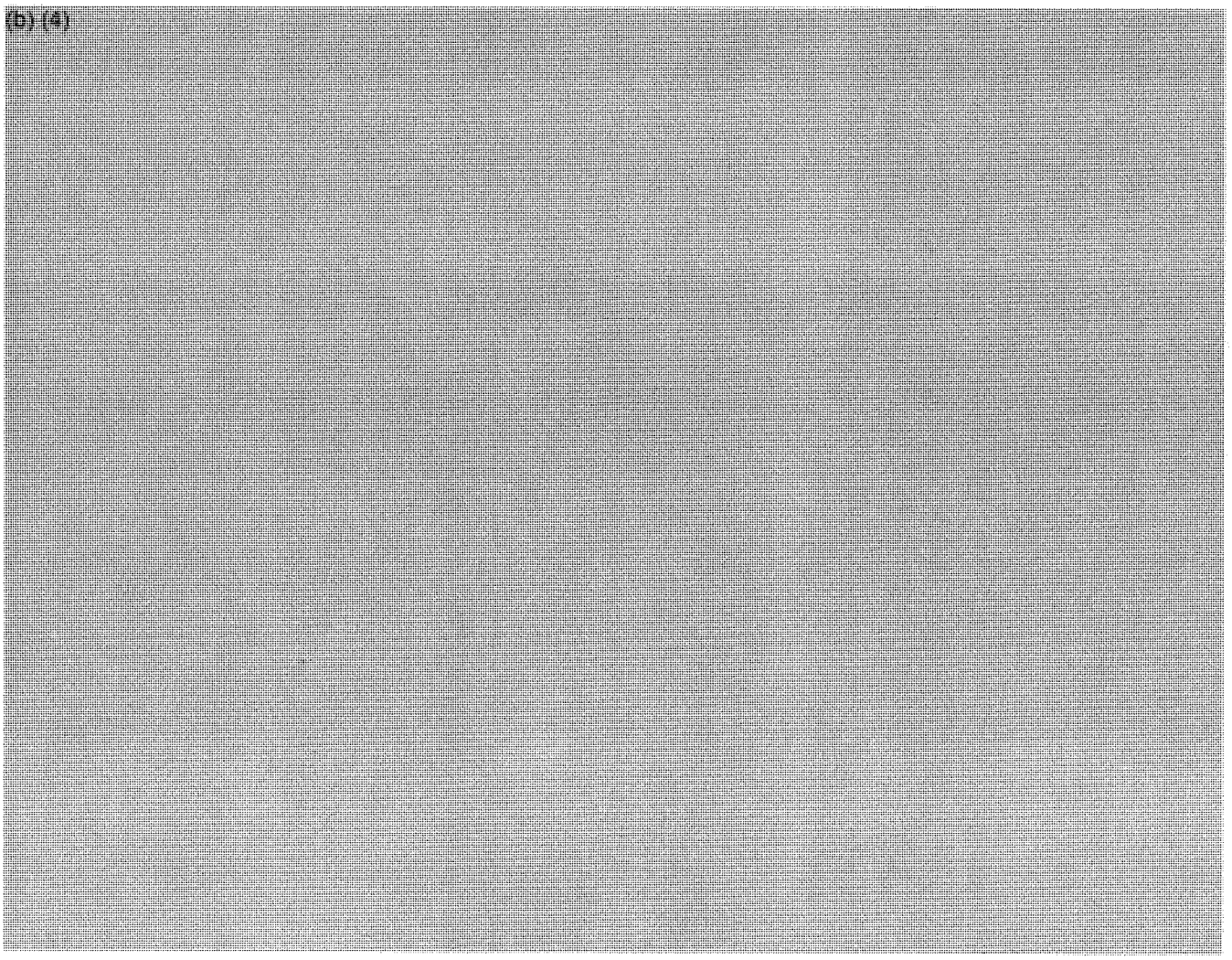
The procedures and tests that will take place at each of the weekly study visits are presented below.

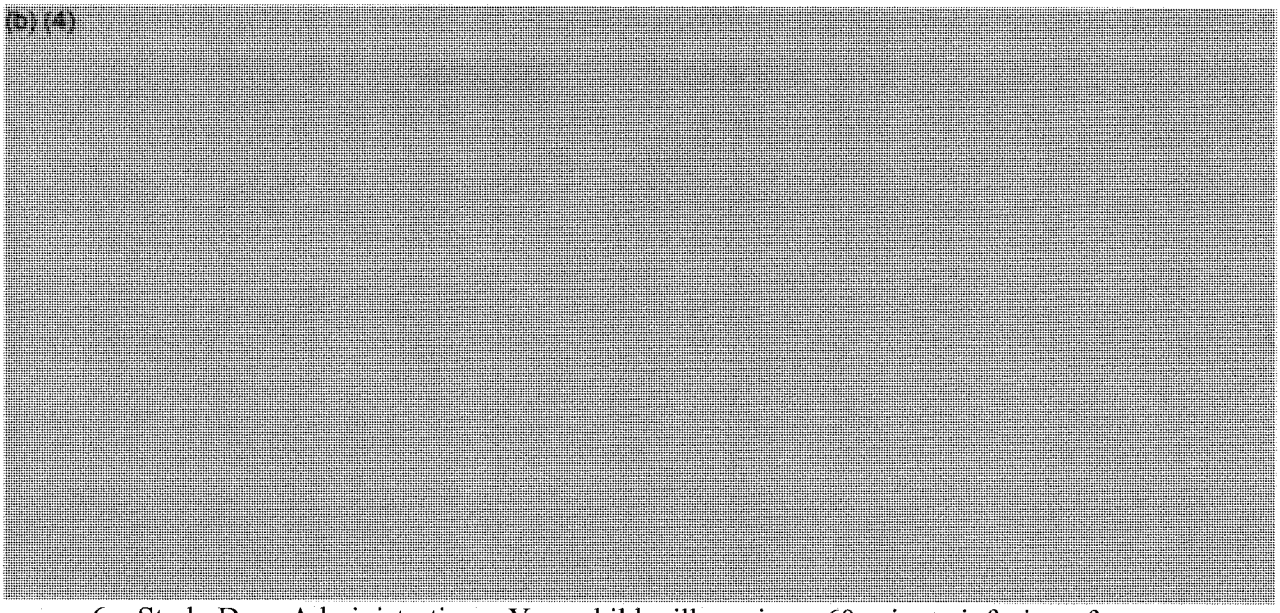
If a situation occurs that your child is unable to attend a scheduled visit and your child is at risk of missing a weekly dose, you must immediately notify the study doctor. It is very important that no more than 2 doses are missed in a 6-month period. If your child misses more than 6 doses during the 80 week study, he may be withdrawn from the study.

Screening/Baseline Period

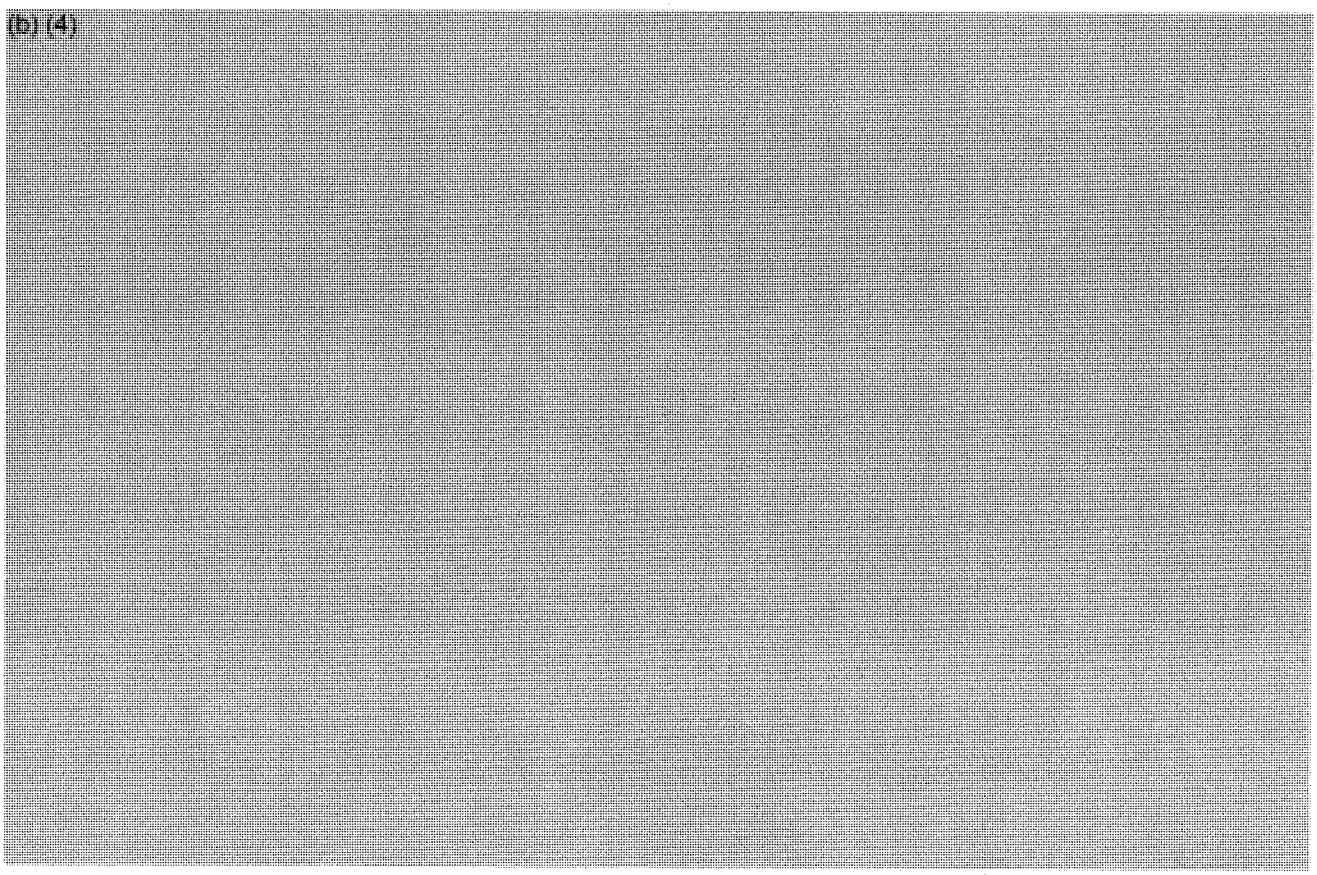
Because this is an extension study for children who successfully completed Study 4658-us-201, there will be no formal screening period for this study. Instead, the study doctor will review the details of this study with you, obtain your consent and your child's agreement (assent) to take part in this study, and make sure this study is right for your child at the last visit (Week 28) of Study 4658-us-201.

In addition to procedures and tests specific to Study 4658-us-201, the following procedures will be performed at (b) (4) of Study 4658-us-201:

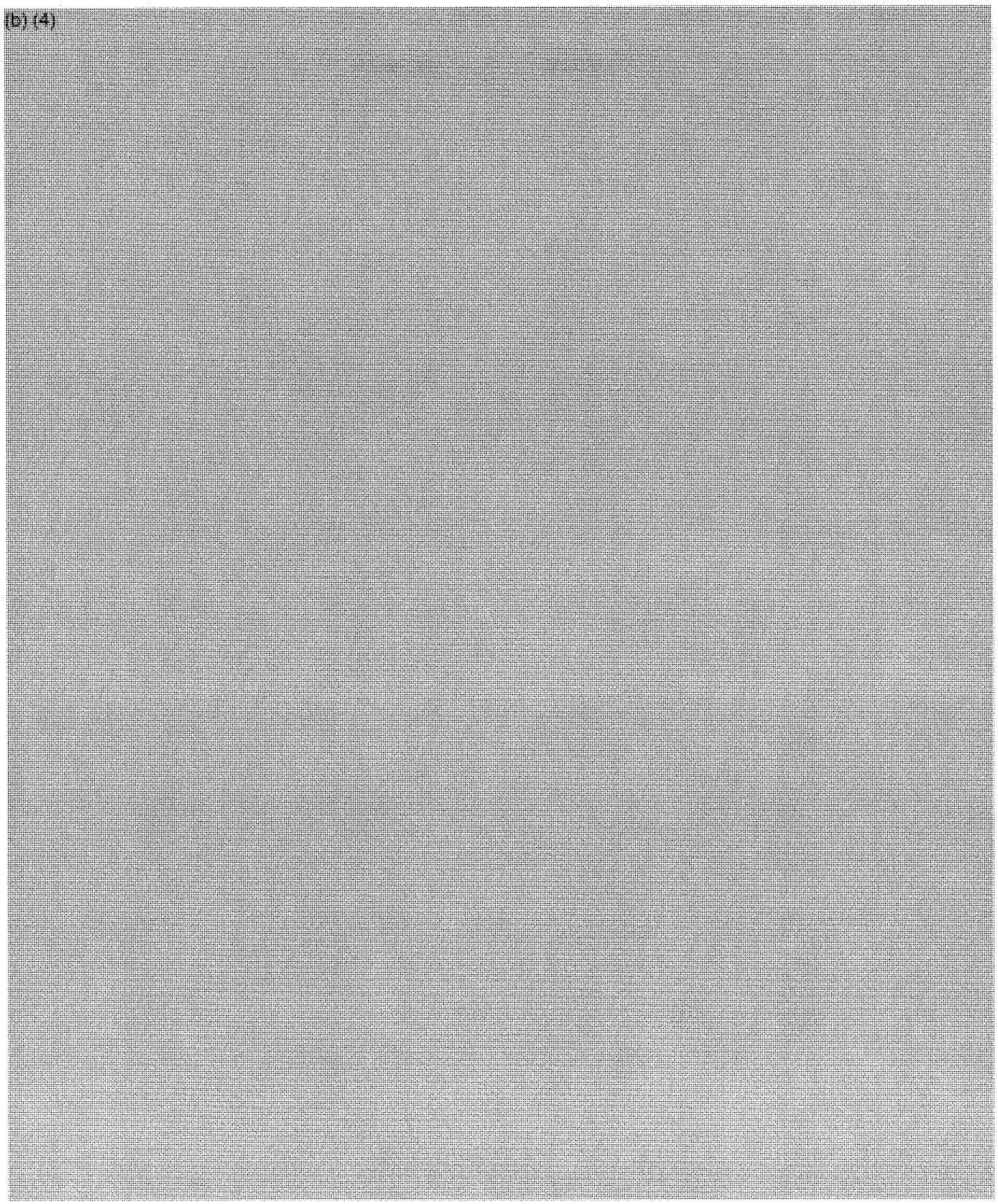


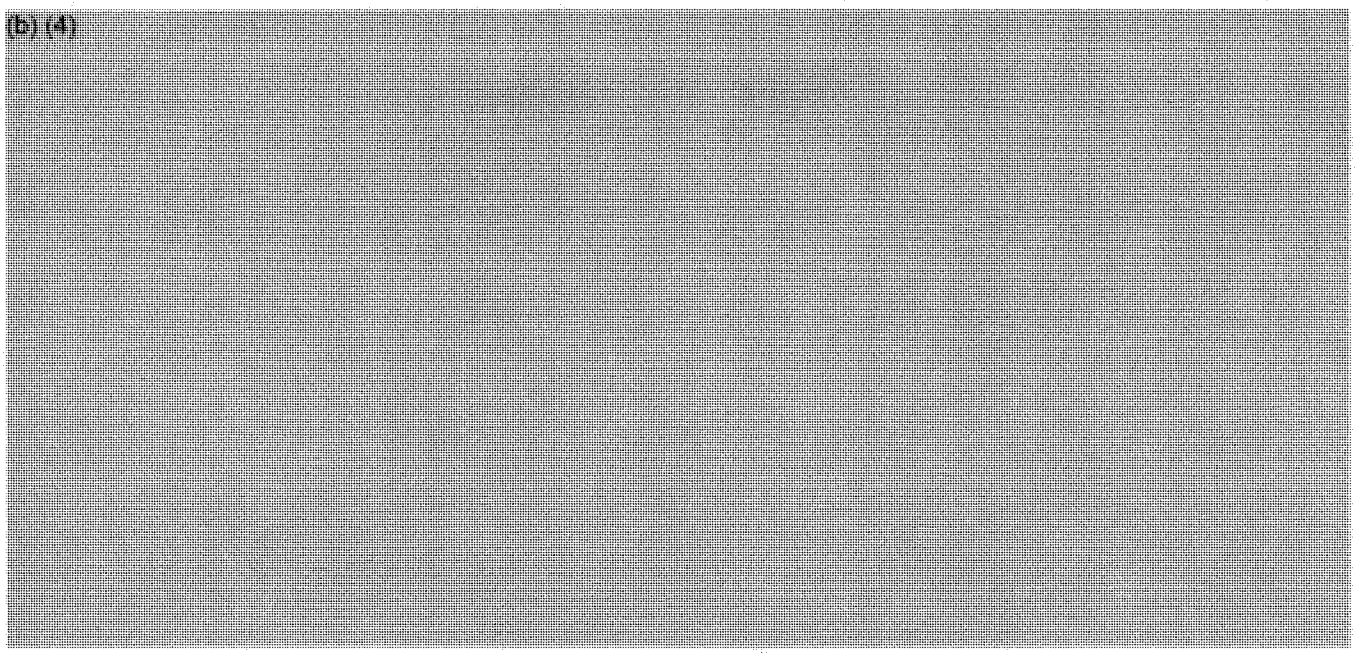


6. Study Drug Administration – Your child will receive a 60-minute infusion of eteplirsen. A topical anesthetic (numbing) cream (e.g., lidocaine 2.5%, prilocaine 2.5%, or LMX4) may be applied to your child's skin prior to the infusion, if needed. After the infusion ends, your child will be observed for at least 1 hour to make sure that he is doing okay. As long as he is okay and all other tests and procedures have been completed, the study doctor will then let you and your child go home.



(b) (4)





WHAT ARE THE RISKS OF BEING IN THIS STUDY?

Two clinical studies have been done with eteplirsen in children with DMD in the United Kingdom and study 4658-us-201 has been completed in the US. The first study was a placebo-controlled study of several doses of eteplirsen in 7 boys with DMD aged 10 to 17 years. Doses ranged from 0.09 mg to 0.9 mg/kg and were given by a single injection into a small muscle on the foot (this is called an intramuscular or IM injection). Several of the boys showed an increase in dystrophin protein in the muscle of the foot that had been injected with eteplirsen.

The second study was an open-label study of eteplirsen administered into the vein (this is called an intravenous or IV injection or infusion). This study enrolled 19 boys with DMD, who were 5 to 15 years of age, and patients received up to 12 weekly infusions of eteplirsen. Doses ranged from 0.5 to 20.0 mg/kg. In this second study, levels of dystrophin protein were increased at the end of the study in 7 out of the 17 patients that had muscle biopsies taken before starting eteplirsen and at the end of the study.

In both studies, eteplirsen was well-tolerated over the doses given (up to 20.0 mg/kg). Overall, the problems that occurred (called adverse events) were generally mild or moderate in intensity. The common side effects of eteplirsen were:

- headache (42%)
- upper respiratory tract infection (42%)
- back pain (37%)
- rhinitis (inflammation of the mucous membrane of the nose that may cause nasal congestion and itching, and sneezing) (37%)
- falling (26%)
- myalgia (pain in the muscle) (21%)

One subject, who had a pre-existing heart condition due to DMD, had a decrease in his heart function without symptoms while taking 4.0 mg/kg of eteplirsen. This problem was considered possibly related to the eteplirsen and the subject was withdrawn from study drug administration.

The final safety information for study 4658-us-201 is not yet available, but early findings from the results showed that no adverse events were experienced by any subject that were related to the study medication and no subject stopped early in the study. In addition, there were no changes in vital signs, physical examination findings, ECGs, safety laboratory results or several blood markers that test for kidney problems that were related to the study medication.

It is important that you give the study staff your child's complete medical history. Not giving them this information or not completely following the directions of the study could harm your child.

All study drugs may cause some side effects or other reactions. There is no way to predict if your child will experience any of these side effects. Side effects that are not yet known may also occur.

Blood Draw/IV Risk
Drawing blood and starting IVs by placing a needle in a vein may cause pain, lightheadedness and fainting, bleeding, bruising, or swelling at the puncture site. Infection is a rare possibility. Topical anesthetic or numbing cream may be used on the skin to decrease the discomfort, if needed. Although there are no known side effects from the numbing cream, skin irritation or an allergic reaction is possible.

Muscle Biopsy Risk
The common side effects of the muscle biopsies may include discomfort, a scar, infection, bruise, numbness near the biopsy site, and delayed wound healing.

Sedation Risk
Risks from local anesthetic may include pain with infection, and (very rarely) allergic reactions. Minor discomfort during surgery is common, but the likelihood of other risks is extremely small (less than 1%). After use of conscious sedation, your child may get a headache or feel nauseous or dizzy. It is possible that your child will have a reaction to the sedative medication used.

If any of the symptoms listed above are severe, your child must get medical help right away. If you are worried about anything while in this study, please call the study doctor or study nurse at the telephone number on page 1.

Unforeseen Risks
There may be other risks of being in this research study that are not known at this time.

ARE THERE BENEFITS TO TAKING PART IN THIS STUDY?

The potential benefits of eteplirsen in subjects with DMD are unknown. Your child may have some benefits from taking part in this study, but even if your child does not benefit from being in this study, we might learn something that could help others.

WHAT WILL HAPPEN IF NEW INFORMATION IS FOUND OUT ABOUT THE DRUG OR TREATMENT?

If new information is found out during this study that might change your mind about your child taking part or might affect your child's health, your study doctor will discuss it with you and your child as soon as possible.

WHAT OTHER TREATMENTS OR OPTIONS ARE THERE?

Your child's participation in this study is voluntary. It is not necessary to be in this study to get care for this condition. If you decide not to allow your child to be in this study, the study doctor will talk to you and your child about other possible treatments or refer you to your child's regular doctor for care.

WILL THERE BE ANY COSTS TO ME?

It will not cost you or your child anything to be in this study and you or your child will not be paid to be in this study. Travel expenses including airfare (with supporting receipts) for up to two adults and one child for all required visits to Nationwide Children's Hospital will be covered.

CONFIDENTIALITY OF STUDY INFORMATION

The data collected as part of this study will be kept confidential, but may be shared with the individuals and entities and for the purposes described in this Parental Permission Form and the attached HIPAA Authorization form. In all study-related records, a number and initials will identify your child, unless otherwise described in this Parental Permission Form or the attached HIPAA Authorization form. Data collected and recorded on study forms are the property of the sponsor If information about this study is published, your child's identity will remain confidential. However, the U.S. Food and Drug Administration (FDA), Copernicus Group Independent Review Board (IRB), and the study sponsor, AVI BioPharma, Inc. and its representatives may be granted direct access to your child's original medical records for verification of clinical trial procedures or data. By signing this Parental Permission Form, you are authorizing such access. A court of law could order medical records shown to other people, but that is unlikely.

WHAT HAPPENS IF BEING IN THIS STUDY CAUSES INJURIES?

If your child is hurt by the study drug, eteplirsen, or the procedures that are part of the study, you should seek medical treatment for your child's injuries and tell the study doctor as soon as possible at the number on the first page of this form. If it is an emergency, call 911 or go to the nearest emergency department.

If your child is injured as a direct result of the proper administration of the study drug, eteplirsen, or the proper performance of procedures that are required solely for the study, and your child has followed the directions of the study team, (b) (4)

(b) (4)

If the care is provided at Nationwide Children's Hospital, (b) (4)
(b) (4)
(b) (4) This does not mean that you give up any of your or your child's legal rights to seek compensation for your child's injuries.

LEGAL RIGHTS

The above section does not restrict your right to seek legal assistance. By signing this Parental Permission Form you will not waive any of your child's legal rights as a research subject.

WHAT HAPPENS IF MY CHILD DOES NOT FINISH THIS STUDY?

It is your choice to allow your child to be in this study or to stop at any time. If you decide to stop your child from being in this study, it is okay, but you must call the study doctor or the study nurse. If you stop your child from being in the study, there will not be a penalty or loss of benefits to which your child is otherwise entitled.

If at any time the study doctor believes participating in this study is not the best choice of care for your child, the study may be stopped and other care prescribed. If the study instructions are not followed, your child's participation in the study may also be stopped. If unexpected medical problems come up, the study doctor or the sponsor, AVI BioPharma, Inc., may decide to stop your child's participation in the study.

If your child's participation in the study is stopped before completing all of the study activities, your child will be asked to visit the study doctor, «FirstName» «MiddleName» «LastName» «Suffix» (unless you have withdrawn consent), or you may be asked to return to Nationwide Children's Hospital so that the following information can be collected and assessments can be completed:

(b) (4)

In addition, subjects who have not already had their (b) (4) [redacted]

If your child withdraws from the study because he is not feeling well, your child will be encouraged to have follow-up assessments when he feels better.

OTHER IMPORTANT INFORMATION

It is considered a conflict of interest where the parents of a potential subject hold stock of AVI BioPharma, Inc. By signing this consent form, you agree that neither you nor any of your family have stock of or an interest with the potential for financial gain in the sponsor, AVI BioPharma, Inc.

It is important that healthcare providers know about all medicines your child is taking. This includes the study drug being tested in this research study. Because of this, we plan to tell your child's primary care doctor that he is in this research study. This is done so extra care can be taken in prescribing other medicines and looking at any unexplained symptoms that may occur. Your child cannot take part in this study if you do not want us to tell your child's primary care doctor.

The study doctor is being paid by AVI BioPharma, Inc. for the time and knowledge needed to do this study.

Being in more than one research study at the same time may cause injury. Please tell the study doctor if your child is in any other research study so a decision can be made about being in more than one study at the same time.

Keep in mind that your permission for your child's participation in the study will remain valid until such time as you choose to withdraw it. This withdrawal should be in writing and sent to the following address:

«FirstName» «MiddleName» «LastName» «Suffix»
«Company»
«Address» «SuiteDept»
«City» «State» «Zip»

Any information collected prior to this withdrawal may be used but no new information would be collected after the time the withdrawal is received.

WHOM SHOULD I CALL IF I HAVE QUESTIONS OR PROBLEMS?

If you have any questions about your child's participation in this research study or if you feel that your child has experienced a research-related injury or reaction to the study drug, contact:

Investigator Name: **«FirstName» «MiddleName» «LastName» «Suffix»**

Daytime telephone number(s): «Phone»; you can reach the study nurse during business hours at [Study Nurse Phone]

24-hour contact number(s): «Phone2» (7 days a week)

If you have any questions or concerns about your child's rights as a research subject or want to discuss a problem, get information or offer input, you may contact Copernicus Group Independent Review Board (IRB) at 1-888-303-2224 (toll free). An IRB is a group of scientific and non-scientific individuals who perform the initial and ongoing ethical review of the research study with the study subject's rights and welfare in mind. Copernicus Group IRB has reviewed and approved the research study described in this Parental Permission Form. If you have study-related comments, complaints or concerns, you should first contact the study doctor. Please call the IRB if you want to talk to someone other than the study doctor or have difficulty reaching the study doctor. For further information regarding the clinical trials process and your child's role as a research subject, you may visit the Copernicus Group IRB website at www.cgirb.com.

PARENTAL STATEMENT OF PERMISSION

Open-Label, Multiple-Dose, Efficacy, Safety, and Tolerability Study of Eteplirsen in Subjects with Duchenne Muscular Dystrophy who Participated in Study 4658-us-201

I have read this Parental Permission Form and have had a chance to ask questions about this research study, which have been answered to my satisfaction. If I have more questions about participation in this study or a research-related injury, I may contact the study doctor. By signing this Parental Permission Form, I certify that all health information I have given regarding my child is true and correct to the best of my knowledge.

I have been given a copy of the Nationwide Children's Hospital Notice of Privacy Practices. I have been told that my right to my child's patient information that is created or collected in the course of this research can be temporarily suspended for as long as the research is in progress. I also have been told that my right to access will be reinstated upon completion of this research.

I give permission for my child to take part in this study. I will be given a copy of this Parental Permission Form with all the signatures for my own records.

_____
PRINTED NAME OF SUBJECT

_____
PRINTED NAME OF PARENT/LEGAL GUARDIAN

_____ _____
SIGNATURE OF PARENT/LEGAL GUARDIAN | DATE & TIME AM/PM

_____
PRINTED NAME OF SECOND PARENT/ LEGAL GUARDIAN

_____ _____
SIGNATURE OF SECOND PARENT/ LEGAL GUARDIAN | DATE & TIME AM/PM

Permission of the second parent not obtained because (select all that apply):

_____ Other parent is deceased.
_____ Other parent is unknown.
_____ Other parent is not reasonably available.
_____ Only one parent has legal responsibility for the care and custody of subject.

I certify that I have explained the research, its purposes, and the procedures to the patient or subject's parent(s) or legal guardian(s) and have answered all of their questions, before requesting their signature. I believe that he/she understands the information described in this Parental Permission Form and freely consents to have his/her child participate in the study.

PRINTED NAME OF PERSON
OBTAINING CONSENT

SIGNATURE OF PERSON
OBTAINING CONSENT

DATE & TIME AM/PM

PRINTED NAME OF INVESTIGATOR

SIGNATURE OF INVESTIGATOR

DATE & TIME AM/PM

PRINTED NAME OF WITNESS

SIGNATURE OF WITNESS
FOR VA SITES ONLY

DATE & TIME AM/PM

HIPAA AUTHORIZATION

The United States government has issued a privacy rule to protect the privacy rights of patients. This rule was issued under a law called the Health Insurance Portability and Accountability Act of 1996 (HIPAA). The Privacy Rule is designed to protect the confidentiality of your child's personal health information. The document you are reading, called an "Authorization," describes your child's rights and explains how your child's health information will be used and disclosed (shared).

HOW WILL MY CHILD'S STUDY INFORMATION BE KEPT PRIVATE?

Information collected for this study will be kept confidential to the extent provided by law. Health information means the information in your child's medical or other healthcare records, which also may include information that can identify your child. Information that can identify your child is called "protected health information" or PHI. By agreeing to allow your child to be in this study, you are giving permission and authorizing «FirstName» «MiddleName» «LastName» «Suffix» and his study staff to collect, use, and disclose your child's PHI for this research study. The results of the study may be published in scientific journals or presented at medical meetings. In the event of any publication regarding this study, your child's identity will not be revealed.

Your child's PHI collected or created under this research study will be used/disclosed as needed during and even after the end of the study. We will need to use it for research purposes and will release it to other people involved in the research or your child's routine healthcare. We will also generate new healthcare information about your child during the course of the study. This information will come from the tests and procedures and any interviews of your child conducted in connection with the study. The records of this study will be kept for an indefinite period of time, and by signing this Authorization you are authorizing the use of your child's PHI in accordance with this Authorization during that entire period. If you decide to withdraw your child from the study, or if your child is removed from the study by the study doctor or Sponsor (AVI BioPharma, Inc.) you may withdraw, on your child's behalf, your permission for others to use and disclose your child's PHI, except that PHI that has already been collected may still be used by and disclosed to the individuals and entities as described in this Authorization. If you withdraw your permission for the use and disclosure of your child's PHI, your child can no longer take part in this research study.

If you decide to withdraw your permission for the use and disclosure of your child's PHI, this must be in writing. Please send a letter to your study doctor:

«FirstName» «MiddleName» «LastName» «Suffix»
«Company»
«Address» «SuiteDept»
«City» «State» «Zip»

Your child's PHI that may be used or disclosed:
Your child's PHI that may be used and disclosed for this study includes: review of your child's past, current or future health records, procedures such as physical examinations, blood or urine tests or other tests, your child's response to any study drug your child receives, your child's study visits, phone calls, study tests and procedures and any other study related health information, may be collected, used and disclosed to others. Your child's PHI also includes:

- ✓ Name and Date of Birth
- ✓ All medical records, including genetic testing and study tests and procedures
- ✓ Contact information (Addresses, Email addresses, Telephone/fax numbers)
- ✓ Family medical history
- ✓ Photos and videos

Efforts will be made to keep your child's study-related information confidential; however confidentiality cannot be guaranteed. Once disclosed, the PHI may no longer be protected by federal law and may be re-disclosed by those receiving the information.

People or Companies authorized to use, disclose, and receive your child's health information and PHI collected or created by this research study for purposes related to this study:

- «FirstName» «MiddleName» «LastName» «Suffix» and study staff
- The Copernicus Group Independent Review Board (the committee that reviews all human subject research)
- Nationwide Children's Hospital internal auditors
- The Office for Human Research Protections (OHRP) (the federal government office that oversees human patient research)
- AVI BioPharma, Inc, the study sponsor and its designees, representatives and agents (including third parties who are providing services to the sponsor related to the study)
- An independent committee of physicians and experts that will review safety information from this study periodically
- The Food and Drug Administration (FDA) and other governmental health agencies, both within and outside the United States
- Your child's insurance company (if charges are billed to insurance).

Your child's health information and/or PHI also may be used and shared for treatment, payment and healthcare operations. Medical information from this study will become part of your child's hospital medical record.

In order to provide your child with routine care, other people at the hospital may need to review the health information we put into your record. This would include such people as your regular doctors and nurses and the hospital's billing department.

Your personal health information may be further shared by the groups above. If shared by them, the information will no longer be covered by the Privacy Rule. However, these groups are committed to keeping your personal health information confidential.

May I have access to my child's health information and PHI?

You will always have access to your child's medical record. A summary may be made available to you at the completion of the study. You will not have access to your child's research file because all information contained in the research file is either information obtained directly from your child, or was gathered from your child's medical records, to which you do have access. In some cases your child's research file may contain some information not known to you or the researchers that if known, would affect the scientific importance of the study.

AUTHORIZATION

I authorize the release of my child's medical records and personal health information related to this study to the Sponsor, including its affiliates, successors and assigns, both in the U.S. and other countries, and/or any third party working with Sponsor to conduct the study or to analyze or review study-related documents or data, the Copernicus Group Independent Review Board, the FDA and other regulatory agencies, and to the other individuals and entities as described above. I have been told that I will receive a signed and dated copy of this Authorization for my records.

_____
Printed First and Last Name of Subject

_____
Printed First and Last Name of Parent/Legal Guardian

_____ _____
Signature of Parent/Legal Guardian Date

_____
Printed First and Last Name of Parent/Legal Guardian

_____ _____
Signature of Parent/Legal Guardian Date

_____
Printed Name of Person Obtaining Authorization

_____ _____
Signature of Person Obtaining Authorization Date

_____
Printed Name of Investigator

_____ _____
Signature of Investigator Date

APPROVED: Mar 14, 2012
COPERNICUS GROUP IRB

copernicus group independent review board

Approved: «Approved»

PARENTAL PERMISSION FORM AND HIPAA AUTHORIZATION

STUDY TITLE: Open-Label, Multiple-Dose, Efficacy, Safety, and Tolerability Study of Eteplirsen in Subjects with Duchenne Muscular Dystrophy who Participated in Study 4658-US-201

PROTOCOL NUMBER: 4658-us-202

STUDY SPONSOR: AVI BioPharma, Inc.

STUDY DOCTOR:

RESEARCH SITE ADDRESS(ES):

DAYTIME TELEPHONE NUMBER(S):

24-HOUR TELEPHONE NUMBER(S): *(24 hours a day, 7 days a week)*

SUBJECT'S NAME: _____

INTRODUCTION

The purpose of this Parental Permission Form is to give you the information you will need to help you decide whether or not to allow your child to be in this study. Please read this form carefully. You should ask questions about what your child will be asked to do, the risks, the benefits, your child's rights as a subject, or anything else about the research or this form that is not clear to you. When all of your questions have been answered to your satisfaction, you can decide if you want your child to take part in this study or not. If you agree to allow your child to take part in this study and you sign this permission form, you will be given a copy for your records. If your child is 10 years of age or older, he will sign a separate informed consent form called an "Assent." You and your child will be given a copy for your records.

You are being asked to allow your child to be in this research study because your child has a muscle disorder called Duchenne muscular dystrophy (DMD). DMD is caused by a mutation (a change) in the gene that makes dystrophin protein. Dystrophin is important for protecting your muscles from stress and activity. Because of the mutation in your child's gene, your child's body is not able to make enough working dystrophin to protect your child's muscles.

This study is investigating a study drug called eteplirsen, which is designed to skip a certain fragment of the dystrophin gene called exon 51. In people with changes, called deletions, in certain parts of the dystrophin gene (including exons 45-50, 47-50, 48-50, 49-50, 50, 52, 52-63), skipping exon 51 is believed to allow the body to produce a shortened, but still working, form of dystrophin protein.

In this study, all subjects will receive eteplirsen once a week and take part in study-specific tests for 80 weeks.

Participation in this study is voluntary. Please learn enough about this research study, its risks and benefits, to decide whether you should agree to allow your child to take part. The study team will explain the study to you, and give you a chance to ask questions about anything you do not understand. This process is called "informed consent." It is up to you to choose if you want your child to be in this study. You may refuse to allow your child to be in this study or your child may quit this study at any time, and standard medical care will still be available here or at a doctor of your choice without a penalty or loss of benefits to your child. If your child is between 10 and 13 years of age and agrees to take part in the study, he will be asked to sign an Assent Form. You will be given a signed and dated copy of this Parental Permission Form and the Assent Form.

Note: A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you or your child. At most, the Web site will include a summary of the results. You can search this Web site at any time.

WHY ARE WE DOING THIS RESEARCH STUDY?

This study will examine the effects of continued treatment with eteplirsen in children with DMD who have successfully completed the 28-week eteplirsen study, Study 4658-US-201. To better understand how eteplirsen works over a long period of time, the sponsor will use data from both studies (4658-US-201 and 4658-US-202) to compare how your child does in this study to how he was doing before he started eteplirsen in Study 4658-US-201.

AVI BioPharma, Inc. is developing eteplirsen for the treatment of DMD by intravenous (IV, meaning through a vein) administration. Eteplirsen is designed to skip exon 51, which is believed to allow for the production of a shortened, but still working, form of the dystrophin protein and therefore result in improved muscle function for people with DMD.

Eteplirsen is considered experimental. Experimental means that this study drug is currently being tested. Eteplirsen has not been approved by the Food and Drug Administration (FDA) for use in the United States.

WHERE WILL THE STUDY BE DONE AND HOW MANY PARTICIPANTS WILL TAKE PART?

This study will be open to the 12 boys who took part in the previous eteplirsen study, Study 4658-US-201. This study will be done at Nationwide Children's Hospital (the central site) and at up to 12 sites closer to the homes of participating subjects (satellite sites).

To take part in the study your child will need to meet all of the inclusion criteria and none of the exclusion criteria that your child's study doctor will discuss with you. The study doctor will also speak with you about some medicines that should not be taken by your child while participating in this study.

To be enrolled in the study, your child must:

1. Have completed 28 weeks of treatment in Study 4658-US-201
2. Have a parent(s) or legal guardian(s) who is able to understand and comply with all of the study requirements
3. Have a parent(s) or legal guardian(s) who is willing to provide written informed consent for the subject to take part in the study
4. Be willing, if at least age 10, to provide informed assent (agreement)

If your child has a prior or ongoing medical condition that the study doctor believes might affect his safety, or make it difficult for him to attend all of the required study visits and receive all of the study drug, or might affect the results of this study, your child will not be able to take part in this study.

WHAT WILL HAPPEN DURING THE STUDY AND HOW LONG WILL IT LAST?

During this study, your child will receive IV infusions of either 30 or 50 mg/kg eteplirsen once a week for up to 80 weeks (about a year and a half). Your child will receive the same dose of eteplirsen in this study that he received in Study 4658-US-201. That means if your child received the high dose (50 mg/kg) of eteplirsen in 4658-US-201, then he will receive the high dose in this study, and if he received the low dose of eteplirsen in 4658-US-201 (30 mg/kg), then he will receive the low dose in this study. Remember that the dose of eteplirsen that your child receives (high or low) was randomly assigned to him (picked by chance like tossing a coin in the air) during Study 4658-US-201. There was an even chance (50/50) that he would be assigned to the high or low dose.

This study is open-label. Open-label means that the study doctor, the study nurse, the study sponsor (AVI BioPharma, Inc.), you, your child, and everyone else who might work with your child in this study will know your child is receiving eteplirsen.

All infusions of eteplirsen and all study tests will be performed at the central site, Nationwide Children's Hospital, until a suitable satellite site closer to your child's home is identified, the personnel there are trained, and the site is approved to take part in this study. Once the satellite is approved and ready, your child will receive all of his weekly infusions of eteplirsen at that site. You and your child will be asked to sign new Parental Permission and Assent Forms when you transfer to the satellite site. However, you and your child will still need to travel to Nationwide Children's Hospital approximately once every 12 weeks so your child can complete certain study-specific tests.

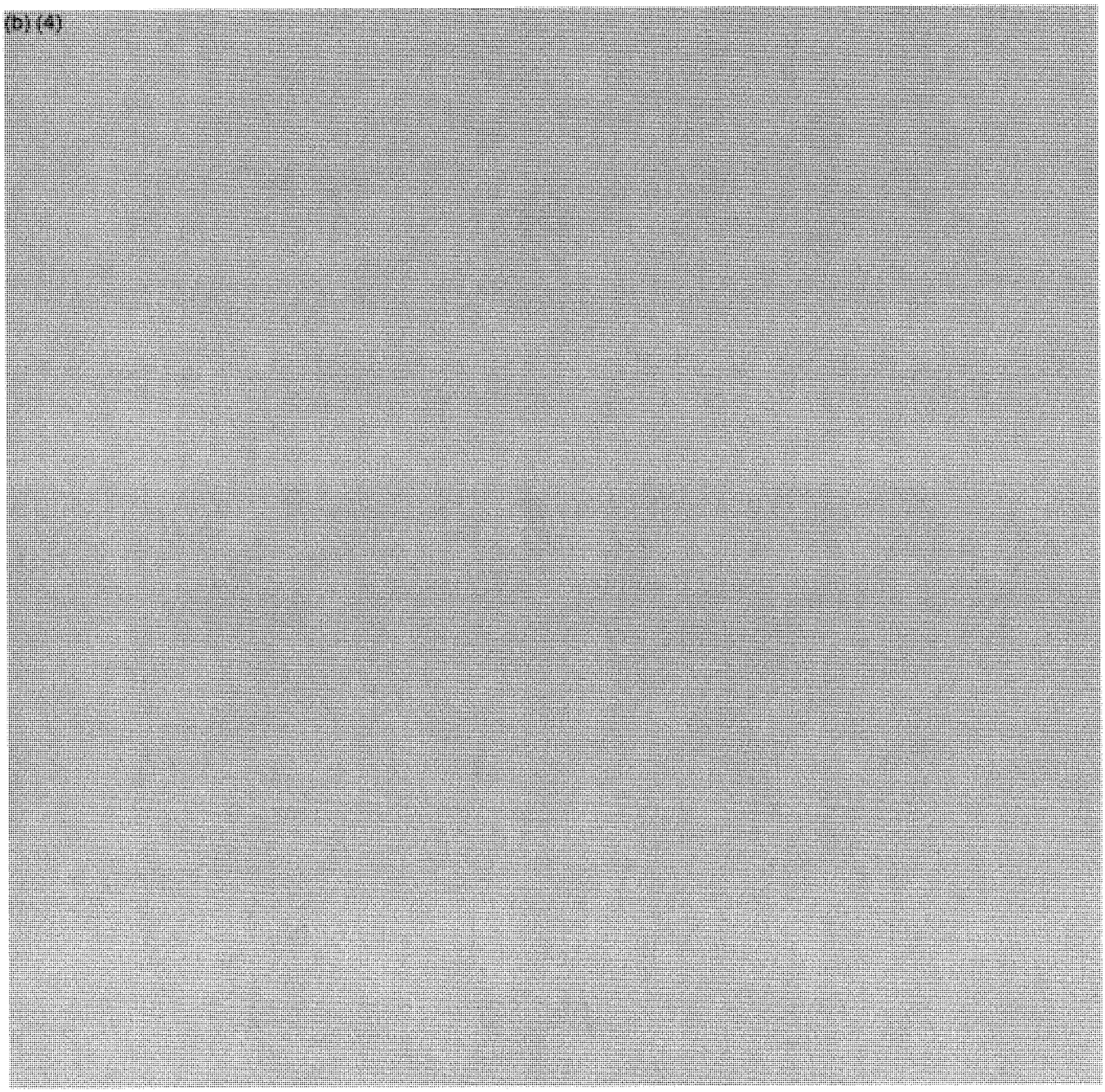
The procedures and tests that will take place at each of the weekly study visits are presented below.

Screening/Baseline Period

Because this is an extension study for children who successfully completed Study 4658-US-201, there will be no formal screening period for this study. Instead, the study doctor will review the details of this study with you, obtain your consent and your child's agreement (assent) to take part in this study, and make sure this study is right for your child at the last visit (Week 28) of Study 4658-US-201.

In addition to procedures and tests specific to Study 4658-US-201, the following procedures will be performed at (b) (4) of Study 4658-US-201:

(b) (4)

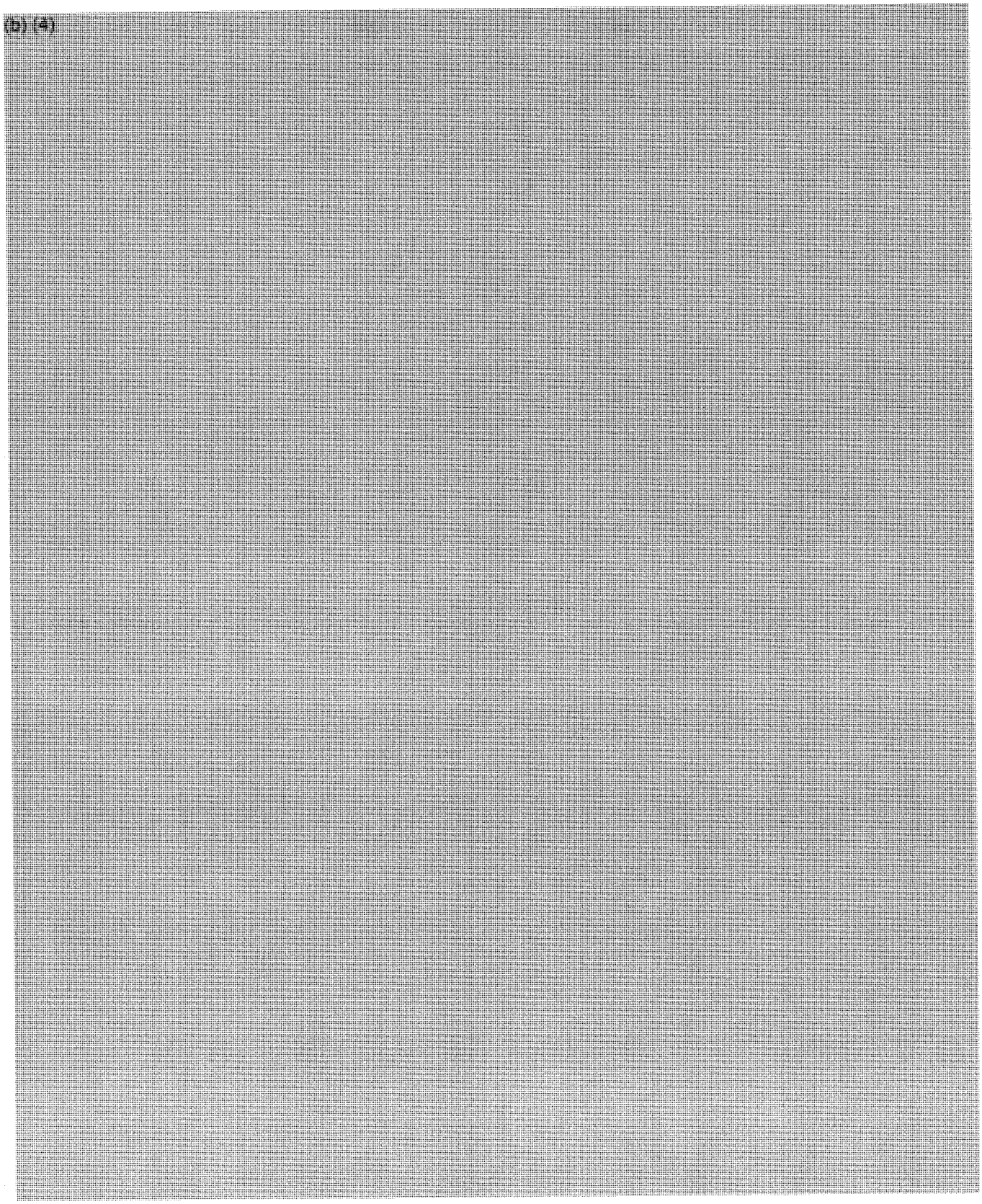


(b) (4)

6. Study Drug Administration – Your child will receive a 60-minute infusion of eteplirsen. A topical anesthetic (numbing) cream (e.g., lidocaine 2.5%, prilocaine 2.5%) may be applied to your child's skin prior to the infusion, if needed. After the infusion ends, your child will be observed for at least 1 hour to make sure that he is doing okay. As long as he is okay and all other tests and procedures have been completed, the study doctor will then let you and your child go home.

(b) (4)

(b) (4)



(b) (4)

WHAT ARE THE RISKS OF BEING IN THIS STUDY?

Two clinical studies have been done with eteplirsen in children with DMD in the United Kingdom. The first study was a placebo-controlled study of several doses of eteplirsen in 7 boys with DMD aged 10 to 17 years. Doses ranged from 0.09 mg to 0.9 mg/kg and were given by a single injection into a small muscle on the foot (this is called an intramuscular or IM injection). Several of the boys showed an increase in dystrophin protein in the muscle of the foot that had been injected with eteplirsen.

The second study was an open-label study of eteplirsen administered into the vein (this is called an intravenous or IV injection or infusion). This study enrolled 19 boys with DMD, who were 5 to 15 years of age, and patients received up to 12 weekly infusions of eteplirsen. Doses ranged from 0.5 to 20.0 mg/kg. In this second study, levels of dystrophin protein were increased at the end of the study in 7 out of the 17 patients that had muscle biopsies taken before starting eteplirsen and at the end of the study.

In both studies, eteplirsen was well-tolerated over the doses given (up to 20.0 mg/kg). Overall, the problems that occurred (called adverse events) were generally mild or moderate in intensity. The common side effects of eteplirsen were:

- headache (42%)
- upper respiratory tract infection (42%)
- back pain (37%)
- rhinitis (inflammation of the mucous membrane of the nose that may cause nasal congestion and itching, and sneezing) (37%)
- falling (26%)
- myalgia (pain in the muscle) (21%)

One subject, who had a pre-existing heart condition due to DMD, had a decrease in his heart function without symptoms while taking 4.0 mg/kg of eteplirsen. This problem was considered possibly related to the eteplirsen and the subject was withdrawn from study drug administration.

It is important that you give the study staff your child's complete medical history. Not giving them this information or not completely following the directions of the study could harm your child.

All study drugs may cause some side effects or other reactions. There is no way to predict if your child will experience any of these side effects. Side effects that are not yet known may also occur. This includes any that may become known from study 4658-US-201.

Blood Draw/IV Risk
Drawing blood and starting IVs by placing a needle in a vein may cause pain, lightheadedness and fainting, bleeding, bruising, or swelling at the puncture site. Infection is a rare possibility. Topical anesthetic or numbing cream may be used on the skin to decrease the discomfort, if needed. Although there are no known side effects from the numbing cream, skin irritation or an allergic reaction is possible.

Muscle Biopsy Risk
The common side effects of the muscle biopsies may include discomfort, a scar, infection, bruise, numbness near the biopsy site, and delayed wound healing.

Sedation Risk
Risks from local anesthetic may include pain with infection, and (very rarely) allergic reactions. Minor discomfort during surgery is common, but the likelihood of other risks is extremely small (less than 1%). After use of conscious sedation, your child may get a headache or feel nauseous or dizzy. It is possible that your child will have a reaction to the sedative medication used.

If any of the symptoms listed above are severe, your child must get medical help right away. If you are worried about anything while in this study, please call the study doctor or study nurse at the telephone number on page 1.

Unforeseen Risks
There may be other risks of being in this research study that are not known at this time.

ARE THERE BENEFITS TO TAKING PART IN THIS STUDY?
The potential benefits of eteplirsen in subjects with DMD are unknown. Your child may have some benefits from taking part in this study, but even if your child does not benefit from being in this study, we might learn something that could help others.

WHAT WILL HAPPEN IF NEW INFORMATION IS FOUND OUT ABOUT THE DRUG OR TREATMENT?
If new information is found out during this study that might change your mind about your child taking part or might affect your child's health, your study doctor will discuss it with you and your child as soon as possible.

WHAT OTHER TREATMENTS OR OPTIONS ARE THERE?
Your child's participation in this study is voluntary. It is not necessary to be in this study to get care for this condition. If you decide not to allow your child to be in this study, the study doctor will talk to you and your child about other possible treatments or refer you to your child's regular doctor for care.

WILL THERE BE ANY COSTS TO ME?
It will not cost you or your child anything to be in this study and you or your child will not be paid to be in this study. Travel expenses including airfare (with supporting receipts) for up to two adults and one child for all required visits to Nationwide Children's Hospital will be covered.

CONFIDENTIALITY OF STUDY INFORMATION

The data collected as part of this study will be kept confidential, but may be shared with the individuals and entities and for the purposes described in this Parental Permission Form and the attached HIPAA Authorization form. In all study-related records, a number and initials will identify your child, unless otherwise described in this Parental Permission Form or the attached HIPAA Authorization form. Data collected and recorded on study forms are the property of the sponsor If information about this study is published, your child's identity will remain confidential. However, the U.S. Food and Drug Administration (FDA), Copernicus Group Independent Review Board (IRB), and the study sponsor, AVI BioPharma, Inc. and its representatives may be granted direct access to your child's original medical records for verification of clinical trial procedures or data. By signing this Parental Permission Form, you are authorizing such access. A court of law could order medical records shown to other people, but that is unlikely.

WHAT HAPPENS IF BEING IN THIS STUDY CAUSES INJURIES?

If your child is hurt by the study drug, eteplirsen, or the procedures that are part of the study, you should seek medical treatment for your child's injuries and tell the study doctor as soon as possible at the number on the first page of this form. If it is an emergency, call 911 or go to the nearest emergency department.

If your child is injured as a direct result of the proper administration of the study drug, eteplirsen, or the proper performance of procedures that are required solely for the study, and your child has followed the directions of the study team, (b) (4)

(b) (4)

If the care is provided at Nationwide Children's Hospital, (b) (4)

(b) (4)

(b) (4) This does not mean that you give up any of your or your child's legal rights to seek compensation for your child's injuries.

LEGAL RIGHTS

The above section does not restrict your right to seek legal assistance. By signing this Parental Permission Form you will not waive any of your child's legal rights as a research subject.

WHAT HAPPENS IF MY CHILD DOES NOT FINISH THIS STUDY?

It is your choice to allow your child to be in this study or to stop at any time. If you decide to stop your child from being in this study, it is okay, but you must call the study doctor or the study nurse. If you stop your child from being in the study, there will not be a penalty or loss of benefits to which your child is otherwise entitled.

If at any time the study doctor believes participating in this study is not the best choice of care for your child, the study may be stopped and other care prescribed. If the study instructions are not followed, your child's participation in the study may also be stopped. If unexpected medical problems come up, the study doctor or the sponsor, AVI BioPharma, Inc., may decide to stop your child's participation in the study.

If your child's participation in the study is stopped before completing all of the study activities, your child will be asked to visit the study doctor, «FirstName» «MiddleName» «LastName» «Suffix» (unless you have withdrawn consent), or you may be asked to return to Nationwide Children's Hospital so that the following information can be collected and assessments can be completed:

(b) (4)

In addition, subjects who have not already had their (b) (4)

If your child withdraws from the study because he is not feeling well, your child will be encouraged to have follow-up assessments when he feels better.

OTHER IMPORTANT INFORMATION

It is considered a conflict of interest where the parents of a potential subject hold stock of AVI BioPharma, Inc. By signing this consent form, you agree that neither you nor any of your family have stock of or an interest with the potential for financial gain in the sponsor, AVI BioPharma, Inc.

It is important that healthcare providers know about all medicines your child is taking. This includes the study drug being tested in this research study. Because of this, we plan to tell your child's primary care doctor that he is in this research study. This is done so extra care can be taken in prescribing other medicines and looking at any unexplained symptoms that may occur. Your child cannot take part in this study if you do not want us to tell your child's primary care doctor.

The study doctor is being paid by AVI BioPharma, Inc. for the time and knowledge needed to do this study.

Being in more than one research study at the same time may cause injury. Please tell the study doctor if your child is in any other research study so a decision can be made about being in more than one study at the same time.

Keep in mind that your permission for your child's participation in the study will remain valid until such time as you choose to withdraw it. This withdrawal should be in writing and sent to the following address:

«FirstName» «MiddleName» «LastName» «Suffix»
«Company»
«Address» «SuiteDept»
«City» «State» «Zip»

Any information collected prior to this withdrawal may be used but no new information would be collected after the time the withdrawal is received.

WHOM SHOULD I CALL IF I HAVE QUESTIONS OR PROBLEMS?

If you have any questions about your child's participation in this research study or if you feel that your child has experienced a research-related injury or reaction to the study drug, contact:

Investigator Name: **«FirstName» «MiddleName» «LastName» «Suffix»**

Daytime telephone number(s): «Phone»; you can reach the study nurse during business hours at [Study Nurse Phone]

24-hour contact number(s): «Phone2» (7 days a week)

If you have any questions or concerns about your child's rights as a research subject or want to discuss a problem, get information or offer input, you may contact Copernicus Group Independent Review Board (IRB) at 1-888-303-2224 (toll free). An IRB is a group of scientific and non-scientific individuals who perform the initial and ongoing ethical review of the research study with the study subject's rights and welfare in mind. Copernicus Group IRB has reviewed and approved the research study described in this Parental Permission Form. If you have study-related comments, complaints or concerns, you should first contact the study doctor. Please call the IRB if you want to talk to someone other than the study doctor or have difficulty reaching the study doctor. For further information regarding the clinical trials process and your child's role as a research subject, you may visit the Copernicus Group IRB website at www.cgirb.com.

PARENTAL STATEMENT OF PERMISSION

Open-Label, Multiple-Dose, Efficacy, Safety, and Tolerability Study of Eteplirsen in Subjects with Duchenne Muscular Dystrophy who Participated in Study 4658-US-201

I have read this Parental Permission Form and have had a chance to ask questions about this research study, which have been answered to my satisfaction. If I have more questions about participation in this study or a research-related injury, I may contact the study doctor. By signing this Parental Permission Form, I certify that all health information I have given regarding my child is true and correct to the best of my knowledge.

I have been given a copy of the Nationwide Children's Hospital Notice of Privacy Practices. I have been told that my right to my child's patient information that is created or collected in the course of this research can be temporarily suspended for as long as the research is in progress. I also have been told that my right to access will be reinstated upon completion of this research.

I give permission for my child to take part in this study. I will be given a copy of this Parental Permission Form with all the signatures for my own records.

_____
PRINTED NAME OF SUBJECT

_____
PRINTED NAME OF PARENT/LEGAL GUARDIAN

_____ _____
SIGNATURE OF PARENT/LEGAL GUARDIAN | DATE & TIME AM/PM

_____
PRINTED NAME OF SECOND PARENT/ LEGAL GUARDIAN

_____ _____
SIGNATURE OF SECOND PARENT/ LEGAL GUARDIAN | DATE & TIME AM/PM

Permission of the second parent not obtained because (select all that apply):

_____ Other parent is deceased.
_____ Other parent is unknown.
_____ Other parent is not reasonably available.
_____ Only one parent has legal responsibility for the care and custody of subject.

I certify that I have explained the research, its purposes, and the procedures to the patient or subject's parent(s) or legal guardian(s) and have answered all of their questions, before requesting their signature. I believe that he/she understands the information described in this Parental Permission Form and freely consents to have his/her child participate in the study.

_____
PRINTED NAME OF PERSON
OBTAINING CONSENT

_____ _____
SIGNATURE OF PERSON DATE & TIME AM/PM
OBTAINING CONSENT

_____
PRINTED NAME OF INVESTIGATOR

_____ _____
SIGNATURE OF INVESTIGATOR DATE & TIME AM/PM

_____
PRINTED NAME OF WITNESS

_____ _____
SIGNATURE OF WITNESS DATE & TIME AM/PM
FOR VA SITES ONLY

HIPAA AUTHORIZATION

The United States government has issued a privacy rule to protect the privacy rights of patients. This rule was issued under a law called the Health Insurance Portability and Accountability Act of 1996 (HIPAA). The Privacy Rule is designed to protect the confidentiality of your child's personal health information. The document you are reading, called an "Authorization," describes your child's rights and explains how your child's health information will be used and disclosed (shared).

HOW WILL MY CHILD'S STUDY INFORMATION BE KEPT PRIVATE?

Information collected for this study will be kept confidential to the extent provided by law. Health information means the information in your child's medical or other healthcare records, which also may include information that can identify your child. Information that can identify your child is called "protected health information" or PHI. By agreeing to allow your child to be in this study, you are giving permission and authorizing «FirstName» «MiddleName» «LastName» «Suffix» and his study staff to collect, use, and disclose your child's PHI for this research study. The results of the study may be published in scientific journals or presented at medical meetings. In the event of any publication regarding this study, your child's identity will not be revealed.

Your child's PHI collected or created under this research study will be used/disclosed as needed during and even after the end of the study. We will need to use it for research purposes and will release it to other people involved in the research or your child's routine healthcare. We will also generate new healthcare information about your child during the course of the study. This information will come from the tests and procedures and any interviews of your child conducted in connection with the study. The records of this study will be kept for an indefinite period of time, and by signing this Authorization you are authorizing the use of your child's PHI in accordance with this Authorization during that entire period. If you decide to withdraw your child from the study, or if your child is removed from the study by the study doctor or Sponsor (AVI BioPharma, Inc.) you may withdraw, on your child's behalf, your permission for others to use and disclose your child's PHI, except that PHI that has already been collected may still be used by and disclosed to the individuals and entities as described in this Authorization. If you withdraw your permission for the use and disclosure of your child's PHI, your child can no longer take part in this research study.

If you decide to withdraw your permission for the use and disclosure of your child's PHI, this must be in writing. Please send a letter to your study doctor:

«FirstName» «MiddleName» «LastName» «Suffix»
«Company»
«Address» «SuiteDept»
«City» «State» «Zip»

Your child's PHI that may be used or disclosed:
Your child's PHI that may be used and disclosed for this study includes: review of your child's past, current or future health records, procedures such as physical examinations, blood or urine tests or other tests, your child's response to any study drug your child receives, your child's study visits, phone calls, study tests and procedures and any other study related health information, may be collected, used and disclosed to others. Your child's PHI also includes:

- ✓ Name and Date of Birth
- ✓ All medical records, including genetic testing and study tests and procedures
- ✓ Contact information (Addresses, Email addresses, Telephone/fax numbers)
- ✓ Family medical history
- ✓ Photos and videos

Efforts will be made to keep your child's study-related information confidential; however confidentiality cannot be guaranteed. Once disclosed, the PHI may no longer be protected by federal law and may be re-disclosed by those receiving the information.

People or Companies authorized to use, disclose, and receive your child's health information and PHI collected or created by this research study for purposes related to this study:

- «FirstName» «MiddleName» «LastName» «Suffix» and study staff
- The Copernicus Group Independent Review Board (the committee that reviews all human subject research)
- Nationwide Children's Hospital internal auditors
- The Office for Human Research Protections (OHRP) (the federal government office that oversees human patient research)
- AVI BioPharma, Inc, the study sponsor and its designees, representatives and agents (including third parties who are providing services to the sponsor related to the study)
- An independent committee of physicians and experts that will review safety information from this study periodically
- The Food and Drug Administration (FDA) and other governmental health agencies, both within and outside the United States
- Your child's insurance company (if charges are billed to insurance).

Your child's health information and/or PHI also may be used and shared for treatment, payment and healthcare operations. Medical information from this study will become part of your child's hospital medical record.

In order to provide your child with routine care, other people at the hospital may need to review the health information we put into your record. This would include such people as your regular doctors and nurses and the hospital's billing department.

Your personal health information may be further shared by the groups above. If shared by them, the information will no longer be covered by the Privacy Rule. However, these groups are committed to keeping your personal health information confidential.

May I have access to my child's health information and PHI?
You will always have access to your child's medical record. A summary may be made available to you at the completion of the study. You will not have access to your child's research file because all information contained in the research file is either information obtained directly from your child, or was gathered from your child's medical records, to which you do have access. In some cases your child's research file may contain some information not known to you or the researchers that if known, would affect the scientific importance of the study.

AUTHORIZATION

I authorize the release of my child's medical records and personal health information related to this study to the Sponsor, including its affiliates, successors and assigns, both in the U.S. and other countries, and/or any third party working with Sponsor to conduct the study or to analyze or review study-related documents or data, the Copernicus Group Independent Review Board, the FDA and other regulatory agencies, and to the other individuals and entities as described above. I have been told that I will receive a signed and dated copy of this Authorization for my records.

_____
Printed First and Last Name of Subject

_____
Printed First and Last Name of Parent/Legal Guardian

_____ _____
Signature of Parent/Legal Guardian Date

_____
Printed First and Last Name of Parent/Legal Guardian

_____ _____
Signature of Parent/Legal Guardian Date

_____
Printed Name of Person Obtaining Authorization

_____ _____
Signature of Person Obtaining Authorization Date

_____
Printed Name of Investigator

_____ _____
Signature of Investigator Date

NATIONWIDE CHILDREN'S
When your child needs a hospital, everything matters.™

Study Title: Open-Label, Multiple-Dose, Efficacy, Safety, and Tolerability Study of Eteplirsen in Subjects with Duchenne Muscular Dystrophy who Participated in Study 4658-us-201

Protocol No.: 4658-us-202 **Study Sponsor:** Sarepta Therapeutics, Inc.

Study Doctor: Jerry Mendell, MD **Contact Telephone Number:** 614-722-2203
(24 hours a day, 7 days a week)

ASSENT - To Participate In A Clinical Research Study
Optional Biopsy Addendum Assent

SUBJECT'S NAME: _____ **DATE OF BIRTH:** _____

1) **INTRODUCTION**
You are being asked to have an additional biopsy done as an **optional** part of this study. You do not have to agree to have the biopsy. Collection of this biopsy sample is entirely voluntary. You can still be in the main study if you do want to have the biopsy. If you agree to have the biopsy and then change your mind, you should tell your parents and the study staff. Listed below is a description of how the biopsy be collected, what it will be used for and any possible risks.

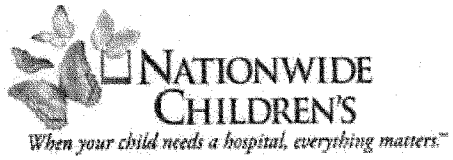
2) **WHAT WILL HAPPEN?**
[redacted]

3) **WHAT WILL THE SAMPLES BE USED FOR?**
The optional biopsy is being done to collect additional information on the long-term effect of receiving eteplirsen.

4. **WHAT ARE THE RISKS:**
Common side effects of muscle biopsies may include discomfort, a scar, infection, bruise, numbness near the biopsy site, and delayed wound healing.

The medicine used to put you to sleep may make cause a headache or upset stomach or make you feel dizzy after you wake up.

5. **WHAT GOOD THINGS CAN POSSIBLY HAPPEN DURING THIS STUDY?**
There will be no benefit to your child from being having the additional biopsy but we might learn something from your information that could help others.



6. **WILL THERE BE ANY COSTS TO ME:**
There will be no cost to you or your parents for participating in the additional biopsy sample collection portion of the study. You will not be paid to participate in this optional sample draw.

Some new products might be developed and sold because of the research done on your child's biopsy sample but you will not receive money for this.

Subject's Name _____ **Date of Birth**_____

Signing the assent form

I have read (or someone has read to me) this form. I have had a chance to ask questions before making up my mind. I want to be in this research study.

_____ _____ **AM/PM**
Signature or printed name of Participant **Date and time**

Investigator/Research Staff

I have explained the research to the participant before requesting the signature above. There are no blanks in this document. A copy of this form has been given to the participant or his/her representative.

_____ _____
Printed name of person obtaining consent Signature of person obtaining consent

_____ AM/PM
Date and time

APPROVED: Sep 09, 2014
COPERNICUS GROUP IRB

copernicus group independent review board

Approved:

CHILDREN'S ASSENT FORM
(For Subjects Ages 10 and Older)

Study Title: Open-Label, Multiple-Dose, Efficacy, Safety, and Tolerability Study of Eteplirsen in Subjects with Duchenne Muscular Dystrophy who Participated in Study 4658-US-201

Protocol Number: 4658-us-202

Protocol Amendment: 07 (Dated 14Aug2014)

Study Sponsor: Sarepta Therapeutics, Inc.

Study Doctor:

Research Site Address(es):

Daytime telephone number(s):

24-hour telephone number(s):

Subject's Name: _____

If you would like to read more information about this study, you can ask for a copy of the form that your parent/guardian will read and sign.

You are being asked to be in a research study. Studies are done to find out if there are better ways to treat people or to understand things better.

- This form will tell you about the study to help you decide whether or not you want to volunteer to take part.
- You should ask any questions you have before making up your mind. You can think about it and discuss it with your family or friends before you decide.
- It is okay to say "No" if you don't want to be in the study. If you say "Yes," you can change your mind and stop being in the study at any time without getting in trouble.
- If you decide you want to be in the study, an adult (usually a parent) will also need to give permission for you to be in this study.

What is this study about?

The purpose of this study is to learn about the long-term effects of eteplirsen in children who have Duchenne muscular dystrophy (DMD). People with DMD have a problem in the gene (a gene provides the plan for how our body is made and works) that makes dystrophin, which is important for protecting muscles from stress and activity. Because of this problem, people with DMD are not able to make enough dystrophin to protect their muscles.

Sarepta Therapeutics, Inc. has made eteplirsen (also called AVI-4658) to see if it will help people who have DMD make the dystrophin that their bodies need to protect their muscles. Eteplirsen is experimental, meaning that it is currently being tested. It has not been approved by the Food and Drug Administration (FDA) for use in the United States and no one knows yet whether or how much eteplirsen will affect the health and strength of your muscles.

This study is only for people who have completed the 28-week study of eteplirsen called Study 4658-us-201. If you and your parent(s) or legal guardian(s) decide to take part in this study and the study doctor decides that this study is right for you, you will receive eteplirsen once a week for 212 weeks (about 4 years) and take part in several tests so that we can see how eteplirsen is affecting your muscles and general health over time. You will take the same dose of eteplirsen that you took in Study 4658-us-201. For example, if you took the high dose (50 mg/kg) of eteplirsen in Study 4658-us-201 then you will take that dose in this study. If you took the low dose (30 mg/kg) of eteplirsen in 4658-us-201 then you will receive the low dose in this study. Remember that the dose of eteplirsen that you receive (high or low) was randomly assigned to you (picked by chance like tossing a coin) during Study 4658-us-201. There was an even chance (50/50) that you would be assigned to the high or low dose.

This study will be done at a medical facility close to your home (satellite site) where you will receive your weekly infusions of eteplirsen through a small tube that is placed in your vein.

After your Week 124 visit, you may have the option of having a visiting nurse come to your house to give you your weekly infusions. You will need to speak with your Study Doctor to get more information about this.

You will still need to go to Nationwide Children's Hospital about every 24 weeks (about every 6 months) for some tests.

This study is open-label, which means that the study doctor, the study nurse, the visiting nurse, the study sponsor (Sarepta Therapeutics, Inc.), you, your parents or guardians, and everyone else who might work with you in this study will know you are receiving eteplirsen.

What will I need to do (what will be done to me) if I am in this study?
First you and your parent(s) or legal guardian(s) will be told why we are doing this research study and we will explain all the procedures that are part of it. You can ask all the questions you have and take all the time you need to think about participating. If you decide to be in this research study, you will first sign this assent form, and your parent(s) or legal guardian(s) will sign the permission form.

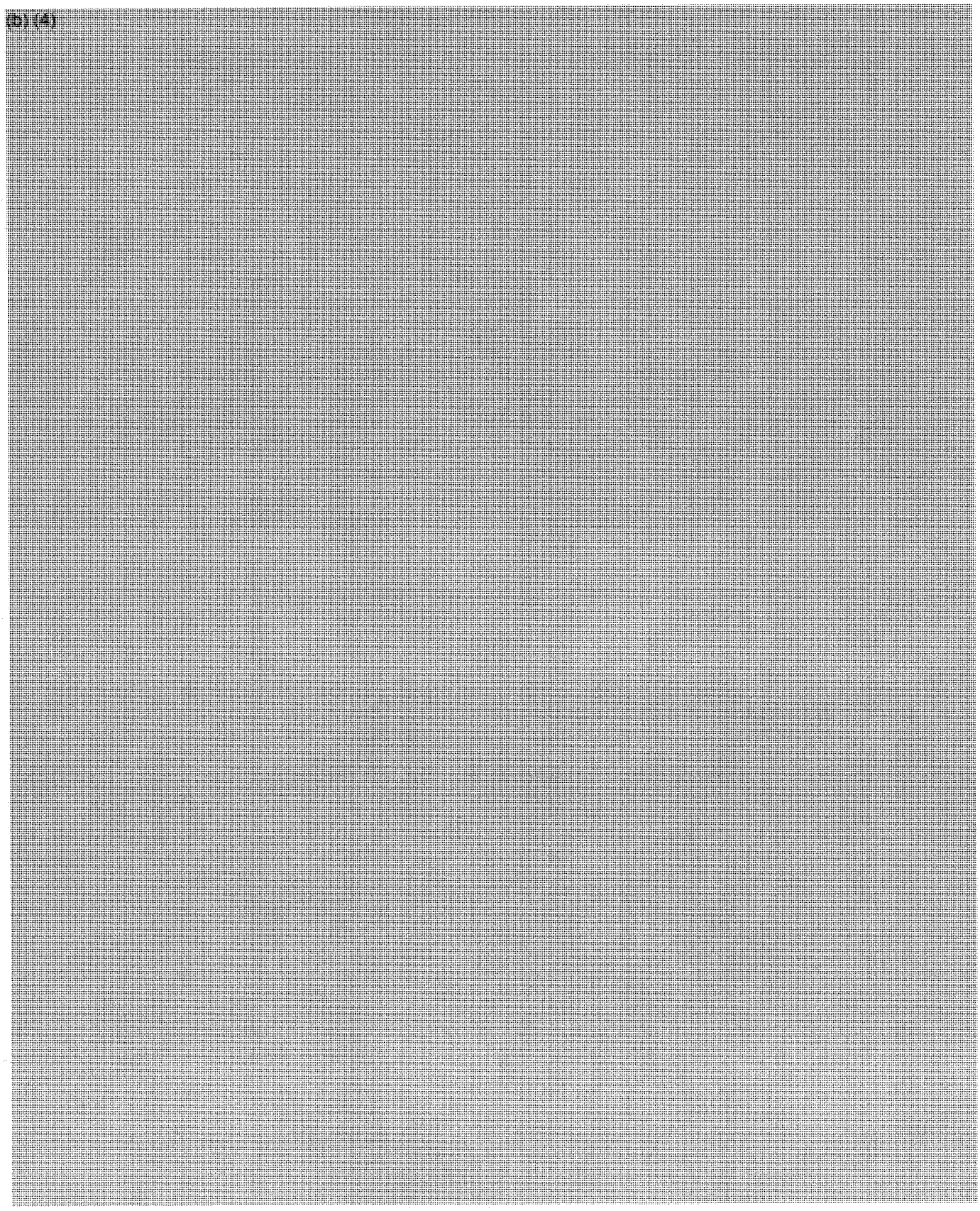
If you want to be in the study, it is important that you do everything the doctors and nurses tell you to do. You have to tell them how you are feeling and tell them about any medicines you are taking, especially if you are feeling bad while you are in this study.

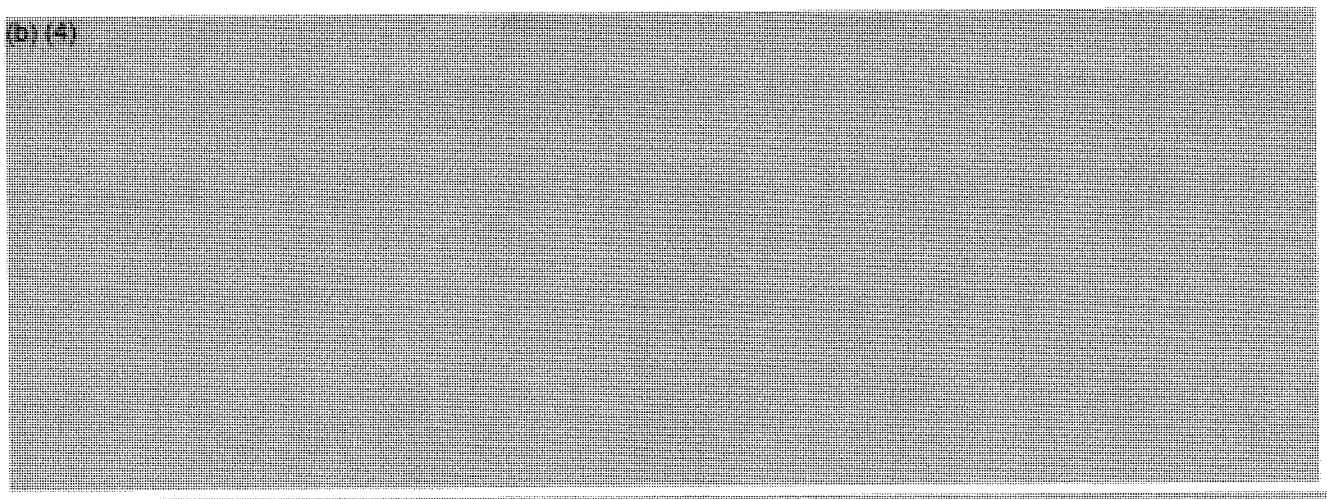
Once you and your parent(s) or legal guardian(s) have decided that you will participate in this study, then your doctor will make sure that this study is right for you. All of this will happen at your last visit for Study 4658-US-201 (b) (4), so the study doctor will mostly use information from that study to make sure that that this study is right for you. The only extra thing that he will do is ask you some more questions about how you're doing and about you're medical history.

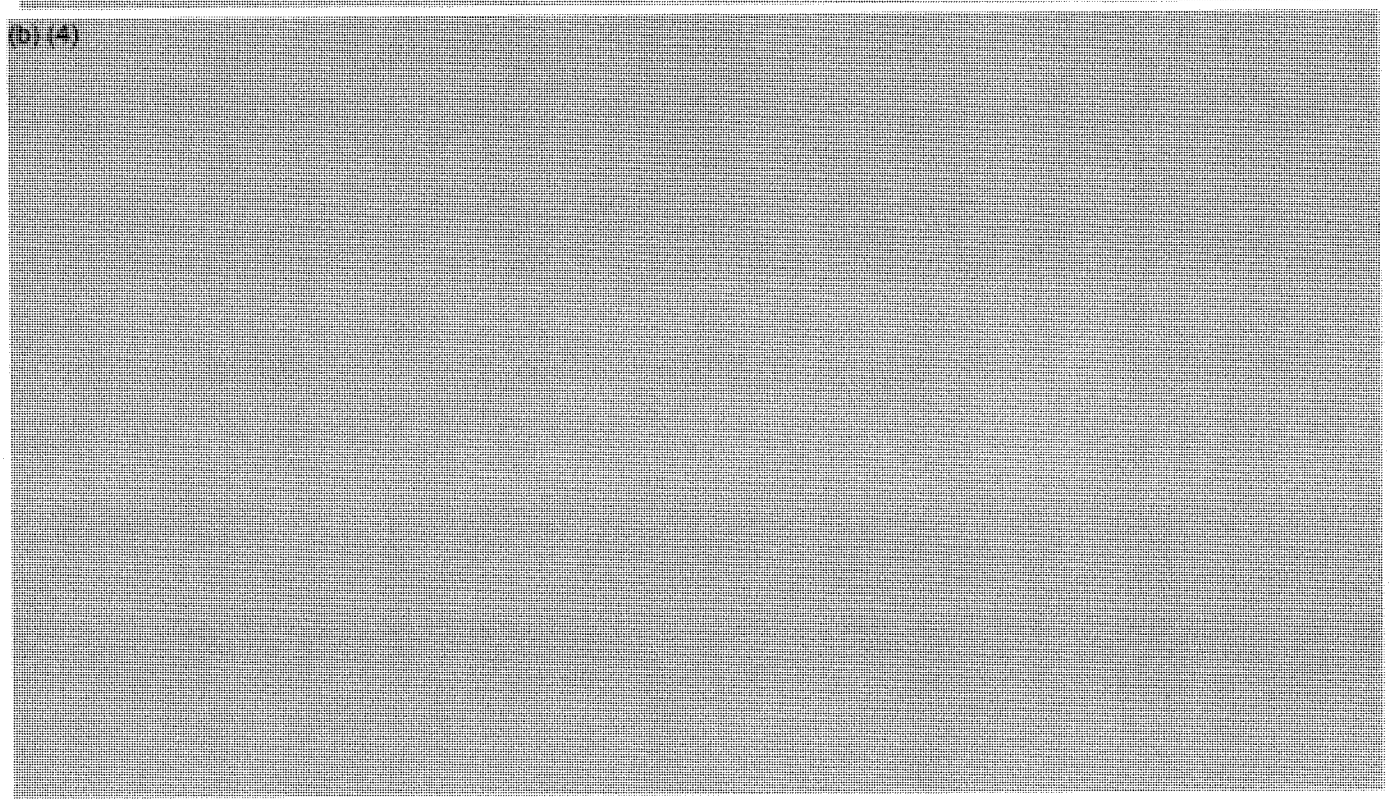
If the study doctor says that it is okay for you to take part in this study, you will need to make a total of 164 weekly visits to either Nationwide Children's Hospital or to a hospital or clinic nearer to your home, or have a visiting nurse come to your home, in order for you to receive eteplirsen and complete tests for the study. Below is a summary of what will happen at those weekly visits.

(b) (4)

(b) (4)







Can I stop being in the study?
Yes. You may stop being in the study at any time.

What bad things might happen to me if I am in the study?
Some bad things can happen with eteplirsen. These things don't always happen, but they do happen sometimes. The most common bad things (side effects) that other subjects experienced while on eteplirsen are:

a. headache
b. throat infection
c. back pain

d. congestion and itching in your nose, and sneezing
e. falling
f. muscle pain

Subjects from other studies of eteplirsen generally had these side effects at either mild (63%) or moderate (32%) level.

There may be other effects that may be harmful, which are not known at this time.

Blood Draw/IV Risk
Drawing blood and starting IVs by placing a needle in a vein may cause pain, dizziness and fainting, bleeding, bruising, or swelling at the needle site. Infection is a rare possibility.

Biopsy Risk
The common side effects of the muscle biopsies may include discomfort, a scar at the site of the biopsy, infection, bruise, or numbness.

Your disease may not get better or may become worse while you are in this study.

What good things might happen to me if I am in the study?
You may experience some good things from participating in this study. However, good things may not happen to you by being in this research study. If you do not benefit from being in this study, the study doctors might learn something that could help others.

Will I be given anything for being in this study?
You will not be paid to be in this study.

*****INTERNAL NOTE - PI Specific Comp – delete template wording as appropriate*****

What happens to the information that is learned about me in the study?
What is learned about you will only be shared with people who need to know. Most people will not know that your information belongs to you. The information we learn about you may be used for research publication and/or presentation. The people who can see your information that personally identifies you are:

- The study doctors and nurses and other people who need it to care for you.
- Researchers who run this study or other studies using Eteplirsen

Who can I talk to about the study?
If you have any questions about taking part in this research study, or if you feel that you have experienced a research-related injury or reaction to the study drug, you or your parents (or legal guardians) may contact:

Investigator Name:

Daytime telephone number(s):

24-hour contact number(s):

If you have any questions or concerns about your rights as a research subject or want to discuss a problem, get information or offer input, you or your parents (or legal guardian(s)) may contact Copernicus Group Independent Review Board (IRB) at 1-888-303-2224 (toll free). An IRB is a group of scientific and non-scientific individuals who perform the initial and ongoing ethical review of the research study with the study subject's rights and welfare in mind. Copernicus Group IRB has reviewed and approved the research study described in this Children's Assent Form. If you have study-related comments, complaints or concerns, you or your parents (or legal guardian[s]) should first contact the study doctor. Please have your parents (or legal guardian[s]) call the IRB if you want to talk to someone other than the study doctor or have difficulty reaching the study doctor. For further information regarding the clinical trials process and your role as a research subject, you or your parents (or legal guardian[s]) may visit the Copernicus Group IRB website at www.cgirb.com.

SUBJECT ASSENT

Open-Label, Multiple-Dose, Efficacy, Safety, and Tolerability Study of Eteplirsen in Subjects with Duchenne Muscular Dystrophy who Participated in Study 4658-US-201

I have read (or someone has read to me) this Assent Form. I have had a chance to ask questions before making up my mind.

I have been told what is involved if I take part in this study in a way that that I can understand. I have to tell my parent(s) or legal guardian(s) whether I do or do not want to take part in this study.

I have been told that I do not have to take part and can stop at any time. I have been told that I may refuse to take part in the study without any problems.

The tests for this study have been explained to me by my parent(s) or legal guardian(s) and the study staff.

Discomforts and risks that I may have by taking part in this study have been explained to me by my parent(s) or legal guardian(s) and the study staff.

I am free now, and in the future, to ask any questions about the study.

I want to be in this research study.

_____

Printed Name of Subject

_____ _____

Signature of Subject **Date and Time**
(For Subjects 10 Years and Older)

_____

Printed Name of Parent

_____ _____

Signature of Parent **Date and Time**
For VA Sites Only

Approved

Investigator/Research Staff

I have explained the research to the subject and have answered all of his/her questions before requesting the signature above. I believe that the subject understands the information described in this Children's Assent Form and freely consents to participate in the study. There are no blanks in this document. A copy of this form has been given to the subject or his legal representative.

Printed Name of Person Obtaining Assent Assent	**Signature of Person Obtaining**
	Date and Time **AM/PM**
Printed Name of Investigator	**Signature of Investigator**
	Date and Time **AM/PM**

APPROVED: Apr 23, 2014
COPERNICUS GROUP IRB

copernicus group independent review board

Approved:

CHILDREN'S ASSENT FORM
(For Subjects Ages 10 and Older)

Study Title: Open-Label, Multiple-Dose, Efficacy, Safety, and Tolerability Study of Eteplirsen in Subjects with Duchenne Muscular Dystrophy who Participated in Study 4658-US-201

Protocol Number: 4658-us-202

Study Sponsor: Sarepta Therapeutics, Inc.

Study Doctor:

Research Site Address(es):

Daytime telephone number(s):

24-hour telephone number(s):

Subject's Name: _____

If you would like to read more information about this study, you can ask for a copy of the form that your parent/guardian will read and sign.

You are being asked to be in a research study. Studies are done to find out if there are better ways to treat people or to understand things better.

- This form will tell you about the study to help you decide whether or not you want to volunteer to take part.
- You should ask any questions you have before making up your mind. You can think about it and discuss it with your family or friends before you decide.
- It is okay to say "No" if you don't want to be in the study. If you say "Yes," you can change your mind and stop being in the study at any time without getting in trouble.
- If you decide you want to be in the study, an adult (usually a parent) will also need to give permission for you to be in this study.

What is this study about?

The purpose of this study is to learn about the long-term effects of eteplirsen in children who have Duchenne muscular dystrophy (DMD). People with DMD have a problem in the gene (a gene provides the plan for how our body is made and works) that makes dystrophin, which is important for protecting muscles from stress and activity. Because of this problem, people with DMD are not able to make enough dystrophin to protect their muscles.

Sarepta Therapeutics, Inc. has made eteplirsen (also called AVI-4658) to see if it will help people who have DMD make the dystrophin that their bodies need to protect their muscles. Eteplirsen is experimental, meaning that it is currently being tested. It has not been approved by the Food and Drug Administration (FDA) for use in the United States and no one knows yet whether or how much eteplirsen will affect the health and strength of your muscles.

This study is only for people who have completed the 28-week study of eteplirsen called Study 4658-US-201. If you and your parent(s) or legal guardian(s) decide to take part in this study and the study doctor decides that this study is right for you, you will receive eteplirsen once a week for 164 weeks (about 3 years) and take part in several tests so that we can see how eteplirsen is affecting your muscles and general health over time. You will take the same dose of eteplirsen that you took in Study 4658-US-201. For example, if you took the high dose (50 mg/kg) of eteplirsen in Study 4658-US-201 then you will take that dose in this study. If you took the low dose (30 mg/kg) of eteplirsen in 4658-US-201 then you will receive the low dose in this study. Remember that the dose of eteplirsen that you receive (high or low) was randomly assigned to you (picked by chance like tossing a coin) during Study 4658-US-201. There was an even chance (50/50) that you would be assigned to the high or low dose.

This study will be done at a medical facility close to your home (satellite site) where you will receive your weekly infusions of eteplirsen through a small tube that is placed in your vein.

After your Week 124 visit, you may have the option of having a visiting nurse come to your house to give you your weekly infusions. You will need to speak with your Study Doctor to get more information about this.

You will still need to go to Nationwide Children's Hospital about every 24 weeks (about every 6 months) for some tests.

This study is open-label, which means that the study doctor, the study nurse, the visiting nurse, the study sponsor (Sarepta Therapeutics, Inc.), you, your parents or guardians, and everyone else who might work with you in this study will know you are receiving eteplirsen.

What will I need to do (what will be done to me) if I am in this study?

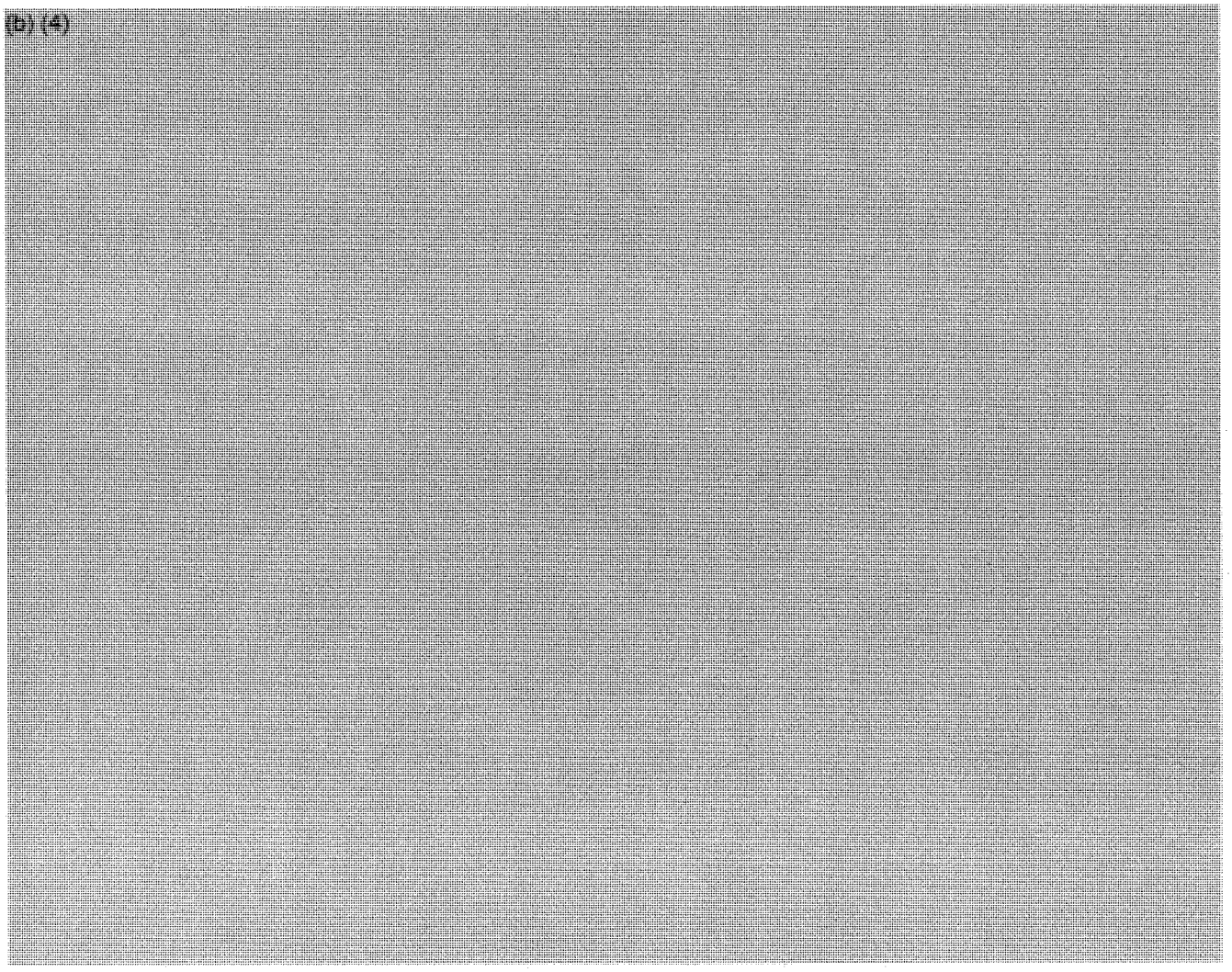
First you and your parent(s) or legal guardian(s) will be told why we are doing this research study and we will explain all the procedures that are part of it. You can ask all the questions you have and take all the time you need to think about participating. If you decide to be in this research study, you will first sign this assent form, and your parent(s) or legal guardian(s) will sign the permission form.

If you want to be in the study, it is important that you do everything the doctors and nurses tell you to do. You have to tell them how you are feeling and tell them about any medicines you are taking, especially if you are feeling bad while you are in this study.

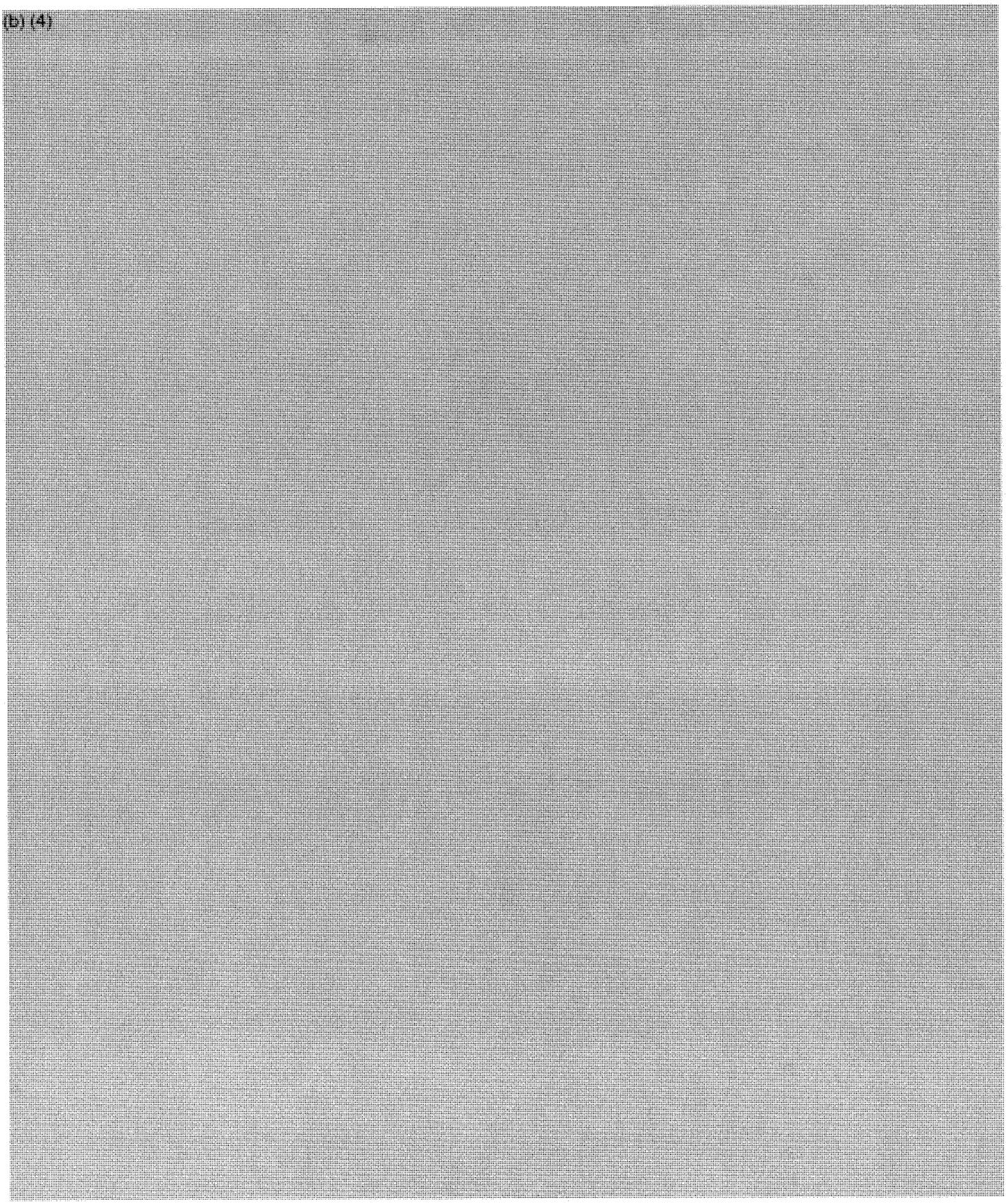
Once you and your parent(s) or legal guardian(s) have decided that you will participate in this study, then your doctor will make sure that this study is right for you. All of this will happen at your last visit for Study 4658-US-201 (b) (4) so the study doctor will mostly use information from that study to make sure that that this study is right for you. The only extra thing that he will do is ask you some more questions about how you're doing and about you're medical history.

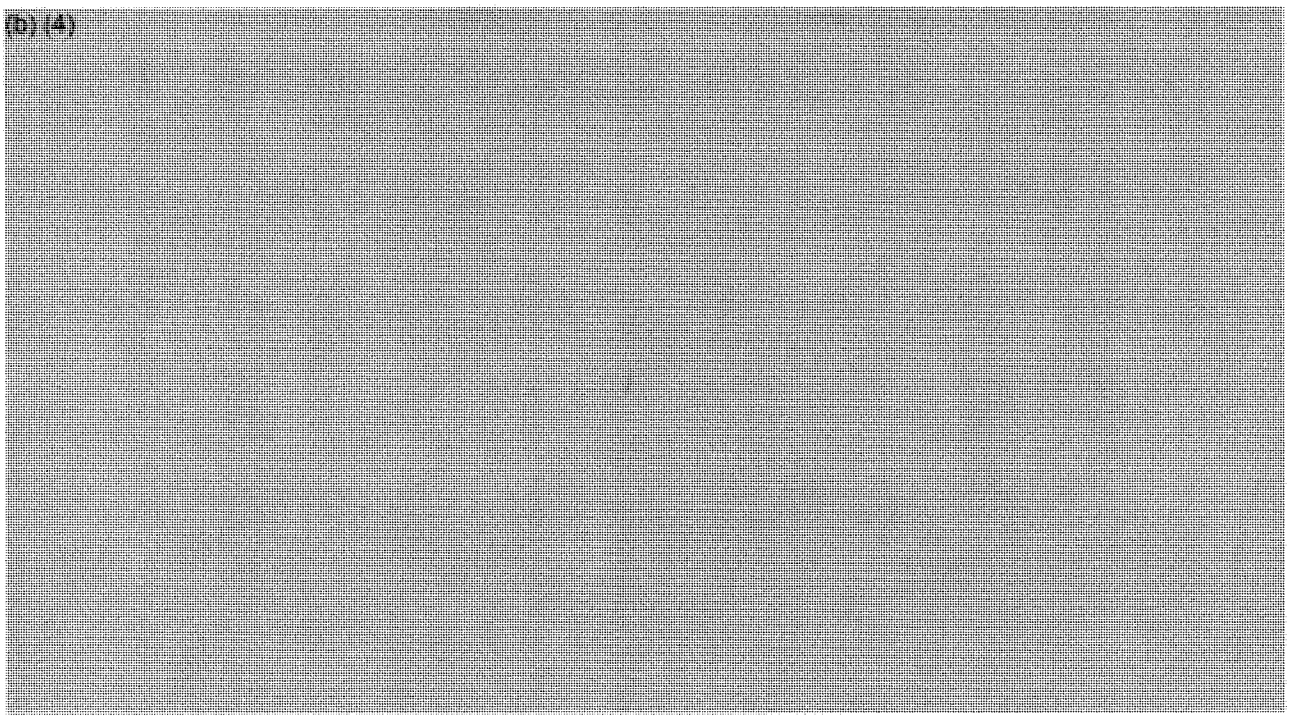
If the study doctor says that it is okay for you to take part in this study, you will need to make a total of 164 weekly visits to either Nationwide Children's Hospital or to a hospital or clinic nearer to your home, or have a visiting nurse come to your home, in order for you to receive eteplirsen and complete tests for the study. Below is a summary of what will happen at those weekly visits.

(b) (4)



(b) (4)





Can I stop being in the study?

Yes. You may stop being in the study at any time.

What bad things might happen to me if I am in the study?

Some bad things can happen with eteplirsen. These things don't always happen, but they do happen sometimes. The most common bad things (side effects) that other subjects experienced while on eteplirsen are:

a. headache
b. throat infection
c. back pain
d. congestion and itching in your nose, and sneezing
e. falling
f. muscle pain

Subjects from other studies of eteplirsen generally had these side effects at either mild (63%) or moderate (32%) level.

There may be other effects that may be harmful, which are not known at this time.

Blood Draw/IV Risk

Drawing blood and starting IVs by placing a needle in a vein may cause pain, dizziness and fainting, bleeding, bruising, or swelling at the needle site. Infection is a rare possibility.

Biopsy Risk

The common side effects of the muscle biopsies may include discomfort, a scar at the site of the biopsy, infection, bruise, or numbness.

Your disease may not get better or may become worse while you are in this study.

What good things might happen to me if I am in the study?

You may experience some good things from participating in this study. However, good things may not happen to you by being in this research study. If you do not benefit from being in this study, the study doctors might learn something that could help others.

Will I be given anything for being in this study?

You will not be paid to be in this study.

What happens to the information that is learned about me in the study?

What is learned about you will only be shared with people who need to know. Most people will not know that your information belongs to you. The information we learn about you may be used for research publication and/or presentation. The people who can see your information that personally identifies you are:

- The study doctors and nurses and other people who need it to care for you.
- Researchers who run this study or other studies using Eteplirsen

Who can I talk to about the study?

If you have any questions about taking part in this research study, or if you feel that you have experienced a research-related injury or reaction to the study drug, you or your parents (or legal guardians) may contact:

Investigator Name:

Daytime telephone number(s):

24-hour contact number(s):

If you have any questions or concerns about your rights as a research subject or want to discuss a problem, get information or offer input, you or your parents (or legal guardian(s)) may contact Copernicus Group Independent Review Board (IRB) at 1-888-303-2224 (toll free). An IRB is a group of scientific and non-scientific individuals who perform the initial and ongoing ethical review of the research study with the study subject's rights and welfare in mind. Copernicus Group IRB has reviewed and approved the research study described in this Children's Assent Form. If you have study-related comments, complaints or concerns, you or your parents (or legal guardian[s]) should first contact the study doctor. Please have your parents (or legal guardian[s]) call the IRB if you want to talk to someone other than the study doctor or have difficulty reaching the study doctor. For further information regarding the clinical trials process and your role as a research subject, you or your parents (or legal guardian[s]) may visit the Copernicus Group IRB website at www.cgirb.com.

SUBJECT ASSENT

Open-Label, Multiple-Dose, Efficacy, Safety, and Tolerability Study of Eteplirsen in Subjects with Duchenne Muscular Dystrophy who Participated in Study 4658-US-201

I have read (or someone has read to me) this Assent Form. I have had a chance to ask questions before making up my mind.

I have been told what is involved if I take part in this study in a way that that I can understand. I have to tell my parent(s) or legal guardian(s) whether I do or do not want to take part in this study.

I have been told that I do not have to take part and can stop at any time. I have been told that I may refuse to take part in the study without any problems.

The tests for this study have been explained to me by my parent(s) or legal guardian(s) and the study staff.

Discomforts and risks that I may have by taking part in this study have been explained to me by my parent(s) or legal guardian(s) and the study staff.

I am free now, and in the future, to ask any questions about the study.

I want to be in this research study.

_____

Printed Name of Subject

_____ _____

Signature of Subject (For Subjects 10 Years and Older) **Date and Time**

_____

Printed Name of Parent

_____ _____

Signature of Parent ***For VA Sites Only*** **Date and Time**

Approved

Investigator/Research Staff

I have explained the research to the subject and have answered all of his/her questions before requesting the signature above. I believe that the subject understands the information described in this Children's Assent Form and freely consents to participate in the study. There are no blanks in this document. A copy of this form has been given to the subject or his legal representative.

Printed Name of Person Obtaining Assent	**Signature of Person Obtaining Assent**
	Date and Time **AM/PM**
Printed Name of Investigator	**Signature of Investigator**
	Date and Time **AM/PM**

FDACDER_SAR_0022793

APPROVED: Jul 12, 2013
COPERNICUS GROUP IRB

copernicus group independent review board

Approved: «Approved»

CHILDREN'S ASSENT FORM
(For Subjects Ages 10 and Older)

Study Title: Open-Label, Multiple-Dose, Efficacy, Safety, and Tolerability Study of Eteplirsen in Subjects with Duchenne Muscular Dystrophy who Participated in Study 4658-US-201

Protocol Number: 4658-us-202

Study Sponsor: Sarepta Therapeutics, Inc.

Study Doctor:

Research Site Address(es):

Daytime telephone number(s):

24-hour telephone number(s): (*24 hours a day, 7 days a week*)

Subject's Name: _____

If you would like to read more information about this study, you can ask for a copy of the form that your parent/guardian will read and sign.

You are being asked to be in a research study. Studies are done to find out if there are better ways to treat people or to understand things better.

- This form will tell you about the study to help you decide whether or not you want to volunteer to take part.
- You should ask any questions you have before making up your mind. You can think about it and discuss it with your family or friends before you decide.
- It is okay to say "No" if you don't want to be in the study. If you say "Yes," you can change your mind and stop being in the study at any time without getting in trouble.
- If you decide you want to be in the study, an adult (usually a parent) will also need to give permission for you to be in this study.

What is this study about?

The purpose of this study is to learn about the long-term effects of eteplirsen in children who have Duchenne muscular dystrophy (DMD). People with DMD have a problem in the gene (a gene provides the plan for how our body is made and works) that makes dystrophin, which is important for protecting muscles from stress and activity. Because of this problem, people with DMD are not able to make enough dystrophin to protect their muscles.

Sarepta Therapeutics, Inc. has made eteplirsen (also called AVI-4658) to see if it will help people who have DMD make the dystrophin that their bodies need to protect their muscles. Eteplirsen is experimental, meaning that it is currently being tested. It has not been approved by the Food and Drug Administration (FDA) for use in the United States and no one knows yet whether or how much eteplirsen will affect the health and strength of your muscles.

This study is only for people who have completed the 28-week study of eteplirsen called Study 4658-US-201. If you and your parent(s) or legal guardian(s) decide to take part in this study and the study doctor decides that this study is right for you, you will receive eteplirsen once a week for 164 weeks (about 3 years) and take part in several tests so that we can see how eteplirsen is affecting your muscles and general health over time. You will take the same dose of eteplirsen that you took in Study 4658-US-201. For example, if you took the high dose (50 mg/kg) of eteplirsen in Study 4658-US-201 then you will take that dose in this study. If you took the low dose (30 mg/kg) of eteplirsen in 4658-US-201 then you will receive the low dose in this study. Remember that the dose of eteplirsen that you receive (high or low) was randomly assigned to you (picked by chance like tossing a coin) during Study 4658-US-201. There was an even chance (50/50) that you would be assigned to the high or low dose.

This study will be done at a medical facility close to your home (satellite site) where you will receive your weekly infusions of eteplirsen through a small tube that is placed in your vein and perform all tests at Nationwide Children's Hospital. After several weeks, however, you may start receiving your weekly infusions of eteplirsen closer to where you live. You will still need to go to Nationwide Children's Hospital about every 24 weeks (about every 6 months) for some tests and this means that on the weeks that you go to Nationwide Children's Hospital you will also go to the satellite site for your weekly infusion.

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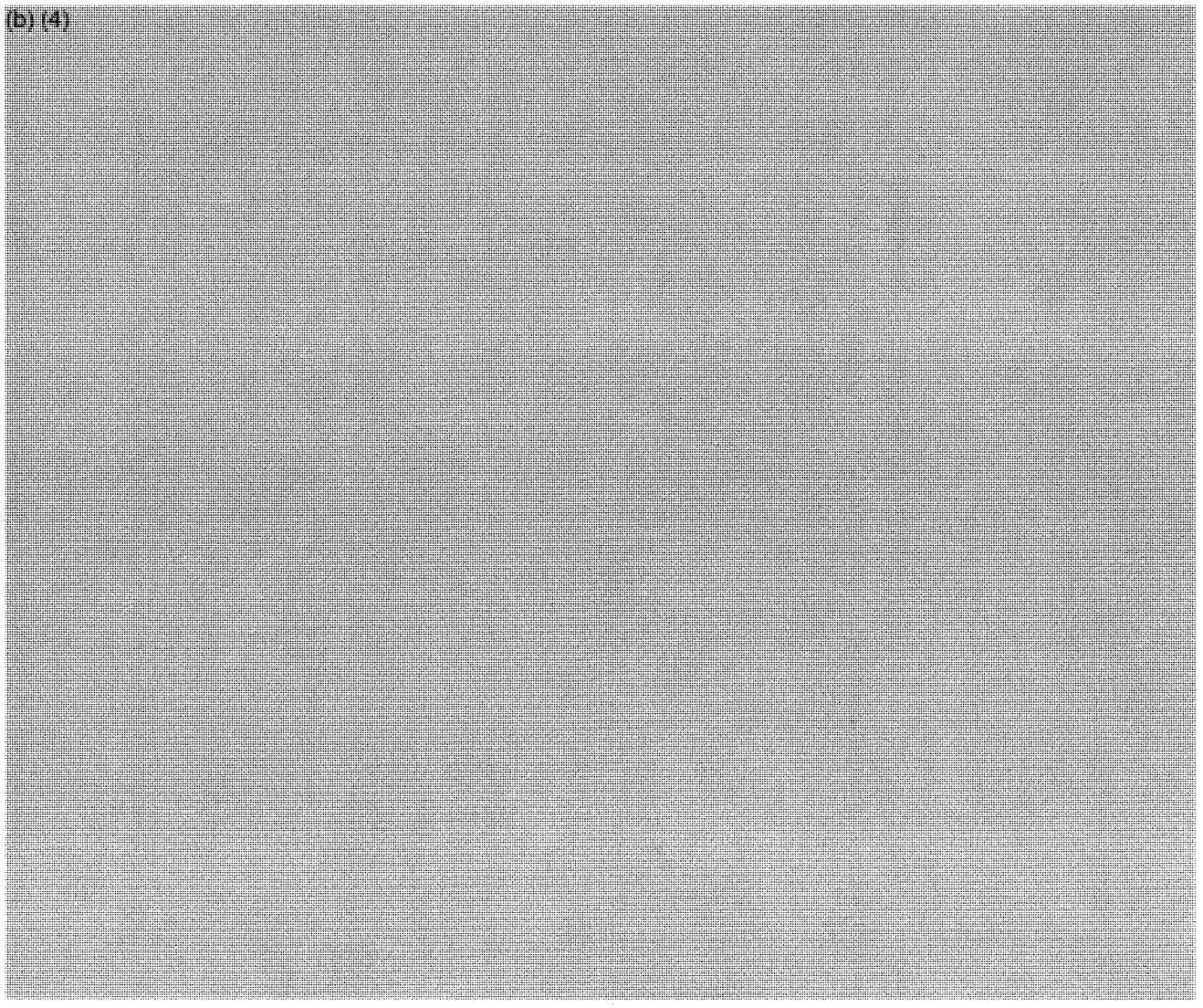
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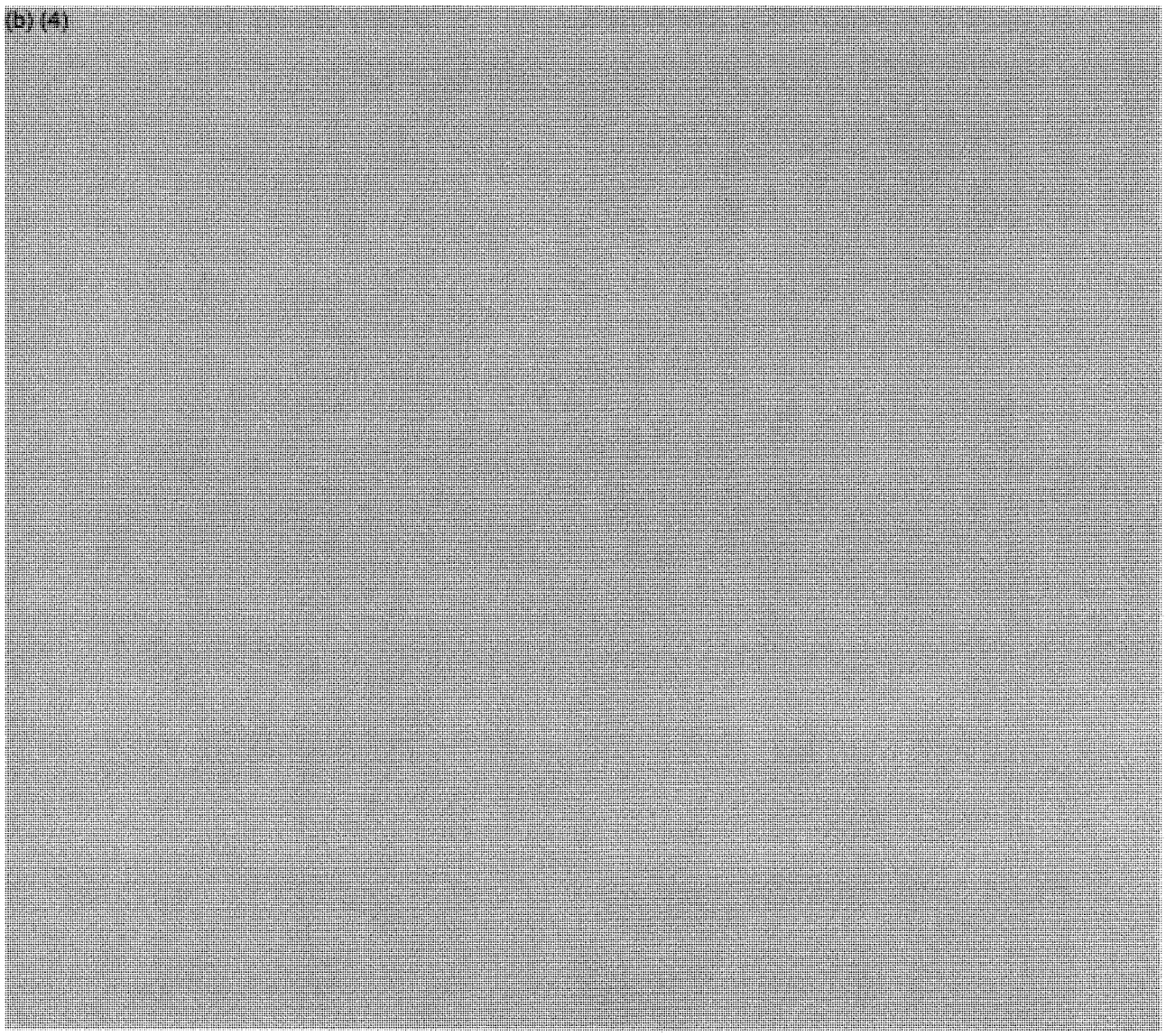
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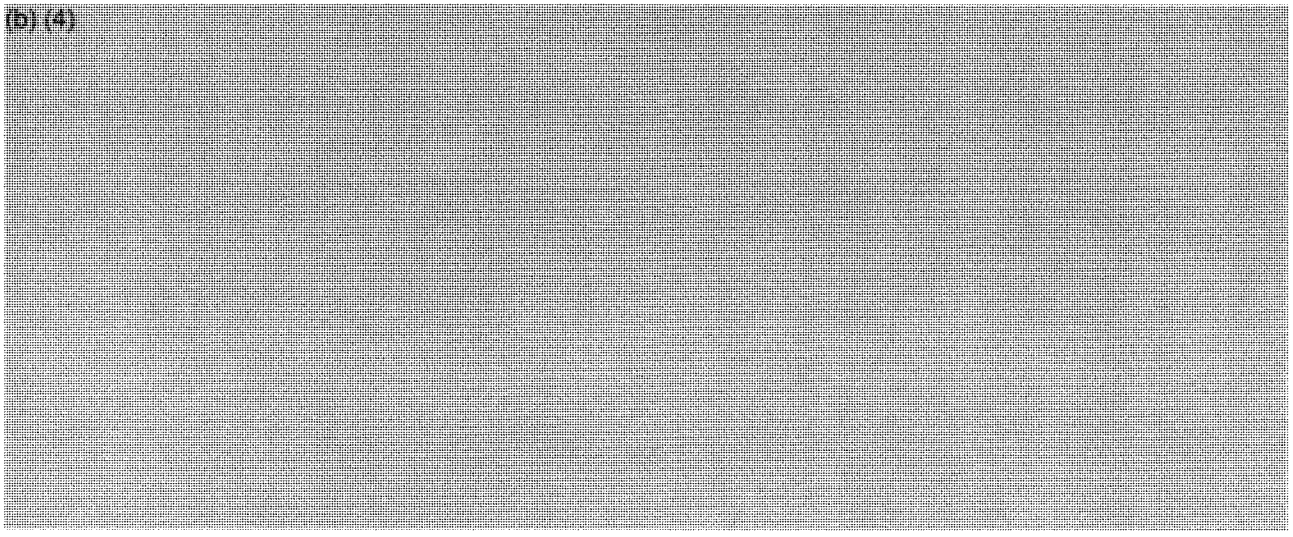
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(b) (4)



(b) (4)



(b) (4)

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Drawing blood and starting IVs by placing a needle in a vein may cause pain, dizziness and fainting, bleeding, bruising, or swelling at the needle site. Infection is a rare possibility.

Biopsy Risk

The common side effects of the muscle biopsies may include discomfort, a scar at the site of the biopsy, infection, bruise, or numbness.

Your disease may not get better or may become worse while you are in this study.

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What happens to the information that is learned about me in the study?

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- The study doctors and nurses and other people who need it to care for you.
- Researchers who run this study or other studies using Eteplirsen

Who can I talk to about the study?

If you have any questions about taking part in this research study, or if you feel that you have experienced a research-related injury or reaction to the study drug, you or your parents (or legal guardians) may contact:

Investigator Name: **«FirstName» «MiddleName» «LastName» «Suffix»**

Daytime telephone number(s): «Phone»

24-hour contact number(s): «Phone2»

If you have any questions or concerns about your rights as a research subject or want to discuss a problem, get information or offer input, you or your parents (or legal guardian(s)) may contact Copernicus Group Independent Review Board (IRB) at 1-888-303-2224 (toll free). An IRB is a group of scientific and non-scientific individuals who perform the initial and ongoing ethical review of the research study with the study subject's rights and welfare in mind. Copernicus Group IRB has reviewed and approved the research study described in this Children's Assent Form. If you have study-related comments, complaints or concerns, you or your parents (or legal guardian[s]) should first contact the study doctor. Please have your parents (or legal guardian[s]) call the IRB if you want to talk to someone other than the study doctor or have difficulty reaching the study doctor. For further information regarding the clinical trials process and your role as a research subject, you or your parents (or legal guardian[s]) may visit the Copernicus Group IRB website at www.cgirb.com.

SUBJECT ASSENT

Open-Label, Multiple-Dose, Efficacy, Safety, and Tolerability Study of Eteplirsen in Subjects with Duchenne Muscular Dystrophy who Participated in Study 4658-US-201

I have read (or someone has read to me) this Assent Form. I have had a chance to ask questions before making up my mind.

I have been told what is involved if I take part in this study in a way that that I can understand. I have to tell my parent(s) or legal guardian(s) whether I do or do not want to take part in this study.

I have been told that I do not have to take part and can stop at any time. I have been told that I may refuse to take part in the study without any problems.

The tests for this study have been explained to me by my parent(s) or legal guardian(s) and the study staff.

Discomforts and risks that I may have by taking part in this study have been explained to me by my parent(s) or legal guardian(s) and the study staff.

I am free now, and in the future, to ask any questions about the study.

I want to be in this research study.

_____

Printed Name of Subject

_____ _____

Signature of Subject **Date and Time**
(For Subjects 10 Years and Older)

_____

Printed Name of Parent

_____ _____

Signature of Parent **Date and Time**
For VA Sites Only

Investigator/Research Staff

I have explained the research to the subject and have answered all of his/her questions before requesting the signature above. I believe that the subject understands the information described in this Children's Assent Form and freely consents to participate in the study. There are no blanks in this document. A copy of this form has been given to the subject or his legal representative.

Printed Name of Person Obtaining Assent	**Signature of Person Obtaining Assent**
	Date and Time **AM/PM**
Printed Name of Investigator	**Signature of Investigator**
	Date and Time **AM/PM**

APPROVED: Mar 14, 2012
COPERNICUS GROUP IRB

copernicus group independent review board

Approved: «Approved»

CHILDREN'S ASSENT FORM
(For Subjects Ages 10 and Older)

Study Title: Open-Label, Multiple-Dose, Efficacy, Safety, and Tolerability Study of Eteplirsen in Subjects with Duchenne Muscular Dystrophy who Participated in Study 4658-US-201

Protocol Number: 4658-us-202

Study Sponsor: AVI BioPharma, Inc.

Study Doctor:

Research Site Address(es):

Daytime telephone number(s):

24-hour telephone number(s): (*24 hours a day, 7 days a week*)

Subject's Name: _____

If you would like to read more information about this study, you can ask for a copy of the form that your parent/guardian will read and sign.

You are being asked to be in a research study. Studies are done to find out if there are better ways to treat people or to understand things better.

- This form will tell you about the study to help you decide whether or not you want to volunteer to take part.
- You should ask any questions you have before making up your mind. You can think about it and discuss it with your family or friends before you decide.
- It is okay to say "No" if you don't want to be in the study. If you say "Yes," you can change your mind and stop being in the study at any time without getting in trouble.
- If you decide you want to be in the study, an adult (usually a parent) will also need to give permission for you to be in this study.

What is this study about?

The purpose of this study is to learn about the long-term effects of eteplirsen in children who have Duchenne muscular dystrophy (DMD). People with DMD have a problem in the gene (a gene provides the plan for how our body is made and works) that makes dystrophin, which is important for protecting muscles from stress and activity. Because of this problem, people with DMD are not able to make enough dystrophin to protect their muscles.

AVI BioPharma, Inc. has made eteplirsen (also called AVI-4658) to see if it will help people who have DMD make the dystrophin that their bodies need to protect their muscles. Eteplirsen is experimental, meaning that it is currently being tested. It has not been approved by the Food and Drug Administration (FDA) for use in the United States and no one knows yet whether or how much eteplirsen will affect the health and strength of your muscles.

This study is only for people who have completed the 28-week study of eteplirsen called Study 4658-US-201. If you and your parent(s) or legal guardian(s) decide to take part in this study and the study doctor decides that this study is right for you, you will receive eteplirsen once a week for 80 weeks (about 1½ years) and take part in several tests so that we can see how eteplirsen is affecting your muscles and general health over time. You will take the same dose of eteplirsen that you took in Study 4658-US-201. For example, if you took the high dose (50 mg/kg) of eteplirsen in Study 4658-US-201 then you will take that dose in this study. If you took the low dose (30 mg/kg) of eteplirsen in 4658-US-201 then you will receive the low dose in this study. Remember that the dose of eteplirsen that you receive (high or low) was randomly assigned to you (picked by chance like tossing a coin) during Study 4658-US-201. There was an even chance (50/50) that you would be assigned to the high or low dose.

This study will be done at Nationwide Children's Hospital (the central site) and at up to 12 sites nearer to the homes of the children who are taking part in this study (satellite sites). In the beginning, you will receive your weekly infusions of eteplirsen through a small tube that is placed in your vein and perform all tests at Nationwide Children's Hospital. After several weeks, however, you may start receiving your weekly infusions of eteplirsen closer to where you live. You will still need to go to Nationwide Children's Hospital about every 12 weeks (about every 3 months) for some tests and this means that on the weeks that you go to Nationwide Children's Hospital you will also go to the satellite site for your weekly infusion.

This study is open-label, which means that the study doctor, the study nurse, the study sponsor (AVI BioPharma, Inc.), you, your parents or guardians, and everyone else who might work with you in this study will know you are receiving eteplirsen

What will I need to do (what will be done to me) if I am in this study?

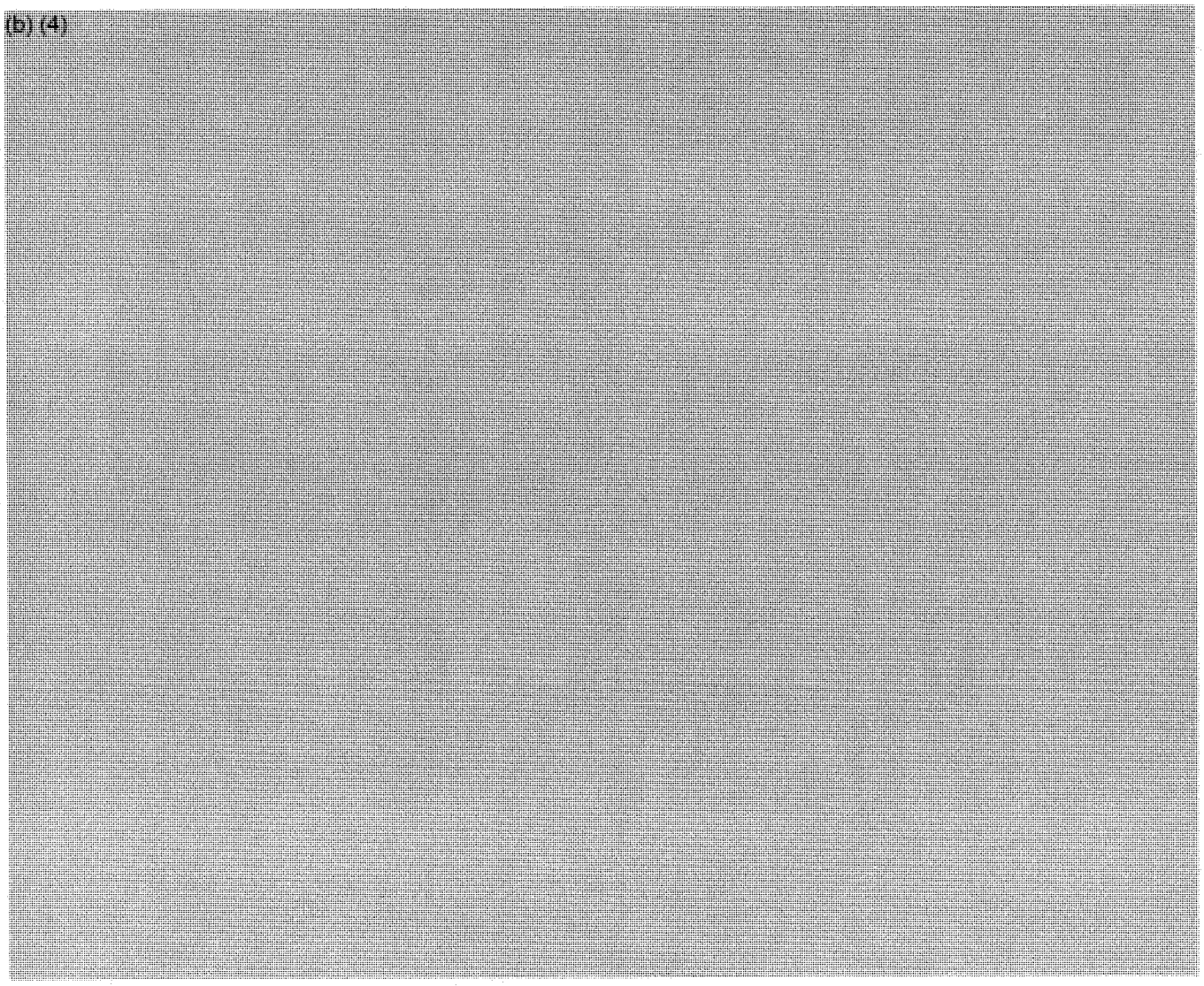
First you and your parent(s) or legal guardian(s) will be told why we are doing this research study and we will explain all the procedures that are part of it. You can ask all the questions you have and take all the time you need to think about participating. If you decide to be in this research study, you will first sign this assent form, and your parent(s) or legal guardian(s) will sign the permission form.

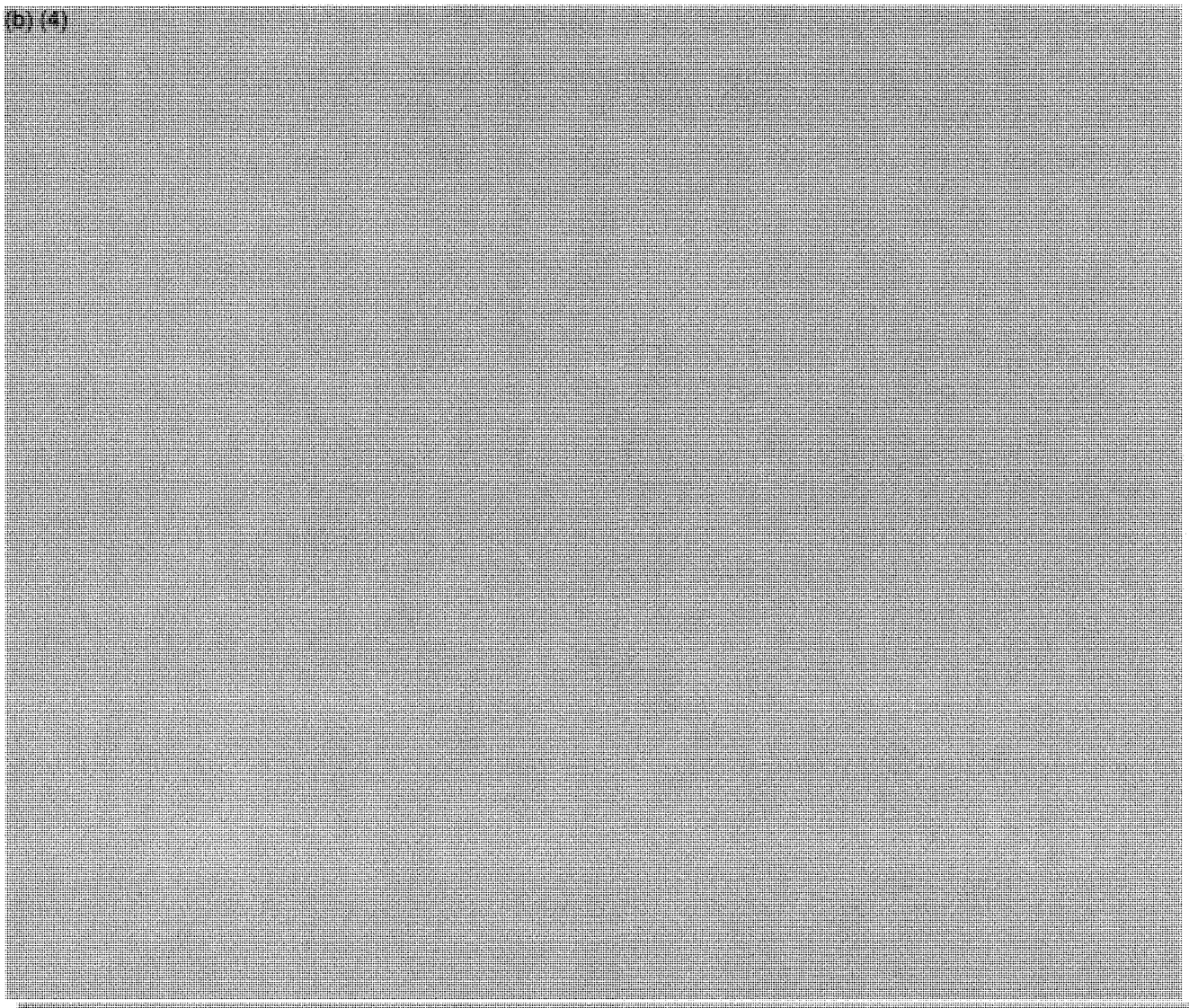
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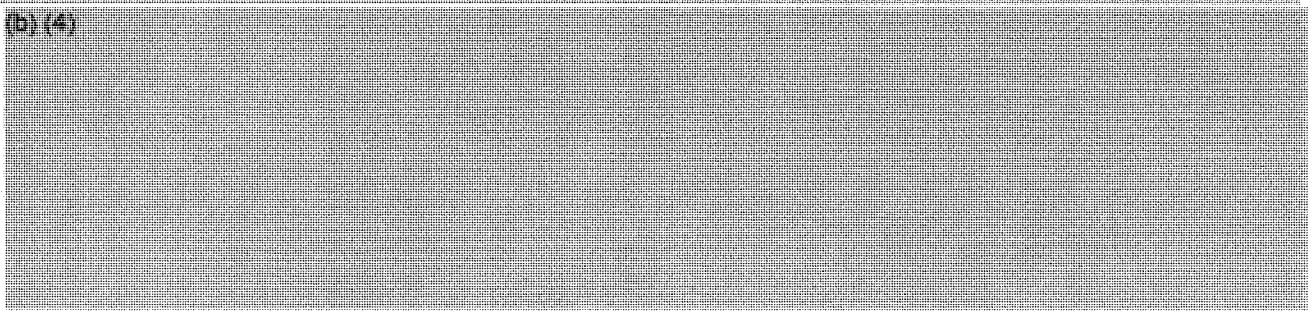
Once you and your parent(s) or legal guardian(s) have decided that you will participate in this study, then your doctor will make sure that this study is right for you. All of this will happen at your last visit for Study 4658-US-201 (b) (4) so the study doctor will mostly use information from that study to make sure that that this study is right for you. The only extra thing that he will do is ask you some more questions about how you're doing and about you're medical history.

If the study doctor says that it is okay for you to take part in this study, you will need to make a total of 80 weekly visits to either Nationwide Children's Hospital or to a clinic nearer to your home in order to receive eteplirsen and complete tests for the study. Below is a summary of what will happen at those weekly visits.

(b) (4)







Can I stop being in the study?
Yes. You may stop being in the study at any time.

What bad things might happen to me if I am in the study?
Some bad things can happen with eteplirsen. These things don't always happen, but they do happen sometimes. The most common bad things (side effects) that other subjects experienced while on eteplirsen are:

a. headache
b. throat infection
c. back pain
d. congestion and itching in your nose, and sneezing
e. falling
f. muscle pain

Subjects from other studies of eteplirsen generally had these side effects at either mild (63%) or moderate (32%) level.

There may be other effects that may be harmful, which are not known at this time.

Blood Draw/IV Risk
Drawing blood and starting IVs by placing a needle in a vein may cause pain, dizziness and fainting, bleeding, bruising, or swelling at the needle site. Infection is a rare possibility.

Biopsy Risk
The common side effects of the muscle biopsies may include discomfort, a scar at the site of the biopsy, infection, bruise, or numbness.

Your disease may not get better or may become worse while you are in this study.

What good things might happen to me if I am in the study?

You may experience some good things from participating in this study. However, good things may not happen to you by being in this research study. If you do not benefit from being in this study, the study doctors might learn something that could help others.

Will I be given anything for being in this study?

You will not be paid to be in this study.

Who can I talk to about the study?

If you have any questions about taking part in this research study, or if you feel that you have experienced a research-related injury or reaction to the study drug, you or your parents (or legal guardians) may contact:

Investigator Name: **«FirstName» «MiddleName» «LastName» «Suffix»**

Daytime telephone number(s): «Phone»

24-hour contact number(s): «Phone2»

If you have any questions or concerns about your rights as a research subject or want to discuss a problem, get information or offer input, you or your parents (or legal guardian(s)) may contact Copernicus Group Independent Review Board (IRB) at 1-888-303-2224 (toll free). An IRB is a group of scientific and non-scientific individuals who perform the initial and ongoing ethical review of the research study with the study subject's rights and welfare in mind. Copernicus

Group IRB has reviewed and approved the research study described in this Children's Assent Form. If you have study-related comments, complaints or concerns, you or your parents (or legal guardian[s]) should first contact the study doctor. Please have your parents (or legal guardian[s]) call the IRB if you want to talk to someone other than the study doctor or have difficulty reaching the study doctor. For further information regarding the clinical trials process and your role as a research subject, you or your parents (or legal guardian[s]) may visit the Copernicus Group IRB website at www.cgirb.com.

SUBJECT ASSENT

Open-Label, Multiple-Dose, Efficacy, Safety, and Tolerability Study of Eteplirsen in Subjects with Duchenne Muscular Dystrophy who Participated in Study 4658-US-201

I have read (or someone has read to me) this Assent Form. I have had a chance to ask questions before making up my mind.

I have been told what is involved if I take part in this study in a way that that I can understand. I have to tell my parent(s) or legal guardian(s) whether I do or do not want to take part in this study.

I have been told that I do not have to take part and can stop at any time. I have been told that I may refuse to take part in the study without any problems.

The tests for this study have been explained to me by my parent(s) or legal guardian(s) and the study staff.

Discomforts and risks that I may have by taking part in this study have been explained to me by my parent(s) or legal guardian(s) and the study staff.

I am free now, and in the future, to ask any questions about the study.

I want to be in this research study.

_____

Printed Name of Subject

_____ _____

Signature of Subject (For Subjects 10 Years and Older) **Date and Time**

_____

Printed Name of Parent

_____ _____

Signature of Parent ***For VA Sites Only*** **Date and Time**

Investigator/Research Staff

I have explained the research to the subject and have answered all of his/her questions before requesting the signature above. I believe that the subject understands the information described in this Children's Assent Form and freely consents to participate in the study. There are no blanks in this document. A copy of this form has been given to the subject or his legal representative.

Printed Name of Person Obtaining Assent	**Signature of Person Obtaining Assent**
	Date and Time **AM/PM**
Printed Name of Investigator	**Signature of Investigator**
	Date and Time **AM/PM**

16.1.4 Principal Investigators

Site Number	Investigator Name	Center Name	Address	City	State	Zip Code	Contact Information
01	Mendell, Jerry MD	Nationwide Children's Hospital	Center for Gene Therapy The Research Institute at Nationwide Children's Hospital 700 Children's Dr.	Columbus	OH	43205	Phone – 614-722-5615 Jerry.mendell@nationwidechildrens.org
(b) (4)							
(b) (4)							
04	Byrne, Barry MD	University of Florida	1600 SW Archer Rd.	Gainesville	FL	32610	Phone: 352-273-6563 bbyrne@ufl.edu
(b) (4)							
08	Heydemann, Peter MD	Rush University Pediatrics-Muscular Dystrophy Clinic	1725 West Harrison Ste. 718	Chicago	IL	60612	Phone: 312-942-4036 peter_heydemann@rush.edu
(b) (4)							

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11	Connolly, Anne MD	Washington University School of Medicine	600 South Euclid Ave, Campus Box 8111	St. Louis	MO	63110	Phone: 314-362-6981 connollya@neuro.wustl.edu
(b) (4)							

FDACDER_SAR_0022811

CURRICULUM VITAE

Name: Jerry R. Mendell, M.D.

Education: 1959-1962 University of Texas, Austin, Texas; BA/BS
1962-1966 University of Texas Southwestern Medical School, Dallas, Texas; M.D.

Neurological Training and Chronology of Employment:

1966 - 1967 Internship, Columbia-Presbyterian
Columbia University College of Physicians and Surgeons, New York, New York

1967 - 1969 Resident in Neurology, New York Neurological Institute, Columbia University College of Physicians and Surgeons, New York, New York

1969 - 1970 Resident in Neurology, Medical
Neurology Branch, NINDS, NIH, Bethesda, Maryland

1970 - 1972 Clinician Researcher, Attending Neurologist, Medical Neurology Branch, NINDS, NIH, Bethesda, Maryland

1972 - 1977 Associate Professor of Neurology, Pediatrics and Pathology, Ohio State University College of Medicine

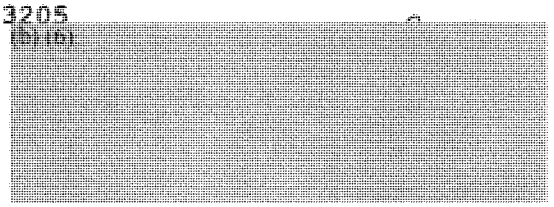
1978 - Present Professor of Neurology, Pediatrics, and Pathology, Ohio State University College of Medicine

1992 - 2004 Helen C. Kurtz Professor and Chair, Department of Neurology, Ohio State University College of Medicine

2004 - Present Professor of Pediatrics

2008 - Present Professor of Physiology and Cell Biology

2004 - Present Director Center for Gene Therapy, Research Institute at Nationwide Children's Hospital, Division of Molecular Medicine, Dept of Pediatrics, Ohio State University College of Medicine, 700 Children's Dr. Columbus, OH.43205



Board Certification:
Certified by the American Board of Psychiatry and Neurology, October, 1972, Certificate No. 43210

Licensed by Texas State Board of Medical Examiners, August, 1966, Certificate No. D3338

Certified by the National Board of Medical Examiners, July 1, 1967, Certificate No. 96701

Licensed by the State of New York June 18, 1968

Licensed by the State of Ohio, December 5, 1972, Certificate Number 35346

Societies:
Alpha Omega Alpha
American Medical Association
American Neurological Association
The American Society for Cell Biology
American Academy of Neurology
New York Academy of Sciences
American Association of Neuropathologists
Central Society for Neurological Research
Peripheral Nerve Study Group
Peripheral Nerve Association of America
American Society for Gene and Cell Therapy

Honors and Special Scientific Recognition:

Nueces County Medical Society Full Four Year Scholarship, 1962

Student Research Award, Southwestern Medical School, 1966

Alpha Omega Alpha, 1966

Senior Investigator Award, Department of Medicine, Ohio State University, College of Medicine, June, 1982

President, Central Society for Neurological Research, 1986-1987

President Medical Review Club, 1990-1991

Presidential Award, American Neurological Association for Outstanding Research 1989

Chair Committee On Qualifications for Neuromuscular Pathology 1995-2003

President Association of University Professors of Neurology 1998-2000

Elected to the Council of the American Neurological Association 1999-2001

Vice-Chair United Council of Neurological Subspecialties 2003-2006

Elected as Honorary Member to American Association of Electromyography and Neuromuscular Medicine for outstanding contributions to the field 2004

S.Mouchly Small Scientific Achievement Award. Muscular Dystrophy Association 2004

Presented the Distinguished Scholar Award of The Ohio State University 2009

Outstanding Researcher for 2009 Research Institute at Nationwide Children's Hospital

Dwight Peters and Juanita Curran Chair in Pediatric Research 2010

Annals of Neurology prize for an outstanding contribution to clinical neuroscience 2011

Honorary Lectures:

Hertafeld lecturer 1992
University of Rochester, Dept of Pediatrics and Neurology, Rochester, NY

Carol Krussen Lecturer 1994 Unversity of Texas Medical School,Southwestern and Texas Scottish-Rite Hospital Departments of Neurology Dallas, Texas

Killam Lecturer 1995 Montreal Neurological Institute
Montreal, Canada

Foster-Elting Bennett Memorial Lecturer,1995
In recognition for contribution to the neurosciences, American Neurological Association Washington, DC

Oh Memorial Lecture, University of Alabama, Dept of Neurology, 1999

Keynote Speaker American Association of Electromyography and Neuromuscular Medicine Gene Therapy for Muscular Dystrophy 2004

William S Fields lecture Current and Evolving Treatment Strategies for Muscular Dystrophy University of Texas Houston 2004

Keynote Speaker American Academy of Neurology "Gene Therapy for Muscular Dystrophy" San Diego, 2006

Presidential Lecture Southern Society for Pediatric Neurology March 2008

National Committees

Member MDA Task Force on Drug Therapy 1979 - 1990

Member Finance Committee of American Neurological Association 1985-1986

Member S. Weir Mitchell Award Committee, American Academy of Neurology 1983-1984

Member Muscular Dystrophy Association, Medical Advisory Committee for Grant Review 1989 -2000

Member Muscular Dystrophy Association Task Force on Gene Therapy 1999 - 2001

Committee on Qualifications Recognition in Neuromuscular Pathology 1995 - 2006

Association of University Professors of Neurology 1992- 2004

Council of American Neurological Association 1999- 2001

MDA task force on translational research (TRAC) 2003-2005

Appointed to NIH task force for muscular dystrophy research 2003-2006

Treat NMD Advisory Committee for Therapeutics - 2009- present

Review Panelist for Howard Hughes Medical Institute applications for medical, dental and veterinary students 2011-present

Chair, Medical Advisory Board The Myositis Association 2010-2011

Chair of Steering Committee for Paul D. Wellstone Centers 2011-present

Editorial Boards:

Muscle and Nerve (Section Editor for Case-of-the-Month) 1992-1999

Neuromuscular Disorders (Section Editor for Rapid Communication for Molecular Abnormalities) 1993-2004

Annals of Neurology 1994-2000

Continuum, A program of the American Academy Neurology 1993 - 1998

Neurology 1996 - 2002

Nature Clinical Practice 2005- 2008

BIBLIOGRAPHY - J.R. MENDELL, M.D.

1. Stern, J., Mendell, J.R., and Clark, K.: H Reflex Suppression by Thalamic Stimulation and Drug Administration. J Neurosurg 29:393-396, 1968.

2. Mendell, J.R., Chase, T.N., and Engel, W.K.: Modification of L-Dopa of a Case of Progressive Supranuclear Palsy. Lancet 1:593, 594, 1970.

3. Mendell, J.R., and Engel, W.K.: The Fine Structure of Type II Muscle Fiber Atrophy. Neurology 21:358-365, 1971.

4. Mendell, J.R. and Markesbery, W.R.: Neuronal Intracystoplasmic Hyaline Inclusions. J Neuropath & Exp Neurol 30: 233- 239, 1971.

5. Mendell, J.R., Engel, W.K. and Derrer, E.C.: Duchenne Muscular Dystrophy: Functional Ischemia Reproduces its Characteristic Lesions. Science 172: 1143-1145, 1971.

6. Mendell, J.R., Chase, T.N., and Engel, W.K.: A Study of Metabolism of Central Monoamines and Treatment with L-Dopa in Amyotrophic Lateral Sclerosis. Trans Am Neurol Assn 96:184-286, 1971.

7. Mendell, J.R.: Unusual Features of the T-System of the Pectoralis Muscle of the chicken. J Ultrastruct Res 37:383-387, 1971.

8. Mendell, J.R., Chase, T.N., and Engel, W.K.: Amyotrophic Lateral Sclerosis: A Study of Central Monoamine Metabolism and Therapeutic Trial of Levodopa. Arch Neurol 25:320-325, 1971.

9. Patten, B., Mendell, J.R., Brunn, B., Curtin, W., and Carter, S.:Double-Blind Study of the Effect of Dexamethasone on Acute Stroke. Neurology 22:377-383, 1972.

10. Mendell, J.R., Roelofs, R.I., and Engel, W.K.: The Ultrastructural Development of Explanted Human Skeletal Muscle in Tissue Culture. J Neuropath & Exp Neurol 31:433-446, 1972.

11. Mendell, J.R., Engel, W.K., and Derrer, E.C.: Plasma Enzyme Concentrations in Rats with Functional Ischemia of Muscle Provide a Possible Model of Duchenne Muscular Dystrophy. Nature 239: 533-544, 1972.

12. Mendell, J.R., Murphy, D.L., Engel, W.K., Chase, T.N., and Gordon, E.: Catecholamines and Indoleamines in Patients with Duchenne Muscular Dystrophy. Arch Neurol 27: 518-520, 1972.

13. Murphy, D.L., Mendell, J.R., and Engel, W.K.: Serotonin and Platelet Function in Patients with Duchenne Muscular Dystrophy. Arch Neurol 28:239-242, 1973.

14. Mendell, J.R., Whitaker, J.N., and Engel, W.K.: The Skeletal Muscle Binding Site of Antistriated Muscle Antibody in Myasthenia Gravis: An Electron Microscopic Immunohistochemical Study Using Peroxidase Conjugated Antibody Fragments. J Immunol 3:847-856, 1973.

15. Parker, J.M., and Mendell, J.R.: 5-HT-Imipramine Induced Proximal Myopathy Simulating Duchenne Dystrophy. Nature 247:103-104, 1974.

16. Bauman, D. and Mendell, J.R.: Method of Re-embedding Tissue for Electron Microscopy. Stain Tech 490:118-119, 1974.

17. Saltis, L.M., and Mendell, J.R.: The Fine Structural Differences in Human Muscle Fiber Types Based on Peroxidatic Activity. J Neuropath & Exp Neurol 33:632-640, 1974.

18. Mendell, J.R., Saida, K., Ganansia, M.F., Jackson, D.B., Weiss, H., Gardier, R.W., Chrisman, V., Allen, N., et al.: Toxic Polyneuropathy Produced by Methyl-n-Butyl Ketone. Science 185:787-789, 1974.

19. Allen, N., Mendell, J.R., Billmaier, D., Fontaine, R.E., O'Neill, J.: Toxic Polyneuropathy Due to Methyl n-Butyl Ketone - An Industrial Outbreak. Arch Neurol 32:209-218, 1974.

20. Couri, D., Hetland, L.B., O'Neill, J.J., Ganansia, M.F., Jackson, D.B., Gardier, R.W., Marks, B.H., Weiss, H., Mendell, J.R., et al: Neurotoxicity of Methylbutyl Ketone. Environmental Toxicology 1974;74-125.

21. Allen, N., Mendell, J.R., Billmaier, D., Fontaine, R.E.: An Outbreak of a Previously Undescribed Toxic Polyneuropathy Due to Industrial Solvent. Trans Am Neurol Assn 99: 23-28, 1975.

22. Saida, K., Mendell, J.R., Weiss, H.S.: Peripheral Nerve Changes Induced by Methyl n-Butyl Ketone and Potentiation by Methyl Ethyl Ketone. J Neuropath & Exp Neurol 35:207-225, 1976.

23. Silverman, L.M., Mendell, J.R. Sahenk, Z., Fontana, M.B.: Significance of Creatine Phosphokinase Isoenzymes in Duchenne Dystrophy. Neurology 26:561-564, 1976.

24. Mendell, J.R., Silverman, L.M., Verrill, H.L., Parker, J.M., Olson, W.H.: Imipramine-Serotonin Induced Myopathy. Neurology 26:968-974, 1976.

25. Malarkey, W.B., Mendell, J.R.: Failure of a Serotonin Inhibitor to Effect Nocturnal GH and Prolactin Secretion in Patients with Duchenne Muscular Dystrophy. J Clin Endocrin Metab 42:889-892, 1976.

26. Sahenk, Z., Mendell, J.R., Rossio, J.L., Hurtubise, P.: Polyradiculoneuropathy Accompanying Procaineamine-Induced Lupus Erythematosis: Evidence for Drug-Induced Enhanced Sensitization to Peripheral Nerve Myelin. Ann Neurol 1:378-384, 1977.

27. Saida, K., Mendell, J.R., Sahenk, Z.: Peripheral Nerve Changes Induced by Local Application of Bee Venom. J Neuropath & Exp Neurol 36:783-796, 1977.

28. Parker, J.M., Allen, J.N., Mendell, J.R.: Peripheral Neuropathy Due to Methyl n-Butyl Ketone and Related Solvents. In:Management of the Poisoned Patient, Rumack, B.H., and Temple, A.R. (eds). Science Press, Princeton, N.J., pp1-8, 1977.

29. Mendell, J.R., Sahenk, Z., Weiss, H.S., Savage, R., Couri, D.: Alterations of Fast Axoplasmic Transport in Experimental Methyl n-Butyl Ketone Neuropathy. Brain Res 133:107-118, 1977.

30. Whitaker, J.N., DiMauro, S., Solomon, S.S., Sabesin, S., Duckworth, W.C., Mendell, J.R.: Corticosteroid-Responsive Skeletal Muscle Disease Associated with Partial Carnitine Deficiency: Studies of Liver and Metabolic Alterations. Am J Med 63: 805-815, 1977.

31. Mendell, J.R., Sahenk, Z., Silverman, L.M.: Relationship of Biogenic Amines to Duchenne Muscular Dystrophy. Excerpta Medica 404:678-684, 1977.

32. Mendell, J.R. and Whitaker, J.N.: Immunocytochemical Localization Studies of Myelin Basic Protein. J Cell Biol 76: 502-511, 1978.

33. Sahenk, Z., Mendell, J.R., Couri, D., Nachtman, J.: Polyneuropathy from Inhalation of N2O Cartridges through a Whipped-Cream Dispenser. Neurology 28:485-487, 1978.

34. Mendell, J.R., Higgins, R., Sahenk, Z., Cosmos, E.: The Relevance of Genetic Animal Models of Muscular Dystrophy to Human Muscular Dystrophies. New York Academy Sciences, 317:409-430, 1979.

35. Warmolts, J.R., Mendell, J.R.: Open-Biopsy EMG: Direct Correlaton of a Pattern of Excessively Recruited, Pathologically Small Motor Unit Potentials with Histologic Evidence of Neuropathy. Arch Neurol 36:406-409, 1979.

36. Mendell, J.R. and Wiechers, D.O.: Allopurinol in Duchenne Muscular Dystrophy: Failure to Confirm a Beneficial Response. Muscle & Nerve 2: 53-56, 1979.

37. Sahenk, Z., and Mendell, J.R.: Analysis of Fast Axoplasmic

Transport in Nerve Ligation and Adriamycin-Induced Neuronal Perikaryon Lesions. Brain Res 171:41-53, 1979.

38. Sahenk, Z., and Mendell, J.R.: Ultrastructural Study of Zinc Pyridinethione Induced Peripheral Neuroapthy. J Neuropath & Exp Neurol 38:532-550, 1979.

39. Warmolts, J.R. and Mendell, J.R.: Neurotonia: Impulse-Induced Repetitive Discharges in Motor Nerve in Peripheral Neuropathy. Ann Neurol 7: 245-250, 1980.

40. Sahenk, Z. and Mendell, J.R.: Axoplasmic Transport in Zinc-Pyridinethione Neuropathy: Evidence for an Abnormality in Distal Turn-Around. Brain Res 186: 343-353, 1980.

41. DiMauro, S., Mendell, J.R., Sahenk, Z., Bachman, D., Scarpa, A., Scofield, R.M., and Reiner, C.: Fatal Infantile Mitochondrial Myopathy and Renal Dysfunction Due to Cytochrome-C-Oxidase Deficiency. Neurology 30: 795-804, 1980.

42. Hofteig, J., Mendell, J.R., Yates, A.: Chemical and Morphological Studies on Garfish Peripheral Nerves. J Comp Neurol 198:265-275, 1981.

43. Brooke, M.H., Griggs, R.C., Mendell, J.R., Fenichel, G.M., Shumate, J.R., Pellegrino, R.: Clinical Trial in Duchenne Dystrophy I. The Design of the Protocol. Muscle and Nerve 4:186-197, 1981.

44. Sahenk, Z. and Mendell, J.R.: Acrylamide and 2,5 Hexanedione Neuropathies: Abnormal Bidirectional Transport Rate in Distal Axons. Brain Res 219:397-405, 1981.

45. Mendell, J.R., Sahenk, Z., Warmolts, J.R., Marshall, J.K., Thibert, P.: The Spontaneously Diabetic BB Wistar Rat: Morphologic and Physiologic Studies of Peripheral Nerve. J Neurol Sci 52: 103-115, 1981.

46. Brooke, M.H., Griggs, R.C., Mendell, J.R., Fenichel, G.M., Shumate, J.R.: The Natural History of Duchenne Muscular Dystrophy: A Caveat for Therapeutic Trials. Trans Am Neurol Assoc, 106: 195-199, 1981.

47. Whitaker, J.N., Bertorini, T.E., Mendell, J.R.:Immunocytochemical Studies on Cathepsin D in Human Skeletal Muscle. Trans Am Neurol Assoc 106:219-221, 1981.

48. Mendell, J.R., Sahenk, Z., Kennedy, M.S.: Treatment of Peripheral Neuropathies. Current Therapy; 773-781,1982.

49. Bachman, D.A., Paulson, G.W., Mendell, J.R.: Acute Inflammatory Polyradiculoneuropathies Following Hymenoptera Stings. JAMA 247:1443-1445, 1982.

50. Whitaker, J.N., Dodd, S.P., Sahenk, Z., Mendell, J.R.: Changes in Sciatic Nerve Cathepsin D after Ligation or Exposure to Neurotoxins. J Neuropath & Exp Neurol 42:87-98, 1983.

51. Whitaker, J.N., Bertorini, T.E., Mendell, J.R.:Immunocytochemical Studies on Cathepsin D in Human Skeletal Muscle. Ann Neurol 13:133-142, 1983.

52. Sahenk, Z. and Mendell, J.R.: Studies on the Morphological Alterations of Axonal Membranous Organelles in Neurofilamentous Neuropathies. Brain Res 268:239-247, 1983.

53. Wanner, W.R., Williams, T.E., Fulkerson, P.K., Mendell, J.R. and Leier, C.V.: Acute Pericarditis Following Thymectomy for Myasthenia Gravis: A Prospective Study for an Overlooked Complication. Chest Med 83:647-649, 1983.

54. Brooke, M.H., Fenichel, G.M., Griggs, R.C., Mendell, J.R., Moxley, R., Miller, J.P., Province, M.A. and the CIDD Group: Clinical Investigation in Duchenne Dystrophy: 2. Determination of the "Power" of Therapeutic Trials Based on the Natural History. Muscle & Nerve 6:91-103, 1983.

55. Bach, P.R., Brooke, M.H., Fenichel, G.M., Griggs, R.C., Mendell, J.R. and the CIDD Group: Determination of Nifepidine in Serum or Plasma by Reversed-Phase Liquid Chromatography. Clin Chem 29:1344-1348, 1983.

56. Sahenk, Z. and Mendell, J.R.: Pathology and Axonal Transport in Hexacarbon Neuropathies. Proc Environmental Toxicology 1983;60-67.

57. Florence, J.M., Pandya, S., King, W.M., Robinson , J.D., Signore, L.C., Wentzell, M., Province, M.A. and the CIDD Group:Clinical Trials in Duchenne Muscular Dystrophy: Reliability Studies. Physical Therapy, 64:41-45, 1984.

58. Mendell, J.R. and Vaughan, A.J.: Duchenne Muscular Dystrophy:

Ethical and Emotional Considerations in Long-Term Management. Sem Neurology 4:98-103, 1984.

59. Mendell, J.R., Griggs, R.C., Moxley, R., Fenichel, G.M., Brooke,M.H., Miller, J.P., Province, M.A., Dodson, E.W. and CIDDGroup: Clinical trial in Duchenne Dystrophy: IV. Double-Blind Controlled Trial of Leucine. Muscle & Nerve 7:535-541, 1984.

60. Sahenk, Z., Mendell, J.R.: Pathology and Axonal Transport in hexacarbon Neuropathies. Proc Experimental Toxicology. 1984:60-67, 1984.

61. Ortman, J.A., Sahenk, Z., Mendell, J.R.: The Experimental Production of Renaut Bodies. J Neurol Sci 62: 233-241, 1983.

62 Clinical Investigation of Duchenne Dystrophy Group: The Use of an Extended Baseline Period in the Evaluation of Treatment in Duchenne Muscular Dystrophy. Controlled Clinical Trials. Stat Med 5:231-241, 1986.

63. Mendell, J.R., Kissel, J.T., Kennedy, M.S., Sahenk, Z.,Grinvalsky, H.T., Pittman, G.L., Kyler, R.S., Roelofs, R.I., Whitaker, J.N., Bertorini, T.E.: Plasma Exchange and immunosuppression in Acute Inflammatory Polyradiculoneuropathy A Controlled-Randomized Trial. J Clin Apheresis 2:332-342, 1985.

64. Mendell, J.R., Sahenk, Z., Whitaker, J.N., Trapp, B.D., Yates, A.J., Griggs, R.C., Quarles, R.H.: Polyneuropathy and IgM Monoclonal Gammopathy: Studies on the Pathogenetic Role ofAnti-Myelin-Associated Glycoprotein Antibody. Ann Neurol 17:243-254, 1985.

65. Mendell, J.R., Kissel, J.T., Kennedy, M.S., Sahenk, Z., Grinvalsky, H.T., Pittman, G.L., Kyler, R.S., Roelofs, R.I., Whitaker, J.N., Bertorini, T.E.: Plasma Exchange and Predinsone in Guillain-Barre Syndrome: A Controlled-Randomized Trial. Neurology 35:1551-1556, 1985.

66. Kissel, J.T., Levy, R.J., Mendell, J.R., Griggs, R.C.: Azathioprine Toxicity in Neuromuscular Disease. Neurology 36:35-39, 1986.

67 Griggs, R.C., Mendell, J.R., Brooke, M.H., Fenichel, G.M., Miller, J.P., Province, M.A., Moxley, R.T., Huntzinger, D.,

Vaughn, A., Cohen, M., Conneally, P.M., Bach, P. and the CIDD Group: Clinical Investigation in Duchenne Dystrophy. V. Use of Creatine Kinase and Pyruvate Kinase in Carrier Detection. Muscle & Nerve 8:60-67, 1985.

68. Moxley, R.T., Brooke, M.J., Fenichel, G.M., Griggs, R.C., Mendell, J.R., Patterson, V.H., Miller, J.P., and the CIDD Group: Clinical Investigation in Duchenne Dystrophy: VI Double-Blind Controlled Trial of Nifepidine. Muscle & Nerve 10:22-33, 1987.

69. Ramirez, J.A., Mendell, J.R., Warmolts, J.R., Griggs, R.C.: Phenytoin Neuropathy: Structural Changes in the Sural Nerve. Ann Neurol 99:162-167, 1986.

70. Kissel, J.T., Beam, W., Bresolin, N., Gibbons, G., DiMauro, S., Mendell, J.R.: The Physiologic Assessment of a Newly Described Metabolic Myopathy, Phosphoglycerate Mutase Deficiency, Through Incremental Exercise Testing. Neurology 33:828-833, 1985.

71. Kissel, J.T., Slivka, A.P., Warmolts, J.R., Mendell, J.R.: The Clinical Spectrum of Necrotizing Angiopathy of the Peripheral Nervous System. Ann Neurol 18:251-257, 1985.

72. O'Shannessy, D.J., Ilyas, A.A., Dalakas, M.C., Mendell, J.R.: Specificity of Human IgM Monoclonal Antibodies from Patients with Peripheral Neuropathy. J Neuroimmunol 11: 131-136, 1986.

73. Kissel, J.T., Mendell, J.R., Rammohan, K.W.: Microvascular Deposition of Complement Membrane Attack Complex in Dermatomyositis. N Engl J Med, 314:329-333, 1986.

74. Collaborative Investigation of Duchenne Dystrophy Group: The Use of an Extended Baseline Period in the Evaluation of Treatment in a Longitudinal Duchenne Muscular Dystrophy Trial. Stat Med 5: 231-241, 1986.

75. Hyser, C.L., Griggs, R.C., Mendell, J.R., Polakowska, R., Quirk, S., Brooke, M.H., Fenichel, G.M., Doherty, R.A.: Use of Serum Creatine Kinase, Pyruvate Kinase and Genetic Linkage for Carrier Detection in Duchenne and Becker Dystrophy. Neurology 37:4-10, 1987.

76. Sahenk, Z., Brady, S.T., Mendell, J.R.: Studies on the Pathogenesis of Vincristine-Induced Neuropathy. Muscle & Nerve 10:80-84, 1987.

77. Kolkin, S., Nahman, N.S. Jr., and Mendell, J.R.: Chronic Nephrotoxicity Complicating Cyclosporine Treatment of Chronic Inflammatory Demyelinating Polyradiculoneuropathy. Neurology 37:147-149, 1987.

78. Hyser, C.L., Kissel, J.T., Mendell, J.R.: Three Cases of Amyotrophic Lateral Sclerosis in a Common Occupational and Environmental Setting. Neurology 234:443-444, 1987.

79. Mendell, J.R., Kolkin, S., Kissel, J.T., Weiss, K.L., Chakeres, D.W., Rammohan, K.: Evidence for Central Nervous SystemDemyelination in Chronic Inflammatory Polyradiculoneuropathy. Neurology 37:1291-1294, 1987.

80. Hyser, C.L., Doherty, R.A., Griggs, R.C., Mendell, J.R., Polakowska, R., Quirk, S., Brooke, M.H., Fenichel, G.M.: Carrier Assessment for Female Relatives of Isolated Duchenne Dystrophy Cases: The Importance of Serum Enzyme Determinations. Neurology 37:1476-1480, 1987.

81. Nahman, S.N., Cosio, F.G., Kolkin, S., Mendell, J.R., Sharma, H.M.:Cyclosporine Nephrotoxicity Without Major Organ Transplantation. Ann Int Med 106:400-402, 1987.

82. Hyser, C.L., Province, M., Griggs, R.C., Mendell, J.R., Fenichel, G.M., Brooke, M.H., Miller, J.P., Polakowska, R., Doherty, R.A., Quirk, S.: Genetic Heterogeneity in Duchenne Dystrophy. Ann Neurol 22: 553-555, 1987.

83. Warmolts, J.R., Mendell, J.R., O'Dorisio, T.M., Cataland, S.: Comparison of the Effects of Continuous Subcutaneous Infusion and Split Mixed Injection of Insulin on Nerve Function in Type I Diabetes Mellitus. J Neurol Sci 82: 161-169, 1987.

84. Mendell, J.R., Province, M.A., Moxley, R.T. III, Griggs, R.C., Brooke, M.H., Fenichel, G.M., Miller, J.P., Kaiser, K.K.,Robison, J., Signore, L., Pandya, S., Florence, J.M.: Clinical Investigation of Duchenne Dystrophy. A Methodology for Therapeutic Trials Based on Natural History Controls. Arch Neurol 44:808-812, 1987.

85. Brooke, M.H., Fenichel, G.M., Griggs, R.C., Mendell, J.R., Moxley, R.T. III, Miller, J.P., Kaiser, K.K., Florence, J.M., Pandya, S., Signore, L., King, W., Robison, J., Province, M., Seyfried, W., Mandel, S.: Clinical Investigation of Duchenne Dystrophy. Interesting Results

in a Trial of Prednisone. Arch Neurol 44:812-818,1987.

86. Fenichel, G.M., Brooke, M.H., Griggs, R.C., Mendell, J.R., Miller, J.P., Moxley, R.T. III, Park, J.H., Province, M.A., Florence, J., Kaiser, K.K., King, W.M. , Pandya, S., Robison, J., Signore, L.: Clinical Investigation in Duchenne Muscular Dystrophy: Double-Blind Controlled Trial of Penicillamine and Vitamin E. Muscle & Nerve 11: 1164-1168, 1988.

87. Mendell, J.R., Barohn, R.J., Kissel, J.T.: Chronic Inflammatory Demyelinating Polyneuropathy. Neurology and Neurosurg Update 7:1-7, 1988.

88. Pakalnis, A., Drake, M.E., Barohn, R.J., Chakeres, D.W., Mendell, J.R.: Evoked Potentials in Chronic Inflammatory Demyelinating Polyneuropathy. Arch Neurol 45:1014-1016, 1988.

89. Kao, L., Krstenasky, J., Mendell, J.R., Rammohan, K.W., Gruenstein, E.: Immunological Identification of a High Molecular Weight Protein as a Candidate for the Product of the Duchenne Muscular Dystrophy Gene. Proc Nat Acad Sci 85: 4491-4495, 1988.

90. Hyser, C.L., Mendell, J.R.: Recent Advances in Duchenne and Becker Muscular Dystrophy. Neurol Clin 6:429-454, 1988.

91. Barohn, R.J., Levine, E.J., Olson, J.O., Mendell, J.R.: Gastric Hypomotility in Duchenne's Muscular Dystrophy - A Possible Manifestation of Smooth Muscle Dystrophin Deficiency. N Engl J Med 319:15-18, 1988.

92. Hyser, C.L., Kissel, J.T., Warmolts, J.R., Mendell, J.R.: Scapuloperoneal Neuropathy: A Distinct ClinicalPathological Entity. J Neurol Sci 87:91-102, 1988.

93. Ross, J.F., Sahenk, Z., Hyser, C., Mendell, J.R., Alden, C.L.: Characterization of a Murine Model for Human Bismuth Encephalopathy. Neurotoxicol 9:581-586, 1988.

94. Brooke, M.H., Fenichel, G.M., Griggs, R.C., Mendell, J.R., Moxley, R., Florence, J., King, W.M., Pandya, S., Robison, J., Schierbecker, J., Signore, L., Miller, P., Gilder, B.F., Kaiser, K.K., Mandel, S., Arfken, C.: Duchenne Muscular Dystrophy: Patterns of Clinical Progression and Effects of Supportive Therapy. Neurology 39:475-480, 1989.

95. Kissel, J.T., Riethman, J.L., Omerza, J., Rammohan, K.W.,

Mendell, J.R.: Peripheral Nerve Vasculitis: Immune Characterization of the Vascular Lesions. Ann Neurol 25: 291-298, 1989.

96. Lombes, A., Mendell, J.R., Nakase,H., Barohn, R.J., Bonilla, E., Zeviani, M., Yates, A.J., Omerza, J., Gales, T.L., Nakahara, K., Rizzuto, R., Engel, W.K., DiMauro, S.: Myoclonic Epilepsy and Ragged-Red Fibers (MERRF) with Cytochrome Oxidase Deficiency: Neuropathology, Biochemistry, and Molecular Genetics. Ann Neurol 26:20-33, 1989.

97. Barohn, R.J., Kissel, J.T., Warmolts, J.R., Mendell, J.R.: Chronic Inflammatory Demyelinating Polyradiculoneuropathy: Clinical Characteristics, Course and Recommendations for Diagnostic Criteria. Arch Neurol 46:878-884, 1989.

98. Mendell, J.R., Moxley, R.T., Griggs, R.C., Brooke, M.H., Fenichel, G.M., Miller, J.P., King, W., Signore, L., Pandya, S., Florence, J., Schierbecker, J., Robison, J., Kaiser, K., Mandel, S., Arfken, C., Gilder, B.: Randomized, Double-Blind Six-Month Trial of Prednisone in Duchenne's Muscular Dystrophy. N Engl J Med 320:1592-1597, 1989.

99. Barohn, R.J., Clanton, T., Sahenk, Z., Mendell, J.R.: Recurrent Respiratory Insufficiency and Depressed Ventilatory Drive Complicating Mitochondrial Myopathies. Neurology 40:103-106, 1990.

100. Sahenk, Z., Whitaker, J.N., Mendell, J.R.: Immunocytochemical Evidence of the Retrograde Transport of Intraaxonal Cathepsin D: Possible Relevance to the Dying Back Process. Brain Res 510, 1-6, 1990.

101. Lo, W.D., Barohn, R.J., Bobulski, R.J., Kean, J., Mendell, J.R.:Centronuclear Myopathy and Type I Hypotrophy Without Central Nuclei: Distinct Nosologic Entities? Arch Neurol 47:273-276, 1990.

102. Mendell, J.R., Jiang, X.S., Warmolts, J.R., Nichols, W.C., Benson, M.D.: Diagnosis of Maryland/German Familial Amyloidotic Polyneuropathy (FAP II) Using Allele-Specific Enzymatically Amplified Genomic DNA. Ann Neurol 27:553-557, 1990.

103. Mendell, J.R., Florence, J.: The Use of Manual Muscle Testing in the Assessment of Duchenne Muscular Dystrophy. In: Proceedings of the Workshop on Clinical Trials (Ed) Fenichel, G. Muscle & Nerve 12:16-20, 1990.

104. Mendell, J.R.: Immunosuppressive Therapy in Duchenne Muscular Dystrophy: Considerations for Myoblast Transfer Studies. Adv Exp Med Biol 1990; 287-295.

105. Griggs, R.C., Moxley, R.T., Mendell, J.R., Fenichel, G.M., Brooke, M.H., Miller, P.J., Mandel, S., Florence, J., Schierkicker, J., Kaiser, K.K., King, W., Pandya, S., Robison, J., Signore, L.: Randomized, Double-Blind Trial of Mazindol in Duchenne Dystrophy. Muscle & Nerve 13:1169-1173, 1990.

106. Prior, T.W., Papp, A.C., Snyder, P.J., Highsmith, W.E, Jr., Friedman, K.J., Perry. T.R., Silverman, L.M., Mendell, J.R.: Determination of Carrier Status in Duchenne and Becker Muscular Dystrophies by Quantitative Polymerase Chain Reaction and Allele-Specific Oligonucleotides. Clin Chem 36:2113-2117, 1990.

107. Kissel, J.R., Halterman, R.K., Rammohan, K.W., Mendell, J.R.: The Relationship of Complement-Mediated Microvasculopathy to the Histologic Features and Clinical Duration of Disease in Dermatomyositis. Arch Neurol 48:26-30, 1991.

108. Kissel, J.T,, Burrow, K.L., Rammohan, K.W., Mendell, J.R. and the CIDD Study Group: Mononuclear Cell Analysis of Muscle Biopsies in Prednisone-Treated Duchenne Muscular Dystrophy. Neurology 41:667-672, 1991.

109. Burrow, K.L., Coovert, D.D., Klein, C.J., Bulman, D.E., Kissel, J.T., Rammohan, K.W., Burghes, A.H.M., Mendell, J.R. and the CIDD Study Group: Dystrophin expression and somatic reversion in prednisone-treated and untreated Duchenne dystrophy. Neurology 41:661-666, 1991

110. Griggs, R.C., Moxley, R.T.III, Mendell, J.R., Fenichel, G.M., Brooke, M.H., Pestronk, A., Miller, J.P., and the CIDD Group: Prednisone in Duchenne Dystrophy: A Randomized, Controlled Trial Defining The Time Course and Dose Response. Arch Neurol 48:383-388, 1991.

111. Fenichel, G.M., Mendell,J.R., Moxley, R.T., Griggs, R.C., Brooke, M.H., Miller, J.P., Pestronk, A., Robison, J., King, W., Signore, L., Pandya, S., Florence, J., Schierbecker, J., Wilson,B.: A Comparison of Daily and Alternate-Day Prednisone Therapy in the Treatment of Duchenne Muscular Dystrophy. Arch Neurol 48:575-579, 1991.

112. Barohn, R.J., Sahenk, Z., Warmolts, J.R., Mendell, J.R.: The Bruns-Garland Syndrome ("Diabetic Amyotrophy"): Revisited 100 Years Later. Arch Neurol 48:1130-1136, 1991.

113. Fenichel, G.M., Florecne, J.M., Pestronk, A., Mendell, J.R., Moxley R.T.III, Griggs, R.C., Brooke, M.H., Miller, J.P.,Robison, J., King, W., Signore, L., Pandya, S., Schierbecker, J., Wilson, B.: Long-Term Benefit From Prednisone Therapy in Duchenne Muscular Dystrophy. Neurology 41:1874-1877, 1991.

114. Mendell, J.R., Sahenk, Z., Gales, T., Paul, L.: Amyloid Filaments in Inclusion Body Myositis: Novel Findings Provide Insight Into Nature of Filaments. Arch Neurol, 48:1229-1234, 1991.

115. Cornblath DR, Asbury AK, Albers JW, Feasby TE, Hahn AF, McLeod JG, Mendell JR, Pollard JD, Thomas PK. Research Criteria for Diagnosis of Chronic Inflammatory Demyelinating Polyneuropathy (CIDP). Neurology 41:617-618,1991

116. Weiffenbach, B., Bagley, R.G., Falls, K., Dubois, J., Hyser, C., Storvick, D., Schultz, P., Mendell, J.R., Milner, E.C.B., Jacobsen, S.J., Griggs, R.C.: Framework Multipoint Map of the Long Arm of Human Chromosome 4 and Telomeric Localization of the Gene for Facioscapulohumeral Muscular Dystrophy. Mammalian Genome 3: 143-150,1992.

117. Prior, T.W., Papp, A.C., Synder, P.J., Mendell, J.R.: Germline Mosaicism in Carriers of Duchenne Muscular Dystrophy Muscle & Nerve 15:960-963,1992.

118. Sahenk, Z., Mendell, J.R.: Alterations in slow transport kinetics induced by estramustine phosphate, and agent binding to microtubule-associated proteins. J Neurosci Res 32:481-493,1992

119. Weiffenbach, B., Bagley, R., Falls, K., Hyser, C., Griggs, R., Storvick, D., Schultz, P., Mendell, J., Milner, E., Jacobsen, S.J.: Linkage Analyses of Four 4q Markers in 24 Facioscapulohumeral Muscular Dystrophy (FSHD) Families. Am J Hum Gen 51:416-423,1992.

120. Kissel JT, Mendell JR. Vasculitic neuropathy. Neurol Clin 10:761-81, 1992

121. Klein, C.J., Coovert, D.D., Bulman, D.E., Ray, P.N., Mendell, J.R., Burghes, A.H.M.: Somatic Reversion/Suppression in Duchenne Muscular Dystrophy (DMD): Evidence Supporting a Frame Restoring Mechanism in Rare Dystrophin Positive Fibers. Am J Hum Gen 50:950-959,1992

122. Williams, L.L., Kissel, J.T., Shannon, B.T., Wright, F.S., and Mendell, J.R.: Expression of Schwann Cell and Peripheral T-Cell Activation Epitopes in Hereditary Motor and Sensory neuropathy. J Neuroimmunol 36:147-155, 1992.

123. Winnard, A.V., Hsu, Y.J., Gibbs, R.A., Mendell, J.R., Burghes, AHM.: Identification of a 2 Base Pair Nonsense Mutation Causing a Cryptic Splice in a DMD Patient. Hum Mol Genet 1:645-646, 1992.

124. Kissel JT, Lynn DJ, Rammohan KW, Klein JP, Griggs RC, Moxley VT,Cwik V, Brooke MH, Mendell JR. Mononuclear Cell Analysis of Muscle Biopsies in Prednisone- and Azathioprine- Treated Duchenne Muscular Dystrophy. Neurology;43:532-536, 1993.

125. Sahenk, Z., Sehareseyon, J., Mendell, JR, Burghes, AHM: Gene Delivery to Spinal Motor Neurons. Brain Res 606:126-129, 1993

126. Amato, AA, Barohn, RJ, Sahenk, Z., Tutschka, P., Mendell, JR: Polyneuropathy Complicating Bone Marrow and Solid Organ Transplantation. Neurology 43:1513-1518, 1993.

127. Mendell, JR., Sahenk, Z: Recent Advances in Diagnosis and Classification of Charcot-Marie-Tooth Disease. Current Opinion in Orthopedics. 4 (5):39-45, 1993.

128. Weiffenbach B, Dubois J, Sturvick D, Tawil R, Jacobsen SJ, Gilbert J, Wijmenga C, Mendell JR, Winukur S, Altherr MR, Schultz P, Ulandt S, Fronts RR, Perciak-Vance M, Griggs RC. Mapping the Facioscapulohumeral Muscular Dystrophy Gene is Complicated by Chromosome 4q35 Recombination Events. Nature Genet 4:165-173, 1993.

129. Prior TW, Papp AC, Snyder PJ, Burghes AHM, Bartolo C, Sedra MS, Western LS, and Mendell JR. A Missense Mutation in the Dystrophin Gene in a Duchenne Muscular Dystrophy Patient. Nature Genet 4:357-360, 1993.

130. Prior TW, Papp AC, Snyder PJ, Burghes AHM, Sedra MS, Western LS,

Bartolo C, and Mendell JR. An Exon 44 Nonsense Mutation in Two Duchenne Muscular Dystrophy Brothers Detected by Heteroduplex Analysis. Human Mutation 2:192-195, 1993.

131. Winnard AV, Klein CJ, Coovert DD, Prior TW, Papp AC, Snyder PJ, Bulman DE, Ray PN, McAndrew P, King W, Moxley RT, Mendell JR, and Burghes AHM. Characterization of Translation Frame Exception Patients in Duchenne/Becker Muscular Dystrophy. Human Molec Genet 2:737-744, 1993.

132. Amato AA, Prior TW, Barohn R, Snyder P, Papp A, and Mendell JR. Kennedy's Disease: A Clinicopathologic Correlation with Mutations in the Androgen Receptor Gene. Neurology 43: 791-794, 1993.

133. Prior TW, Papp AC, Snyder PJ, Burghes AHM, Sedra MS, Western LS, Bartolo C, and Mendell JR. Identification of Two Point Mutations and a One Base Deletion in Exon 19 of the Dystrophin Gene by Heteroduplex Formation. Human Molec Genet 2: 311-314, 1993.

134. Griggs RC, Tawil R, Storvick D, Mendell JR, Altherr MR. Genetics of Facioscapulohumeral dystrophy: New mutations in Sporadic Cases. Neurology 43:2369-2370,1993.

135. Barohn RJ, Sahenk Z, Tutschka PJ, Mendell JR. Polyneuropathy complicating bone marrow and solid organ transplantation. Neurology 43:1513-1517,1993

136. Mendell JR. Chronic Inflammatory Demyelinating Polyradiculopathy Annu Rev Med 44:211-219,1993

137. Griggs RC, Moxley RT, Mendell JR, Fenichel GM, Brooke MH, Pestronk A, Miller JP, Cwik S, Pandya S, Robison J, King W, Signore L, Schierbecker J, Florence J, Matheson-Burden N, Wilson B. Duchenne dystrophy: Randomized, controlled trial of prednisone (18 months) and azathioprine (12 months). Neurology 43:520-526,1993

138. Jackson CJ, Barohn RJ, Mendell JR. Acute paralytic syndrome:comparison to Chinese cases. Arch Neurol 50:732-738,1993.

139. Ptacek LJ, Gouw I, Kwiechnski H, McManis P, Mendell JR, Barohn RJ, George AL, Barchi RL, Robertson M, Leppert M. Sodium channel mutations in hyperkalemic periodic paralysis and paramyotonia congenita. Ann Neurol 33:300-307,1993

140. Matsumura K, Burghes AHM, Mora M, Tome FMS, Morandi L, Cornello F, Leturq F, Marc J, Kaplan C, Reinert P, Fardeau M,Mendell JR, Campbell K. Immunohistochemical Analysis of Dystrophin-Associated Proteins in Becker/Duchenne Muscular Dystrophy with Huge In-Frame Deletions in the N-Terminal and Rod Domains of Dystrophin. J Clin Invest 93:99-105, 1994.

141. Sahenk, Z., Barohn, R., New, P., Mendell, JR: Taxol Neuropathy. Electrodiagnostic and Sural Nerve Biopsy Findings. Arch Neurol, 51:726-729, 1994.

142. Barohn RJ, Mendell JR, Brumback RA. Hyaline body myopathy. Neuromuscular Disorders 4 (3): 257-262,1994.

143. Tsujino S, Shanske S, Nonaka I, Eto Y, Mendell JR, Fenichel GM, DiMauro S. Three new mutations in patients with myophosphorylase deficiency (McArdle's Disease). Am J Hum Genet 54:44-52, 1994.

144. Ptacek LJ, Tawil R, Griggs RC, Meola G, McManis P, Barohn RJ, Mendell JR, Harris c, Spitzer R, Santiago F, Leppert MF. Sodium channel mutations in acetozazolamide-responsive myotonia congenita, paramyotonia congenita, and hyperkalemic periodic paralysis. Neurology 43(8):1500-1503 , 1994

145. DiDonato CJ, Morgan K, Carpten JD, Fuerst P, Ingraham SE, Prescott G, McPherson JD, Wirth B, Zerres K, Hurko O, Wasmuth JJ, Mendell JR, Burghes AHM, Simard LR. Association Between Ag1-CA Alleles and Severity of Autosomal Recessive Proximal Spinal Muscular Atrophy. Am J Hum Genet. 55:1218-1229, 1994.

146. Prior TW, Bartolo C, Papp AC, Snyder PJ, Sedra MS, Burghes AHM, Mendell JR. Identification of a Missense Mutation, Single Base Deletion and a Polymorphism in the Dystrophin Exon 16. Hum Molec Genet 3:1173-1174, 1994.

147. Lynn DJ, Woda RP, Mendell JR. Respiratory Dysfunction in Muscular Dystrophy and other Myopathies. Clin Chest Med. 15:661-674,1994.

148. Tan E, Lynn D.J., Amato, AA, Kissel JT, Rammohan KR, Sahenk Z, Warmolts, JR, Jackson CE, Barohn RJ, Mendell JR. Immunosuppressive Treatment of Motor Neuron Syndromes: Attempts to Distinguish a Treatable Disorder. Arch Neurol 51:194-200, 1994.

149. Prior, TW, Papp AC, Snyder PJ, Sedra MS, Western LS, Bartolo C, Mendell, JR. Heteroduplex Analysis of the Dystrophin Gene: Application to Point Mutation and Carrier Detection. American J Med Genet, 50: 68-73, 1994.

150. Burghes, AHM, Ingraham, SE, Kote-Jarai Z, Rosenfeld S, Herta N, Nadkarni N, DiDonato C, Carpten J, Hurko O, Florence J, Moxley RT, Coblen J, Mendell JR. Linkage Mapping of the Spinal Muscular Atrophy Gene. Human Genet, 93: 305-312, 1994.

151. Nadkarni, N., Prior, TW, Mendell, JR. The Impact of Molecular Genetics on the Care of Patients with Muscle Disease. Current Opinion in Neurol, 7:435-447, 1994.

152. Tan E, Lynn DJ, Amato AA, Kissel JT, Rammohan KW, Sahenk Z, Warmolts JR, Jackson CE, Barohn RJ, Mendell JR. Immunosuppressive Treatment of Motor Neuron Syndromes. Arch Neurol 51:194-200, 1994.

153. Lynn DJ, Woda RP, Mendell JR. Respiratory dysfunction in muscular dystrophy and other myopathies. Clin chest Med 1994;15:661-674.

154. Sahenk Z, Seharaseyon J, Mendell JR. CNTF potentiates peripheral nerve regeneration. Brain Res 1994;655:246-250.

155. Tawil R, McDermott MP, Mendell JR, et al. Facioscapulohumeral muscular dystrophy (FSHD): design of natural history study and results of baseline testing. Neurology 1994;44:442-446.

156. Guida M, Marger RS, Papp AC, Snyder PJ, Sedra MS, Kissel JT, Mendell JR, Prior TW. A Molecular Protocol for Diagnosing Myotonic Dystrophy. Clinical Chemistry, 41:69-72, 1995.

157. Winnard AV, Mendell JR, Prior TW, Florence J, Burghes AHM. Frameshift Deletions of Exons 3-7 and Revertant Fibers in Duchenne Muscular Dystrophy: Mechanisms of Dystrophin production. Am J Hum Genet, 68: 158-166, 1995.

158. Thompson TG, DiDonato CJ, Simard RL, Burghes AHM, Crawford TO, Ohatte C, Mendell JR, Wasmuth JJ. A novel cDNA detects homozygous microdeletions in greater than 50% of type 1 spinal muscular atrophy patients.Nature Genetics, 9:56-62, 1995.

159. Mendell JR, Sahenk Z, Prior TW. The Childhood Muscular Dystrophies: Diseases sharing a common pathogenesis of membrane instablitiy. J Child Neurology 10:150-159,1995.

160. Nadkarni N, Freimer M, Mendell JR. Amyloidosis causing a progressive myopathy. Muscle & Nerve, 18:1016-1018,1995.

161. Tsao Cy, Mendell JR, Lo WD, Batley RJ. Critical illness polyneuropathy in a two-year-old girl with hemmorrhagic shock encephalopathy syndrome. J Child Neurol 1995;10:486-488

162. Mendell JR, Kissel JT, Amato AA, King W, Signore RN, Prior TW,Sahenk Z, Benson BA, McAndrew PE, Rice R, Nagaraja H, Stephens R, Lantry L, Morris GE, Burghes AHM. Randomized,double-blind, one year trial of myoblast transfer in Duchenne muscular dystrophy. N Engl J Med 333:832-838, 1995.

163. Kissel JT, Mendell JR. Neuropathies associated with monoclonal gammopathies. Neuromuscular Disorders Neuromuscular Disord 1995;47:119-122

164. Barohn RJ, Amato AA, Sahenk Z, Kissel JT, Mendell JR. Inclusion Body Myositis: Explanation for poor responsive to Immunosuppressive therapy. Neurology 45:1302-04, 1995.

165. Mendell JR. Mitochondrial Myopathy in the elderly: Exaggerated aging in the pathogenesis of disease Ann Neurol. 37:3-4,1995.

166. Guida M, Marger RS, Papp AC, Snyder PJ, Sedra MS, Kissel JR, Mendell JR, Prior TW. A molecular protocol for diagnosing myotonic dystrophy. Clin Chem 41:69-72, 1995.

167. Griggs RC, Tawil R, McDermott, Forrester J, Figlewicz D,Weiffenbach B. The FSH-DY Group. Monozygotic twins with facioscapulohumeral muscular dystrophy (FSHD): implications for genotype/phenotype correlation. Muscle & Nerve Supp 2:S50-S55, 1995.

168. Prior TW, Bartolo C, Pearl DK, Papp AC, Snyder PJ, Sedra MS, Burghes, AHM, Mendell JR. Spectrum of small mutations in the dystrophin coding region. Am J Hum Genet 57:22-23, 1995.

169. Griggs RC, Askansas V, DiMauro S, Engel A, Karpati G, Mendell JR, Rowland LP. Inclusion Body Myositis and Myopathies. Ann Neurol 38:705-713,1995.

170. Prior TW, Bartolo C, Papp AC, Snyder PJ, Sedra MS, Burghes AHM, Mendell JR. Nonsense mutations in a Becker Muscular Dystrophy and an intermediate patient. Human Mutation 7:72-75, 1996.

171. Tawil R, Forrester J, Griggs RC, Mendell JR, Kissel JT, McDermott M, King W, Weiffenbach B, Figlewicz D, and FSH-Dy Group. Evidence for anticipation and association of deletion size and severity in fascioscapulohumeral muscular dystrophy. Ann Neurol 1996;39:744-748

172. Fouad G, Dalakas M, Servidei S, Mendell JR, Van den Bergh P, Angelini C, Alderson K, Griggs RC, Tawil R, Gregg R, Hogan K, Powers PA, Weinberg N, Malonee W, Ptacek LJ. Genotype-phenotype correlations of the DHP receptor alpha 1-subunit gene mutations in causing hypokalemic periodic paralysis. Neuromuscular disoders 1997;7:33-38.

173. Bartolo C, Papp AC, Snyder PJ, Sedra MS, Burghes AHM, Hall CD, Mendell JR, Prior TW. A novel splice site mutation in a Becker muscular dystrophy patient. J Med Genet. 1996;33:324-327

174. Santorelli FM, Sciacco M, Shanske S, Griggs RC, Mendell JR, Bonilla E, DiMauro S. Mitochondrial DNA deletion in Patients with inclusion body myositis. Ann Neurol 1996;39:789-795

175. Mendell JR, Garcha TS, Kissel JT. The immunopathogenic role of complement in human muscle disease. Current Opinion in Neurol 1996;9:226-234.

176. Parsons DW, McAndrew PE, Monani UR, Mendell, Burghes AHM, Prior TW. An 11 base pair duplication in exon 6 of the SMN gene produces a type I spinal muscular atrophy (SMA) phenotype:further evidence for SMN as the primary SMA-determining gene. Hum Mol Genet 1996;5:1727-1732.

177. DiDonato CJ, Ingraham SE, Mendell JR, Prior TW, Lenard S, Moxley R, Florence J, Burghes AHM. Deletion and conversion in SMA patients: is there a relationship to severity? Ann Neurol 1997;41:230-237.

178. Griggs RC, Tawil R, Brown RH, Shapiro BE, Ptacek LJ, McManis PG, Dalakas MC, Mendell JR, Hahn AF, McDermott MP, and the Working Group on Periodic Paralysis. Recent Advances in Clinical Neurophysiology. 1996;160-169.

179. Sciacco M, Gasparo-Rippa P, Vu TH, Tanji K, Shanske S, Mendell JR, Schon EA, DiMauro S, Bonilla E. Study of mitochondrial DNA depletion in muscle by single-fiber PCR. Muscle Nerve 1998;21:1374-1381.

180. Erdem S, Mendell JR. Contribution of nerve biopsy findings to the diagnosis of disabling neuropathy in the elderly. A retrospective review of 100 consecutive patients. Neurology Network Commentary 1997;1:80-84

181. The FSH-DY Group. A prospective, quantitative study of the natural history of facioscapulohumeral muscular dystrophy (FSHD): implications for therapeutic trials. Neurology 1997;48:38-46.

182. Tawil R, McDermott MP, Pandya S, King W, Kissel J, Mendell JR, Griggs RC. A pilot trial of prednisone in facioscapulohumeral muscular dystrophy (FSHD). Neurology 1997;48:46-49.

183. Prior TW, Bartolo C, Papp AC, Snyder PJ, Sedra MS, Burghes AHM, Kissel JT, Luquette MH, Tsao C-Y, Mendell JR. Dystrophin expression in a Duchenne muscular dystrophy patient with a frame shift deletion. Neurology 1997;48:486-488.

184. Coovert DD, Le TT, McAndrew PE, Strasswimmer J, Crawford TO, Mendell JR, Coulson SE, Androphy EJ, Prior TW, Burghes AHM. The survival motor neuron protein in spinal muscular atrophhy. Hum Mol Genet 1997;6:1205-1214.

185. Bradley WG, Daube J, Mendell JR, Posner J, Richman D, Troost BT, Swift TR.Quality improvement in neurology residency programs. Neurology 1997;49:1205-1207.

186. Kissel JT, Mendell JR, Griggs RC, McDermott M, Tawil R. Pilot-trial of albuteral in facioscapulohumeral muscular dystrophy. Neurology 1998;50:1402-6

187. Menell JT, Panicker SG, Tsao C-Y, Feng B, Sahenk Z, Marzluf GA, Mendell JR. Novel compound heterozygous laminin alpha2-chain (LAMA2)gene mutations (exon 4 nonsense and exon 54 frameshift) in congenital muscular dystrophy. Hum Mutation Mutation in Brief # 159 1997

188. McAndrew PE, Parsons DW, Simard LR, Rochette C, Ray PN, Mendell JR, Prior T, Burghes AHM. Idendtication of proximal spinal

muscular atrophy carriers and patients by analysis of SMN^T and SMN^c gene copy number. Am J Hum Genet 1997;60:1411-1422.

189. FSHdy Consortium. Facioscapulo-humeral dystrophy: a distinct regional myopathy with a novel molecular pathogenesis. Ann Neurol 1998;43:279-82

190. Erdem S, Freimer ML, O'Dorisio T, Mendell JR. Procainamide-induced chronic inflammatory demyelinating polyradiculoneuropathy. Neurology 1998;50:824-825.

191. Mendell JR. Charcot-Marie-Tooth Neuropathies and related disorders. Seminars in Neurology 1998;18:41-48.

192. Erdem S, Mendell JR, Sahenk Z. Fate of Schwann cell in CMT1A and HNPP: Evidence for apoptosis. J Neuropath Exp Neurol 1998;57:635-642.

193. Tawil R, Figlewicz DA, Griggs RC, Weiffenbach B, FSH Consortium. Facioscapulo-humeral dystrophy: a distinct regional myopathy with a novel molecular pathogenesis. Ann Neurol 1998;43:279-82

194. Parsons DW, McAndrew PE, Iannaccone ST, Mendell JR, Burghes AH, Prior TW. Intragenic telSMN mutations: frequency, distribution, evidence of a founder effect, and modification of the spinal muscular atrophy phenotype by cenSMN copy number. Am J Hum Genet 1998;63:1712-1723.

195. Kissel JT, Mendell JR. Muscular dystrophy: historical overview and classification. Seminars Neurology 1999;19:5-9.

196. Sue CM, Bruno C, Andreu AL, Cargan A, Mendell JR, Tsao C-Y, Luquette M,Paolicchi J, Shanske S, DiMauro S, De Vivo DC. Infantile encephalopathy associated with the MELAS A3243G mutation. J Pediatr 1999;134:696-700

197. Vu TH, Sciacco M, Tanji K, Nichter C, Bonilla E, Chatkupt S, Maertens P, Shanske S, Mendell J, Koenigsberger MR, Sharer L, Shcon EA, DiMauro S, De Vivo DC. Clinical manifestations of mitochondrial DNA depletion. Neurology 1998;50:1783-1790.

198. Tsao CY, Mendell JR. The childhood muscular dystrophies: Making order out of chaos. Seminars Neurology 1999;19:9-24.

199. Kissel JT, Mendell JR. Muscular dystrophy: historical overview and classification. Seminars Neurology 1999;19:5-9.

200. Sahenk Z, Chen L, Mendell JR. The effects of PMP22 duplications and deletions on the axonal cytoskeleton. Ann Neurol 1999;45:16-24.

201. Orrell RW, Forrester JD, Tawil R, Kissel JT, Mendell JR, Figlewicz DA, Griggs RC. Definitive molecular diagnosis of facioscapulohumeral muscular dystrophy. Neurology 1999;52:1822-1826.

202. Periquet MI, Novak V, Collins MP, Nagaraja HN, Erdem S, Nash SM Freimer ML, Sahenk Z, Kissel JT, Mendell JR. Painful sensory neuropathy. Prospective evaluation using skin biopsy. Neurology 1999;53:1-10.

203. Sahenk Z, Mendell JR. Alterations in Nodes of Ranvier and Schmidt-Lanterman Incisures in Charcot-Marie-Tooth Neuropathies NY Acad Sciences 1999;883:508-517.

204. Stedman H, Wilson JM, Finke R, Klenke A-L, Mendell JR. Clinical Protocol.Phase I clinical trial utilizing gene therapy for limb girdle muscular dystrophy: α–, β–,γ–, or δ–sarcoglycan gene delivered with intramuscular instillations of adeno-associated vectors. Human Gene Therapy 2000;11:777-790.

205. Tawil R, McDermott MP, Brown R, Shapiro B, Ptacek LJ, McManis PG, Dalakas MC, Spector S, Mendell JR, Hahn AF, Griggs RC. Randomized trials of dichlorphenamide in the Periodic Paralyses. Ann Neurol 2000;47:46-53

206. Feng B, Chen L, Drmanovic Z, Kakabadze I, Mendell JR, Marzluf GA, Sahenk Z. Intracellular processing and toxicity of the truncated androgen receptor: nuclear congophilia-associated cell death. J Neuropath Exp Neurol 2000;59:652-663.

207. Lindenbaum H, Kissel JT, Mendell JR. Treatment strategies for Guillain-Barre syndrome and chronic inflammatory demyelinating polyradiculneuropathy. Neuorologic Clinics 19:1-18,2001

208. Collins MP, Mendell JR, Sahenk Z, Periquet I, Amato A, Gronseth GS, Barohn RJ, Jackson CE, Kissel JT. Superficial peroneal nerve/peroneus brevis muscle biopsy in suspected vasculitic neuropathy: diagnostic yield, characterization of vasculitis cohort, and clinicopathologic predictors. Neurology 2000;55:636-643.

209. Reynolds JE, Mendell JR. Another approach to ventilatory failure in neuromuscular disease. Neurology 2000;55:611-612

210. Tsao CY, Mendell JR, Lo WD, Luquette M, Rusin J. Mitochondrial respiratory-chain defects presenting as nonspecific features in children. J Child Neurol 2000;15:445-448.

211. Tsao CY, Mendell JR, Lo WD, Luquette M, Rennebohm R. Myasthenia gravis and associated autoimmune diseases in children. J Child Neurol 2000;15:767-769.

212. Tsao CY, Mendell JR, Luquette M, Dixon B, Morrow G. Mitochondrial DNA depletion in children. J Child Neurol 2000;15:822-824.

213. Barresi R, Moore SA, Stolle CA, Mendell JR, Campbell KP. Expression of gamma-sarcoglycan in smooth muscle. J Cell Biol 2000;275:38554-38560.

214. Mendell JR, Barohn RJ, Freimer ML,JT Kissel, et al. Randomized Controlled Trial of IVIg in Untreated Chronic Inflammatory Demyelinating Polyradiculoneuropathy. Neurology 2001;56:445-449.

215. Mendell JR. Congenital muscular dystrophy: In search of a definition after 98 years. Neurology 2000;56:993-995.

216. Musumeci O, Naini A, Slonim AE, Slavin N, Hadjigeorgiou GL, Krawiecki N, Weissman BM,C-Ysao C-Y, Mendell JR, Shanske S, DeVivo DC, Hirano M, DiMauro S. Familial cerebellar ataxia with muscle coenzyme Q 10 deficiency. Neurology 2001;56:849-855.

217. Tsao CY, Mendell JR, Barthalomew D. High mtDNA T8993G mutation (>90%) without typical features of Leigh's syndrome and NARP syndrome. J Child Neurol 2001;16:533-535.

218. Mendell JR. New Insights, Current Concepts In the Pathophysiology of Inflammatory Myopathies. Adv Immunotherapy.2001;8:12-16.

219. Novak V, Freimer MI, Kissel JT, Sahenk Z, Periquet IM, Nash SM, Collins MP, Mendell JR. Autonomic impairment in painful neuropathy. Neurology 2001;56:861-869.

220. Fenichel GM, Griggs RC, Kissel JT, Kramer TI, Mendell JR, Moxley RT, Pestronk A, Sheng K, Florence J, King WM, Pandya S, Robison VD. An efficacy and safety trial of oxandrolone in the treatment of Duchenne dystrophy. Neurology 2001;56:1075-1079.

221. Mendell JR, Buzin CH, Feng J, Yan J, Serrano C, Sangani DS, Prior TW, Sommer SS. Diagnosis of Duchenne Dystrophy by Enhanced Detection of Small Mutations. Neurology 2001;57:645-50.

222. Kissel JT, McDermott MP, Mendell JR, King WM, Pandya S, Griggs RC, Tawil R. Randomized, double-blind, placebo-controlled trial of albuteral in facioscapulohumeral dystrophy. Neurology 2001;57:1434-1440.

223. Miller RG, Moore DH, Dronsky V, Kissel JT, Mendell JR, et al. and SMA Study Group. A placebo-controlled trial of gabapentin in spinal muscular atrophy. J Neurol Sci 2001;191:127-131.

224. Lindenbaum Y, Nahman SN, Mendell JR. Fatal Group A Streptococcal Necrotizing Myopathy. J Clin Neuromusc Dis 2002;3:113-115.

225. Tsao CY, Mendell JR, Freimer M, Kissel JT. Lambert Eaton myasthenic syndrome in children. J Child Neurol 2002;17:74-76.

226. Tsao C-Y, Mendell JR. Combined partial deficiencies of carnitine palmitoyltransferase II and mitochondrial complex I presenting as increased creatine kinase level. J Child Neurol 2002;17:304-306.

227. Cohn RD, Henry MD, Michele DE, Baresi R, Saito F, Moore SA, Flanagan JD, Skwarchuk MW, Robbins ME, Mendell JR, Williamson R, Campbell KP. Disruption of Dag1 in differentiated skeletal muscle reveals a role for dystroglycan in muscle regeneration. Cell 2002;110:1-20.

228. Tsao C-Y, Mendell JR, Freimer MI, Kissel JT. Lambert-Eaton myasthenic syndrome in children. J Child Neurol 2002;17:74-76.

229. Wolfe GI, Barohn RJ, Foster BM, Jackson CE, Kissel JT, Day JW, Thornton CA, Nations SP, Bryan WW, Amato AA, Freimer ML, Parry GJ, Mendell JR. Randomized, controlled trial of intravenous immunoglobulin in myasthenia gravis. Muscle Nerve 2002;26:549-552.

230. Flanigan KM, von Niederausern A, Dunn DM, Alder J, Mendell JR, Weiss RB. Rapid Direct Sequence Analysis of the Dystrophin Gene. Am J Hum Genet 2003;72:931-9

231. Collins MP, Periquet MI, Mendell JR, Sahenk Z, Nagaraja HN, Kissel.JT. Nonsystemic vasculitic neuropathy: insights from a clinical cohort. Neurology 2003;61:623-630

232. Mendell JR, Sahenk Z. Painful sensory neuropathy. New Engl J Med 2003;348:1243-1255.

233. Wicklund MW, Mendell JR. Limb-girdle muscular dystrophies. Our ever expanding knowledge. J Clin Neuromusc Dis 2003;5:12-28.

234. Mendell JR, Miller A. Gene Transfer for Neurological Disease: Agencies, Policies, and Process. Neurology 2004:63:2203-2208

235. Buzin C, Feng, J, Yan J, Scaringe W, Liu Q, Mendell JR, Sommer SS. Mutation Rates in the Dystrophin Gene: A Super Hotspot of Mutation at a CpG Dinucleotide. Hum Mutation 2005;25:177-88.

236. Yan J, Feng J, Buzin CH, Scaringe W, Liu Q, Mendell JR, den Dunnen J, Sommer SS.. Three-tiered noninvasive diagnosis in 96% of patients with Duchenne muscular dystrophy (DMD). Hum Mutation 2004;23:203-204.

237. Sahenk Z, Nagaraja HN, McCracken BS, King WM, Freimer ML, Cederbaum JM, Mendell JR. NT-3 Promotes Nerve Regeneration and Sensory Improvement in CMT1A Mouse Models and in Patients. Neurology 2005;65:681-689.

238. Barohn RJ, Herbelin L, Kissel JT, King W, McVey AL, Saperstein DS, Mendell JR. Pilot trial of etanercept in the treatment of inclusion-body myositis. Neurology 2006; 66 (2Suppl 1):S123-124.

239. Mendell JR, Clark KR. Challenges for Gene Therapy for muscular dystrophy. Current Neurology and Neuroscience Reports 2006;6:47-56.

240. Mendell JR, Clark KR. Risks, benefits, and consent in the age of gene therapy. Neurology 2006; 6:47-56.

241. Tsao CY, Mendell JR. Coexisting muscular dystrophies and epilepsy in children. J Child Neurol 2006;21:148-50.

242. Mendell JR, Boue DR, Martin PT. The congenital muscular dystrophies: recent advances and molecular insights. Pediatric and Developmental Pathology 2006;9:427-443.

243. Miller TM, Kim SH, Hester M, Umapathi P, Arnson H, Rizo L, Mendell JR, Gage FH, Cleveland DW, Kaspar BK. Gene transfer demonstrates that muscle is not a primary target for non-cell autonomous toxicity in familial ALS. Proc Natl Acad Sci, USA. December 2006;103:19546-51.

244. Moore SA, Shilling CJ, Westra S, Wall C, Wicklund MP, Stolle C, Brown CA, Michele DE, Piccolo F, Winder TL, Stence A, Barresi R, King N, King W, Florence J, Campbell KP, Fenichel GM, Stedman JJ, Kissel JT, Griggs RC, Pandya S, Mathews KD, Pestronk A, Serrano C, Darvish D, Mendell JR. Limb girdle muscular dystrophy in the United States. J Neuropath Exp Neurol 2006;65:995-1003.

245. Mendell JR, Csimma C, McDonald CM, Escolar DM, Janis S, Porter JD, Hesterlee SE, Howell RR. Challenges in drug development for muscle disease: A Stakeholder's meeting. Muscle Nerve

246. [illegible] R, Nagaraja H N, Matkovic V, Landoll J, Hoyle C, Mendell JR, Kissel, JT. Orthopedic outcomes of long-[illegible] corti[illegible]osteroid treatment in Duchenne muscular [illegible]logy 2007;68:1607-1613.

247. Rodino-[illegible] Chicoine L, Kaspar B, Mendell JR. Gene Therapy for Duchen[illegible]scular Dystrophy: Expectations and Challenges. Arch Neurol [illegible]07;64:1-6

248. Tsao C-Y, Men[illegible]l JR. Autistic disorder in 2 children with mitochondrial disorders. J Child Neurol 2007;22:1121-1123

249. Rodino-Klapac L, Janssen PML, Montgomery CL, Coley BD, Chicoine LG, Clark KR, Mendell JR. A Translational Approach for Limb Vascular Delivery of the Micro-dystrophin Gene without High Volume or High Pressure for Treatment of Duchenne Muscular Dystrophy. J Transl Med 2007;5-45

250. Rodino-Klapac LR, Lee J-S, Mulligan RC, Clark KR, Mendell JR. Lack of toxicity of alpha-sarcoglycan overexpression supports clinical gene transfer in LGMD2D. Neurology. 2008;71:240-247.

251. Rosales XQ, Shilling C, Wall C, Chu M-L, Mendell JR. Fidelity of Serum Gamma-glutamyl transferase in differentiating skeletal muscle from liver disease in Duchenne muscular dystrophy. J Child Neurol 2008;23:748-751.

252. Kannanayakal TJ, Mendell JR, Kuret J. Casein kinase 1 alpha associates with the tau-bearing lesions of inclusion body myositis. Neurosci Lett 2008;431:141-145

253. Wagner KR, Fleckenstein JL, Amato AA, Barohn RJ, Bushby K, Escolar DM, Flanigan KM, Pestronk A, Tawil R, Wolfe GI, Eagle M, Florence JM, King WM, Pandya S, Straub V, Juneau P, Meyers K, Csimma C, Araujo T, Parsons SA, Wozney JM, LaVallie ER,

Mendell JR. A Phase I/II trial of MYO-029 in adult subjects with muscular dystrophy. Ann Neurol 2008;63:543-545.

254. Haidet AM, Rizo L, Handy C, Umapathi P, Eagle A, Shilling C, Boue D, Martin PT, Sahenk Z, Mendell JR, Kaspar BK. Long-term enhancement of skeletal muscle mass and strength By single gene administration of myostatin inhibitors. Proc Nat Acad Sci USA 2008;105:4318-4322.

255. Guenther U-P, Varon R, Stephani U, Tsao CY, Mendell JR, Lutzkendorf S, Hubner C, von Au K, Jablonka S, Dittmar G, Heinemann U, Schuetz S, Schuelke M. Clinical variability in Distal Spinal Muscular Atrophy type 1 (DSMA1): Determination of steady-state IGHMBP2 protein levels in five patients with infantile and juvenile disease. J Molec Med 2009;87:31-41.

256. Tsao C-J, Mendell JR, Sahenk Z, Rusin J, Boue D. Hypotonia, weakness, and pontocerebellar hypoplasia in siblings. Semin Pediatr Neurol 2008;15:151-153.

257. Thrush P, Allen HD, Viollet L, Mendell JR. Re-examination of the Electrocardiogram in Boys with Duchenne Muscular Dystrophy and Correlation with its Dilated Cardiomyopathy American Journal of Cardiology. Am J Cardiology 2009;103(2):262-5.

258. Elsheikh B, Prior T, Zhang X, Miller R, Kolb S, Moore D, Bradley DM, Barohn R, Bryan W, Gelinas D, Iannaccone S, Leshner R, Mendell JR, Mendoza M, Russman B, Smith S, King PT, Kissel JT. An Analysis of Disease Severity Based on SMN2 Copy Number in Adults with Spinal Muscular Atrophy Muscle Nerve. 2009;40:652-6.

259. Rodino-Klapac L, Haidet AM, Kota J, Handy C, Kaspar BK, Mendell JR. Inhibition of myostatin with emphasis on follistatin as therapy for muscle disease. Muscle Nerve 2009;39:283-96

260. Martin PT, Xu R, Rodino-Klapac LR, Oglesbay E, Camboni M, Montgomery CL, Shontz K, Chicoine LG, Clark KR, Sahenk Z, Mendell JR, Janssen PML. Overexpression of Galgt2 in skeletal muscle prevents injury resulting from eccentric contractions in both mdx and wild type mice. Am J Physiol Cell Physiol 2009; 296:C476-488.

261. Elsheikh B, Kissel JT, Christoforidis G Wicklund M, Kehagias DT, Chiocca EA, Mendell JR. Spinal angiography and epidural venography in juvenile muscular atrophy of the distal arm "Hirayama disease". Muscle Nerve 2009;40:206-12.

262. Mendell JR, Rodino-Klapac LR, Rosales-Quintero X, Kota J, Coley BD, Galloway G, Craenen JM, Lewis S, Malik V, Shilling C, Byrne BJ, Conlon T, Campbell KJ, Bremer WG, Viollet L, Walker CM, Sahenk Z, Clark KR. LGMD2D gene therapy restores alpha-sarcoglycan and associated proteins. Ann Neurol 2009;66:290-297

263. Viollet L, Gailey S, Thornton DJ, Friedman N, Flanigan KM, Mahan JD, Mendell JR. Utility of Cystatin C to monitor renal function in Duchenne muscular dystrophy. Muscle Nerve 2009;;40:438-42.

264. Kota J, Chivukula RR, O'Donnell KA, Wentzel EA, Montgomery CL, Hwang H-W, Chang T-C, Vivekanandan P, Torbenson M, Clark KR, Mendell JR, Mendell JT. Therapeutic delivery of miR-26a inhibits cancer cell proliferation and induces tumor-specific apoptosis. Cell 2009;137;1005-1017

265. Flanigan KM, Dunn D, von Niederhausern A, Soltanzadeh P, Gappmaier E, Howard MT, Hart K, Sampson J, Bromberg M, Mendell JR, et al Mutational Spectrum of DMD Mutations in Dystrophinopathy Patients: Application of Modern Diagnostic Techniques to a Large Cohort. Human Mutat 2009 30:1657-66

266. Kaspar RW, Allen HD, Ray WC, Alvarez CE, Kissel JT, Pestronk A, Weiss RB, Flanigan KM, Mendell JR, Montanaro F. Analysis of dystrophin deletion mutations predicts age of cardiomyopathy onset in Becker Muscular Dystrophy. Circulation: Cardiovascular Genet 2009 2:544-51.

267. Flanigan KM, Dunn DM, von Niederman A, Howard MT, Mendell JR, Connolly A, Saunders C, Modricin, A et al. DMD Trp3X nonsense mutation associated with a founder effect in North American families with mild Becker muscular dystrophy. Neuromuscul Disord 2009; 19:743-8 Sep 28 Epub ahead of print.

268. Rodino-Klapac LR, Montgomery CL, Bremer WG, Malik V, Shontz KM, Davis N, Sprinkle S, Campbell KJ, Sahenk Z, Clark KR, Walker CM, Mendell JR, Chicoine LG. Persistent expression of FLAG tagged micro-dystrophin in non-human primates with intramuscular and vascular approaches. Mol Ther 2010;18:109-17. Epub 2Nov 10ePUB Nov 2009

269. Kota J, Handy CR, Haidet A, Montogomery CL, Eagle A, Rodino-Klapac LR, Tucker D, Shilling CJ, Therlfall W, Walker CM, Weisbrode SE, Janssen PML, Clark KR, Sahenk Z, Mendell JR, Kaspar BK. Follistatin Gene Delivery Enhances Muscle Growth

and Strength in Nonhuman Primates. Sci Transl Med 2009;1:6ra15

270. Flanigan KM, Dunn DM, von Niederhausern A, Soltanzadeh P, Gappmaier E, Howard MT, Sampson JB, Mendell JR, et al. United Dystrophinopathy Project Consortium. Mutational spectrum of DMD mutations in dystrophinopathy patients: application of modern diagnostic techniques to a large cohort. Hum Mutat 2009;30:1657-1666.

271. Rosales XQ, Gastier-Foster JM, Lewis S, Malik V, Thrush DL, Astbury C, Pyatt R, Reshmi S, Sahenk Z, Mendell JR. Novel Diagnostic Features of Dysferlinopathies. Muscle Nerve 2010;42:14-21

272. Malik V, Rodio-Klapac LR, Viollet L, Wall C, King W, Al-Dahhak R, Lewis S, Shilling CJ, Kota J, Serrano-Munuera C, Hayes J, Mahan JD, Campbell KJ, Banwell B, Dasouki M, Watts V, Sivakumar K, Bien-Willner R, Flanigan KM, Sahenk Z, Barohn RJ, Walker CM, Mendell JR. Gentamicin-induced readthrough of stop codons in Duchenne muscular dystrophy. Ann Neurol 2010;67:771-80.

273. Soltanzadeh P, Friez MJ, Dunn D, von Niederhausern A, Gurvich OL, Swoboda KJ, Sampson JB, Pestronk A, Connolly AM, Florence JM, Finkel RS, Bonnemann CG, Medne L, Mendell JR, et al. Clinical and genetic characterization of manifesting carriers of DMD mutations. Neuromuscul Disord 2010;20:499-504.

274. Mendell JR, Campbell K, Rodino-Klapac L, Sahenk Z, Shilling C, Lewis S, Bowles D, Gray S, Chengwen L, Galloway G, Malik V, Coley B, Clark R, Li J, Xiao X, Samulski J, McPhee SW, Samulski RJ, Walker CM. Dystrophin Immunity Revealed by Gene Therapy in Duchenne Muscular Dystrophy. N Engl J Med 2010;363:1429-37

275. Saechao C, Valles-Ayoub Y, Esfandiarifard S, Haghighatgoo A, No D, Shook S, Mendell JR, Rosales-Quintero X, Felice KJ, Morel CF, Pietruska M, Darvish D. Novel GNE mutations in hereditary inclusion body myopathy patients of non-Middle Eastern descent. Genet Test Mol Biomarkers. 2010;14:157-62

276. Mendell JR, Rodino-Klapac LR, Malik V. Molecular therapeutic strategies targeting Duchenne muscular dystrophy. J Child Neurol 2010 May 24 ePUB

277. Mendell JR, Rodino-Klapac LR, Rosales XQ, Coley BD, Galloway G, Lewis S, Malik V, Shilling C, Byrne BJ, Conlon T, Campbell KJ, Bremer WG, Taylor LE, Flanigan KM, Kota J, Sahenk Z, Walker CM,

Clark KR. Sustained alpha-sarcoglycan gene expression following gene transfer in LGMD2D. Ann Neurol 2010;68:629-638.

278. Flanigan KM, Dunn DM, von Niederhausern A, Soltanzadeh P, Howard MT, Sampson JB, Swoboda KJ, Bromberg MB, Mendell JR, et al. Nonsense mutation-associated Becker muscular dystrophy: Interplay between exon definition and splicing regulatory elements within the DMD gene. Hum Mutat 2010; Dec 16 Epub

279. Scharner J, Brown CA, Bower M, Iannaccone ST, Khatri IA, Gordon E, Felice K, Crowe CA, Grossman C, Meriggioli MN, Asamoah A, Gnocchi VF, Ellis JA, Mendell JR, Zammit PS. Novel LMNA mutations in patients with Emery-Dreifuss muscular dystrophy and functional characterization of four LMNA mutations. Human Mutation 2011;32:152-167.

280. Peterson JM, Kline W, Canan BD, Ricca DJ, Kaspar B, Delfin DA, DiRienzo K, Clemens PR, Robbins PD, Baldwin AS, Flood P, Kaumaya P, Frietas M, Kornegay JN, Mendell JR, Rafael- Fortney JA, Guttridge DC, Janssen PML. Peptide-based inhibition of NF-κB rescues diaphragm muscle contractile dysfunction in a murine model of Duchenne muscular dystrophy. Molec Med 2011;17:508-517.

281. Sahenk Z, Mendell JR. The muscular dystrophies: distinct pathogenic mechanisms invite novel therapeutic approaches. Current Rheumatology Reports 2011;13:199-207

282. Rodino-Klapac LR, Montgomery CL, Mendell JR, Chicoine LG. AAV-mediated gene therapy to the isolated limb in rhesus macaques. Method Mol Biol 2011;709:287-298.

283. Brown CA, Scharner J, Felice K, Meriggioli MN, Tarnopolsky M, Bower M, Zammit PS, Mendell JR, Ellis JA. Novel and recurrent EMD mutations in patients with Emery-Dreifuss muscular dystrophy, identify exon 2 as a mutation hot spot. J Hum Genet in press

284. Rosales XQ, Moser S, Tran T, McCarthy B, Dunn N, Habib P, Simonetti OP, Mendell JR, Raman, SV. Cardiomyopathy by CMR in Limb Girdle Muscular Dystrophy 2B and 2I. J Cardiovasc Magn Reson 2011; Aug 4 Epub

285. Bevan AK, Duque S, Foust KD, Morales PR, Braun L, Schmelzer L, Chan CM, Mccrate M, Chicoine LG, Coley BD, Porensky PN, Kolb SJ, Mendell JR, Burghes AHM, Kaspar BK. Systemic gene delivery in non-human primates for targeting spinal cord, brain and peripheral tissues for pediatric disorders. Mol Ther 2011;

Aug 2 Epub

286. Haidet-Phillips AM, Hester ME, Miranda CJ, Meyer K, Braun L, Frakes A, Song S, Likhite S, Murtha MJ, Foust KD, Rao M, Eagle A, Kammesheidt A, Christensen A, Mendell JR, Burghes AH, Kaspar BK. Astrocytes from familial and sporadic ALS patients are toxic to motor neurons. Nat Biotechnol. 2011 Aug 10;29(9):824-8.

287. Lowes LP, Alfano L, Viollet L, Rosales XQ, Sahenk, Z, Kaspar BK, Clark KR, Flanigan KM, Mendell JR. Knee extensor strength predicts function in sporadic inclusion body myositis. Muscle and Nerve, 2012;45:163-168

288. Boyden SE, Mahoney L, Kawahara G, Myers JA, Estrella EA, Mitsuhashi S, Duncan AR, Dey F, deChene T, Blasko-Goehringer JM, Darras BT, Mendell JR, Lidov HGW, Nishino I, Beggs AH, Kunkel LM, Kang PB. Mutations in the satellite cell gene *MEGF10* cause a recessive congenital myopathy with minicores. Neurogenetics in press.

289. Cottrell C, Mendell J, Hart-Kothari M, Ell D, Thrush D, Astbury C, Pastore M, Gastier-Foster J, Pyatt R. Maternal uniparental disomy of chromosome 4 in a patient with limb-girdle muscular dystrophy 2E confirmed by SNP array technology. Clin Clin Genet. 2011 Apr 11 (Epub ahead of print)

290. Cottrell CE, Prior TW, Pyatt R, Astbury C, Reshmi S, Bartholomew D, Atkin J, Manickam K, Thrush DL, Pastore M, Mendell J, Tsao CY, Al-Dahhak R, Newmeyer A, Gastier-Foster JM. Unexpected detection of dystrophin gene deletions by array comparative genomic hybridization. Am J Med Genet A. 2010;152A:2301-2307.

291. Mendell JR, Shilling c, Leslie ND, Flanigan KM, al-Dahhak R, Gastier-Foster J, Kneile K, Dunn DM, Duval B, Aoyagi A, Hamil C, Mahmoud M, Roush K, Bird L, Rankin C, Lilly H, Street N, Chandrasekar r, Weiss RB. Evidence Based Path to Newborn Screening for Duchenne Muscular Dystrophy. Ann Neurol Feb 2012 (Epub ahead of print)

292. Boyden SE, Mahoney LJ, Kawahara G, Myers JA, Mitsuhashi S, Estrella EA, Duncan AR, Dey F, DeChene ET, Blasko-Goehringer JM, Bönnemann CG, Darras BT, Mendell JR, LIdov HGW, Nishino I, Beggs AH, Kunkel LM, Kang PB. Mutations in the satellite cell gene *MEGF10* cause a recessive 1 congenital myopathy with minicores. Neurogenetics, In Press.

293. Viollet L, Thrush PT, Flanigan KV, Mendell JR, Allen HD. Effects of Angiotensin-Converting Enzyme Inhibitors and/or β-blockers on the Cardiomyopathy in Duchenne Muscular Dystrophy. The American Journal of Cardiology In press

Chapters

1. Mendell, J.R., and Johnson, E.W.: Anterior Horn Cell Disease of Infancy and Childhood and The Progressive Muscular Dystrophies. Current Diagnosis, Conn, J.F., Ed., W.B. Saunders Co., pp. 965-972, 1974.

2. Mendell, J.R.: A Review of Experimental Models and Their Relationship to Human Neuromuscular Diseases. Handbook of Clin Neurol, Northern Holland Publishing Company, Amsterdam, 40:133-182, 1979.

3. Mendell, J.R. and Sahenk, A.: Chapter 10, Interference of Neuronal Processing and Axoplasmic Transport by Toxic Chemicals. In: Exper & Clin Neurotox. Spencer, P.S. & Schaumburg, H.H. (eds.), Williams & Wilkins, Baltimore, pp.139-160, 1980.

4. Sahenk, Z. and Mendell, J.R.: Chapter 40, Zinc Pyridinethione.Exper & Clin Neurotox. Spencer, P.S. & Schaumburg, H.H. (eds.), Williams & Wilkins, Baltimore, pp. 578-592, 1980.

5. Kissel JT, Mendell JR: Endocrine Myopathies. In: Rowland LP, DiMauro S (eds.) Handbook of Clinical Neurology, Vol. 19 (62) Myopathies. Elsevier Science Publishers New York, 1992 pp.139-160, 1980.

6. Mendell, J.R.: Neurologic Disorders in Sports Medicine. Sports Med, W. B. Saunders Co., pp. 149-174, 1984

7. Kissel JT, Mendell JR: Endocrine Myopathies. In: Rowland LP, DiMauro S (eds.) Handbook of Clinical Neurology, Vol. 19 (62) Myopathies. Elsevier Science Publishers New York, 1992

8. Kissel JT, Mendell JR. Treatment of vasculitic neuropathies. In:Johnson RT and Griffin JW (eds). Current Therapy in Neurological Disease. Mosby-Year Book, New York, 1993.

9. Lynn DJ, Mendell JR. Peripheral Neuropathy. In: Rakel RE ed. Conn's Current Therapy. Philadelphia:WB Saunders, 1993.

10. Mendell, J.R. and Griggs, R.C.: Muscular Dystrophy and Other Chronic Myopathies. In: Harrison's Principles of Internal Medicine. Petersdorf, R.G., Adams, R.D., Baunwald, E., Isselbacher, K.J., Martin, J.B. & Wilson, J.D. (eds.), 11th, 12th, and 13th editions, pp. 2383-2392, 1994.

11. Lynn DJ, Mendell JR. Peripheral Neuropathy. In: Koller WC (ed). Current Practice of Medicine. Philadelphia: Current Medicine, 1996.

12. Mendell JR, Prior TW, Marzluf GA. Introduction to Molecular Genetics and Recombinant DNA Technology. In: Clinical Neurology. Joynt RJ and Griggs RC (eds), pp. 1-20, 1996.

13. Mendell JR. Sporadic Inclusion Body Myositis: Clinical and Laboratory Features and Diagnostic Criteria. In: Askanas V, Serratrice G, Engel WK, eds. Inclusion-Body Myositis and Myopathies. Cambridge:Cambridge University Press, 1998:107-115.

14. Collins MP, Kissel JT, Mendell JR. Vasculitic Neuropathies. In: Neuroimmunology. Antel J, Birnbaum G, Hartung H-P (eds), 1998:316-339.

15. Mendell JR, Griggs RC, Ptacek LJ. Diseases of Muscle. In: Harrison's Principles of Internal Medicine. Fauci AS, Baunwald E, Isselbacher KJ, Wilson JD, Martin JB, Kasper DL, Hauser SL, Longo DL. 14th edition, 1998:2473-2482.

16. Tsao, CY, Mendell JR. The Muscular Dystrophies. Appel SH (eds), Current Neurology Volume 17, Amsterdam,IOS Press, 1997:1-46

17. Tsao CY, Mendell JR.. In: Childhood muscular dystrophy sharing a common pathogenesis of membrane instability Motor Disorders. Younger DS (ed). Phildelphia, Lippencott Williams, and Wilkins, Inc., 1999: 139-148.

18. Sahenk Z, Mendell JR. Pyrithione. In: Experimental and Clinical Neurotoxicology. Spencer PS, Schaumburg HH (eds) Second edition, Oxford University Press, New York, N.Y.,2000:1050-1054.

19. Mendell JR. Approach to Myopathies In: Harrison's Principles of Internal Medicine. Fauci AS, Baunwald E, Isselbacher KJ, Wilson JD, Martin JB, Kasper DL, Hauser SL, Longo DL. 15th edition, 2001:2520-2524.

20. Brown RH, Mendell JR. Diseases of Muscle. In: Harrison's Principles of Internal Medicine. Fauci AS, Baunwald E, Isselbacher KJ, Wilson JD, Martin JB, Kasper DL, Hauser SL, Longo DL. 15th edition, 2001:2524-2527.

21. Mendell JR. Approach to Myopathies In: Harrison's Principles of Internal Medicine Kaspar DL, Baunwald E, Fauci AS, Hauser SL, Longo DL, Jameson JL. 16th edition, 2004:2524-2527.

22. Brown RH, Mendell JR. Diseases of Muscle. In: Harrison's Principles of Internal Medicine. Kaspar DL, Baunwald E, Fauci AS, Hauser SL, Longo DL, Jameson JL. 16th edition, 2004:2527-2540.

23. Mendell JR, Miller A. Gene Transfer for Neurological Disease: Agencies, Policies, and Process. In: Gene Therapy in the Central Nervous System. Kaplitt MG, During MJ. Elsevier, Inc. 2006:77-88.

24. Mendell JR. Muscular Dystrophies and Other Myopathies.In: Harrison's Principles of Internal Medicine Kaspar DL, Baunwald E, Fauci AS, Hauser SL, Longo DL, Jameson JL, Loscalzo J. 17th edition, 2008:2678-2695.

MONOGRAPHS

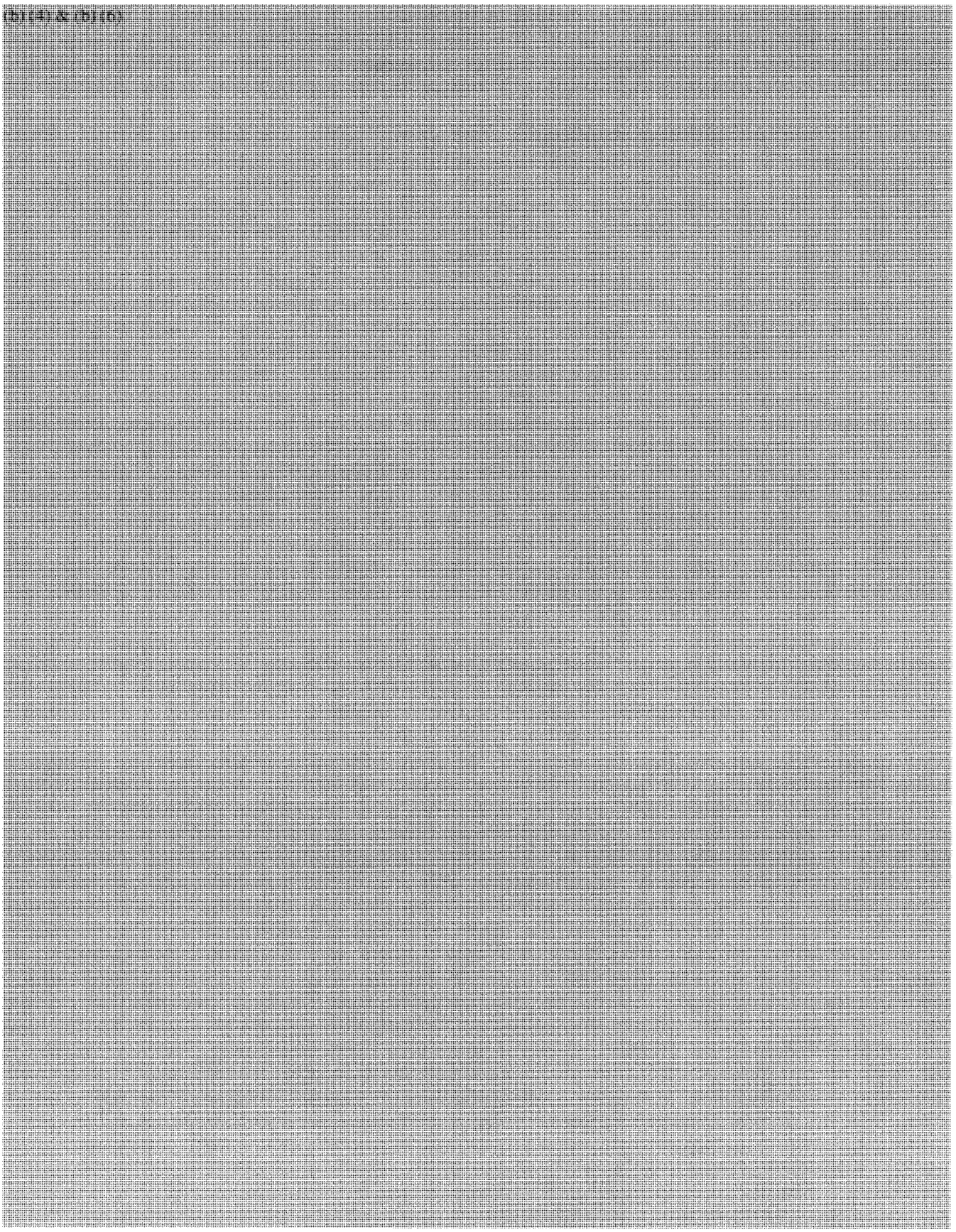
Mendell, JR, Barohn, RJ, Bosch EP, Kissel JT. Peripheral Neuropathies Continuum Series, Advance Star Communications, Cleveland,OH. 1994

Kissel JT, Mendell JR. Muscular Dystrophy. Seminars in Neurology Thieme, New York. 1999

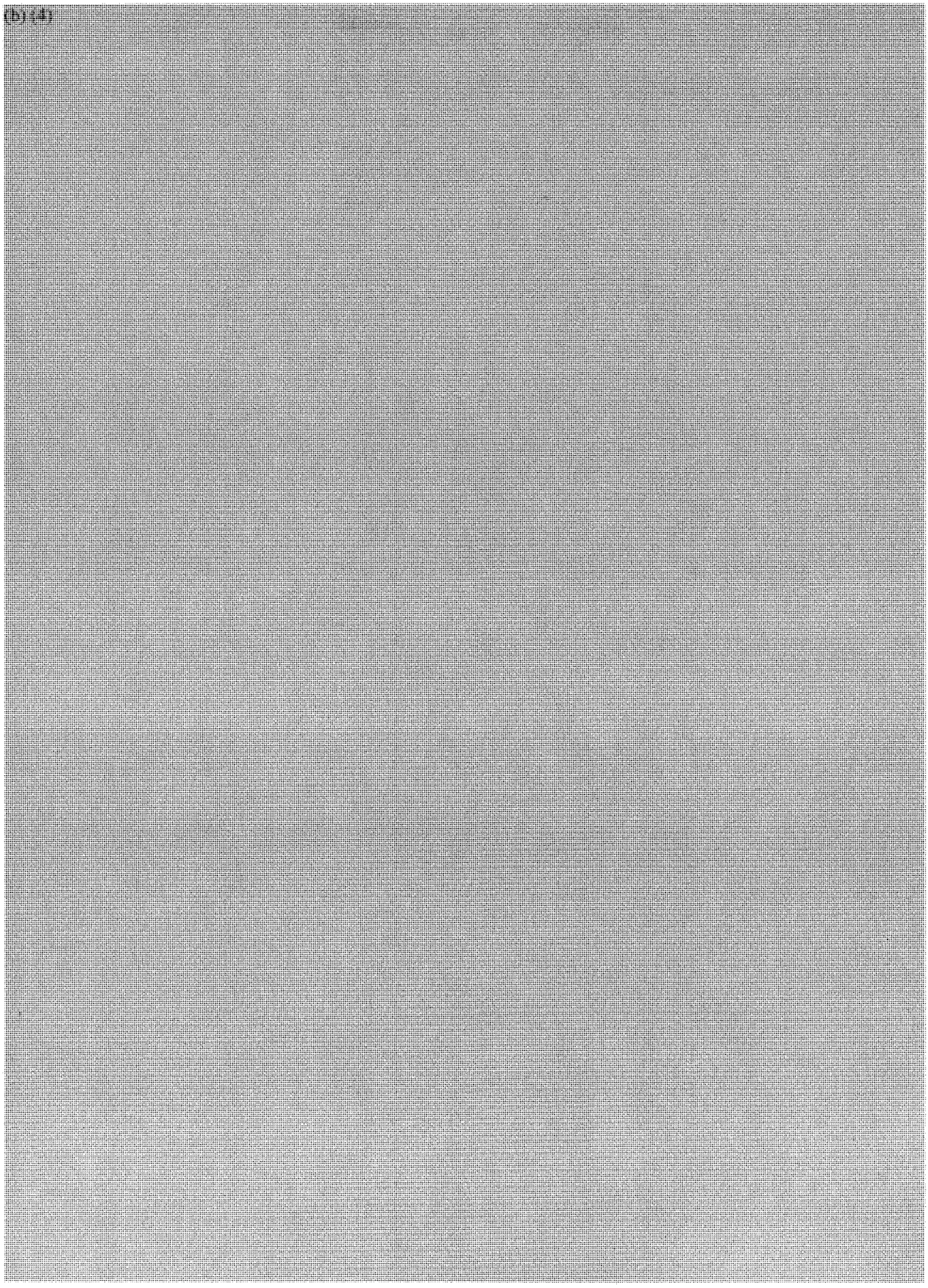
Kissel JT, Amato AA, Barohn RJ, Iannaccone S, Lange D, Mendell JR, Saperstein D. Muscle Disease. Continuum. American Academy of Neurology, Philadelphia, Lipincott Williams and Wilkins. January, 2000

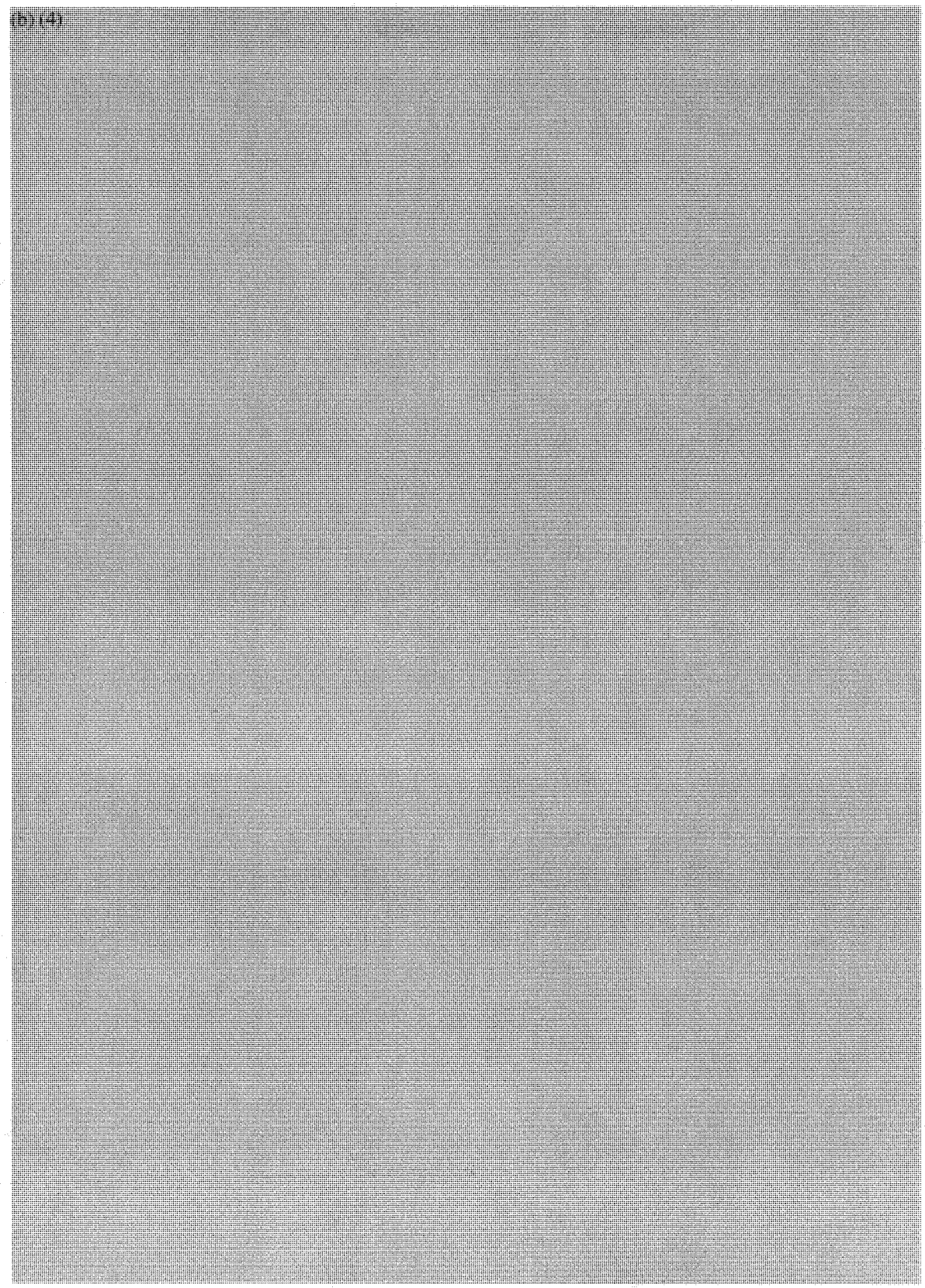
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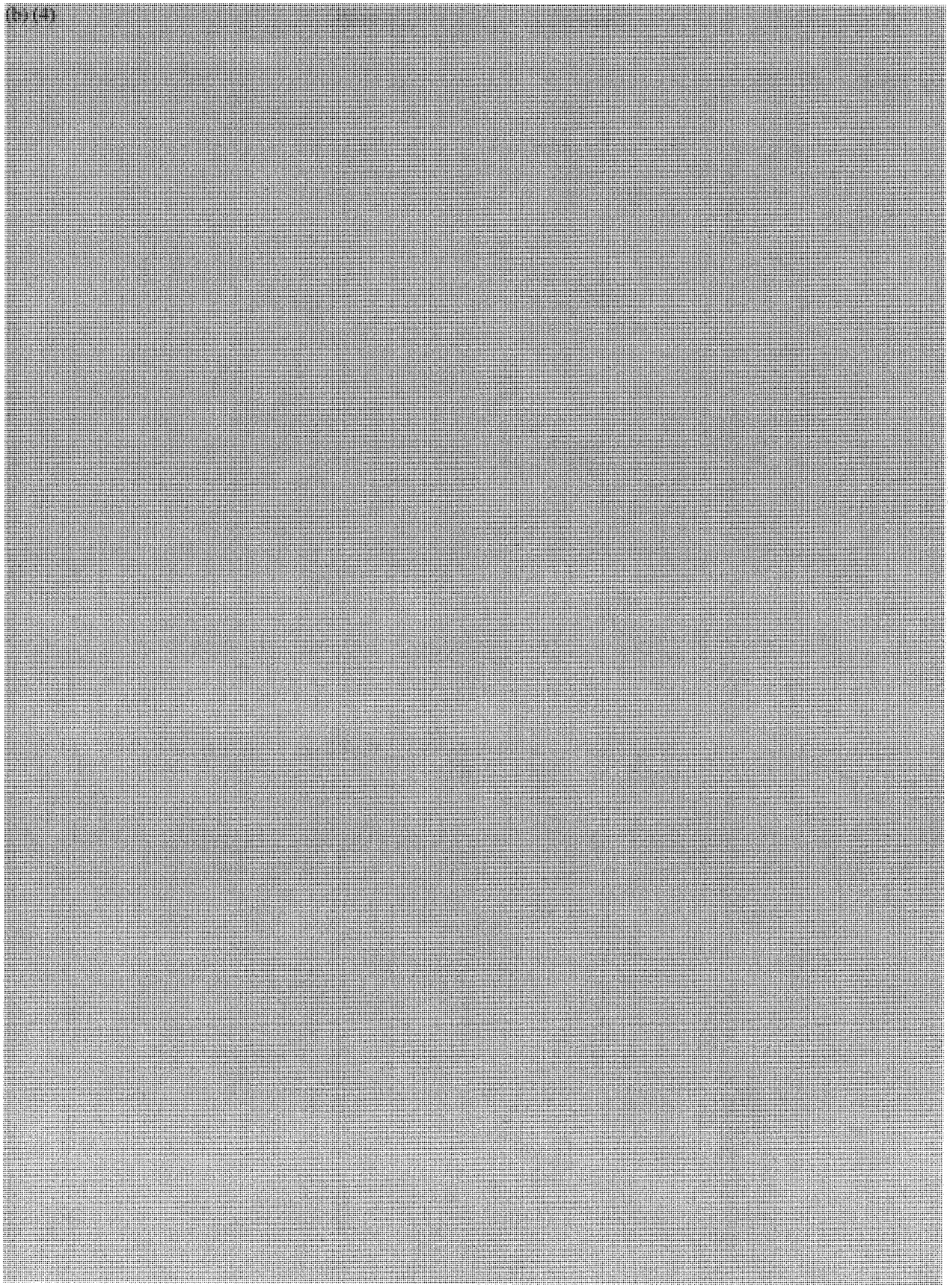


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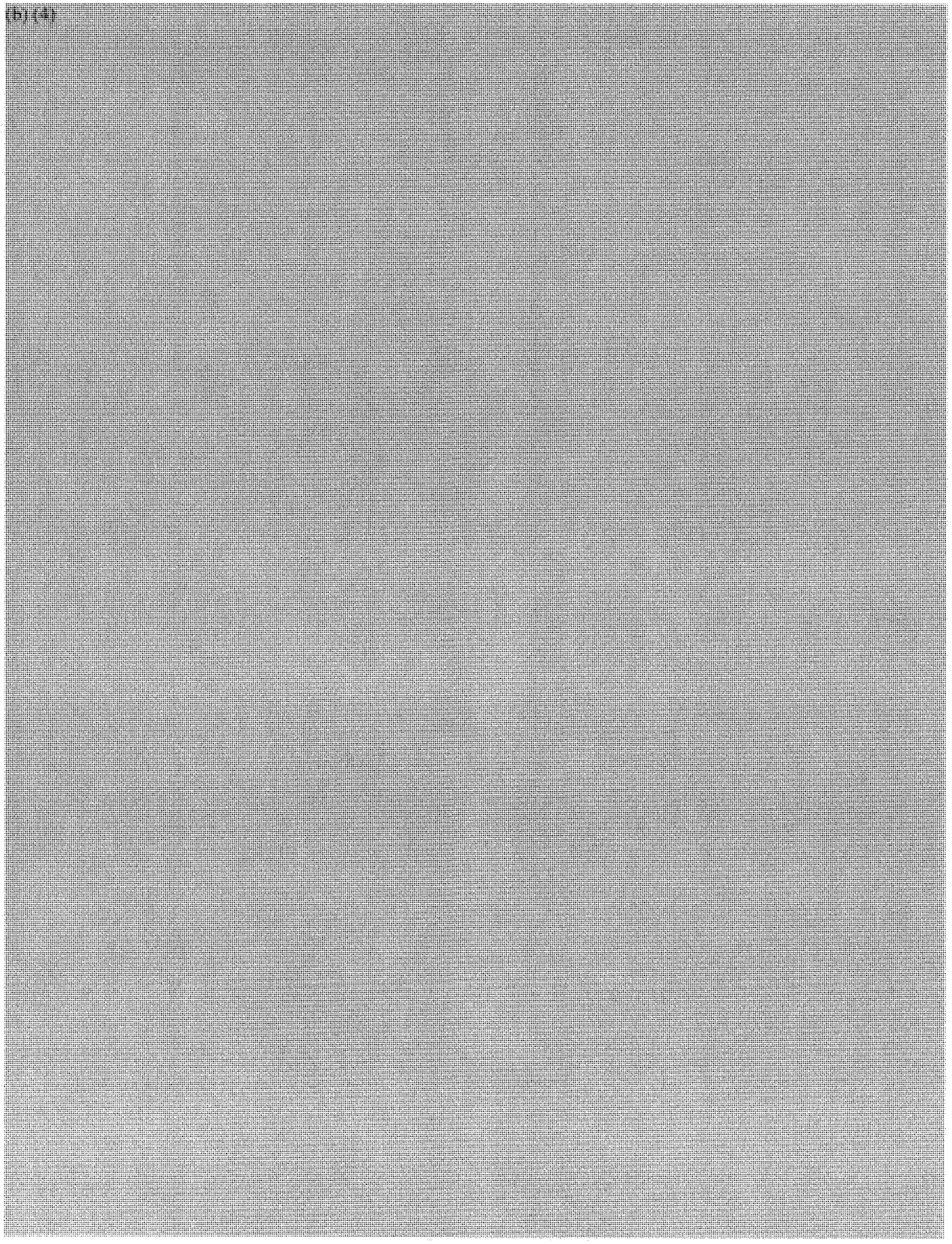



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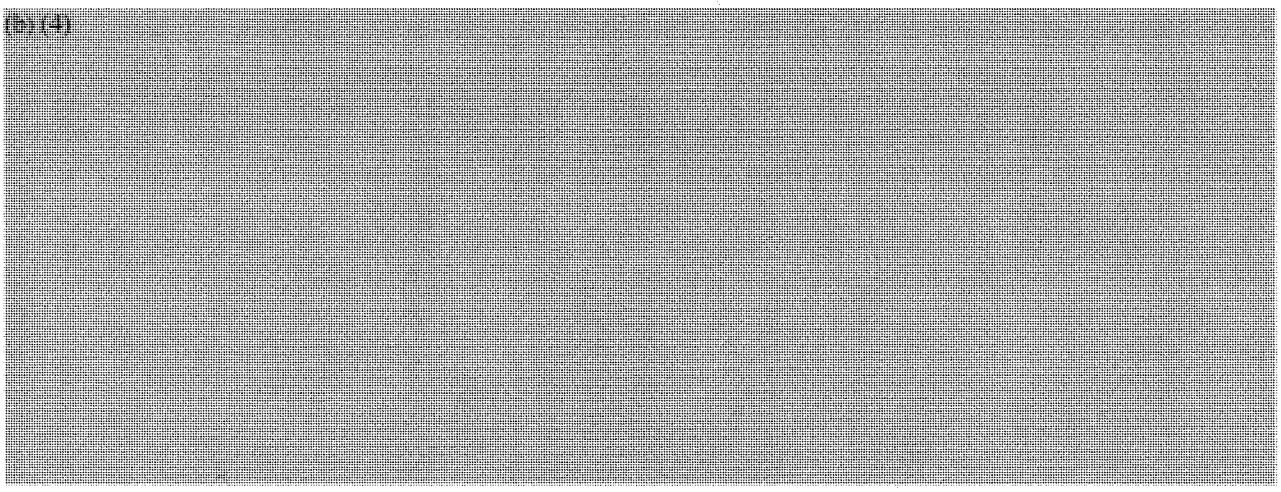
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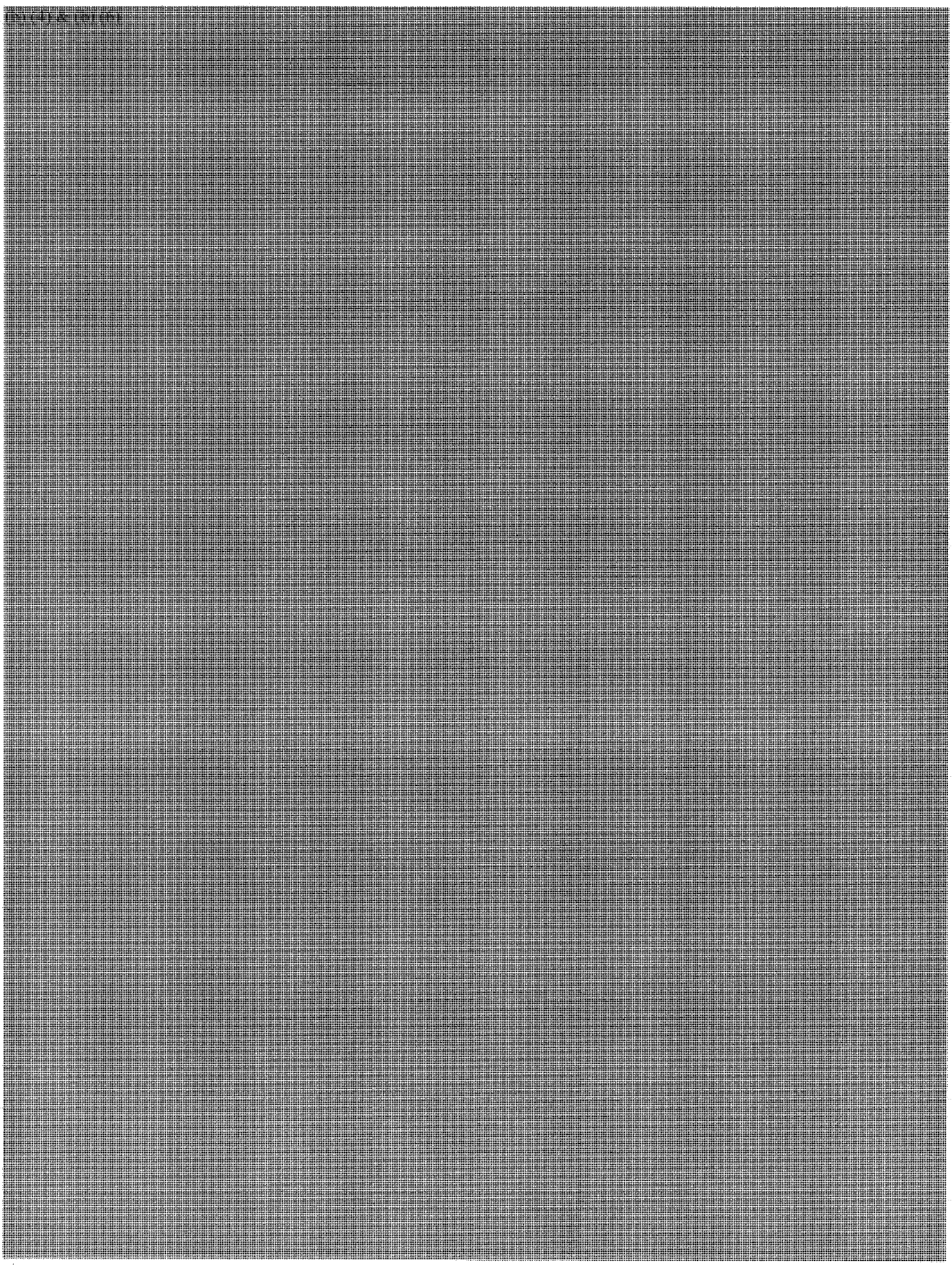
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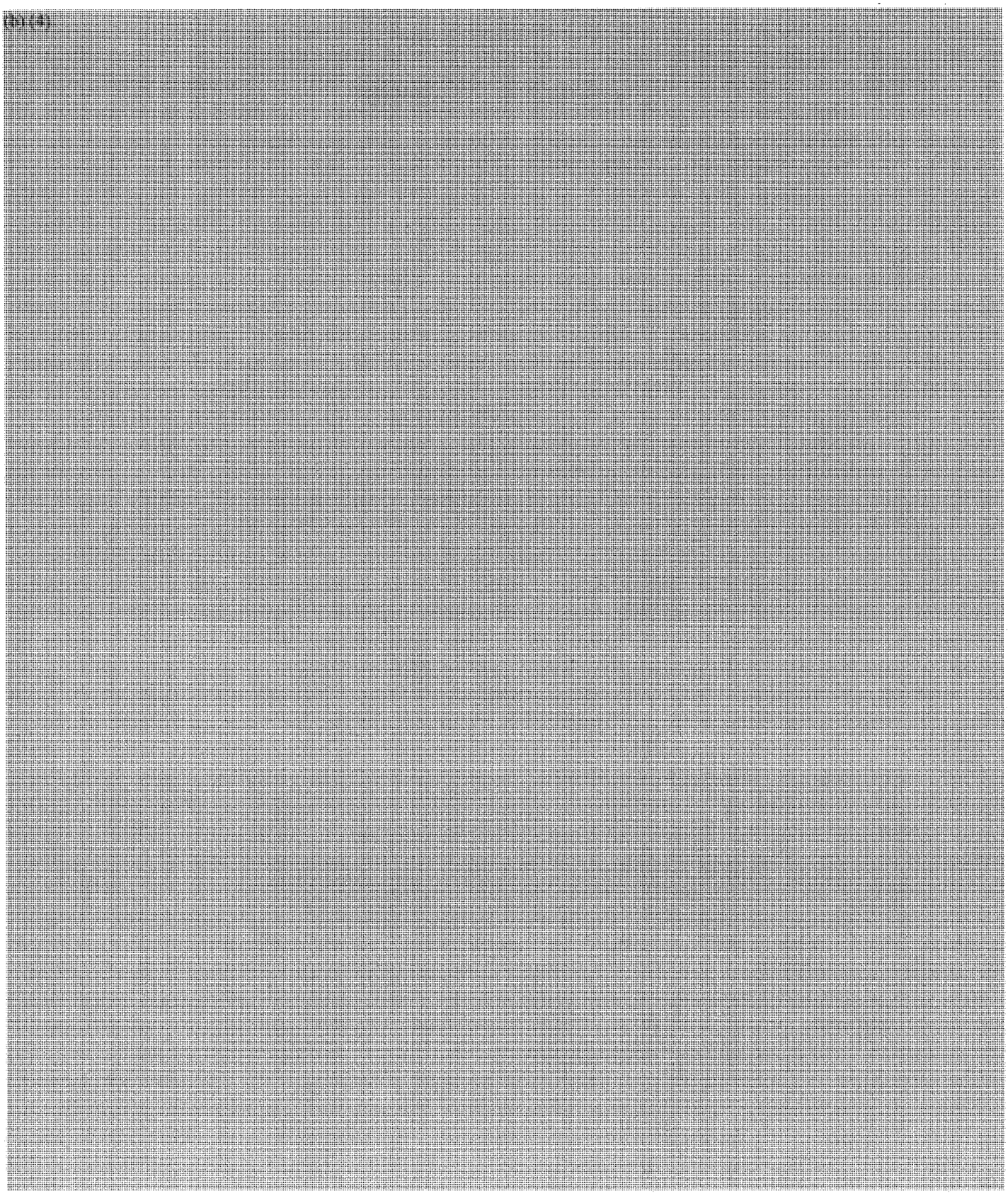
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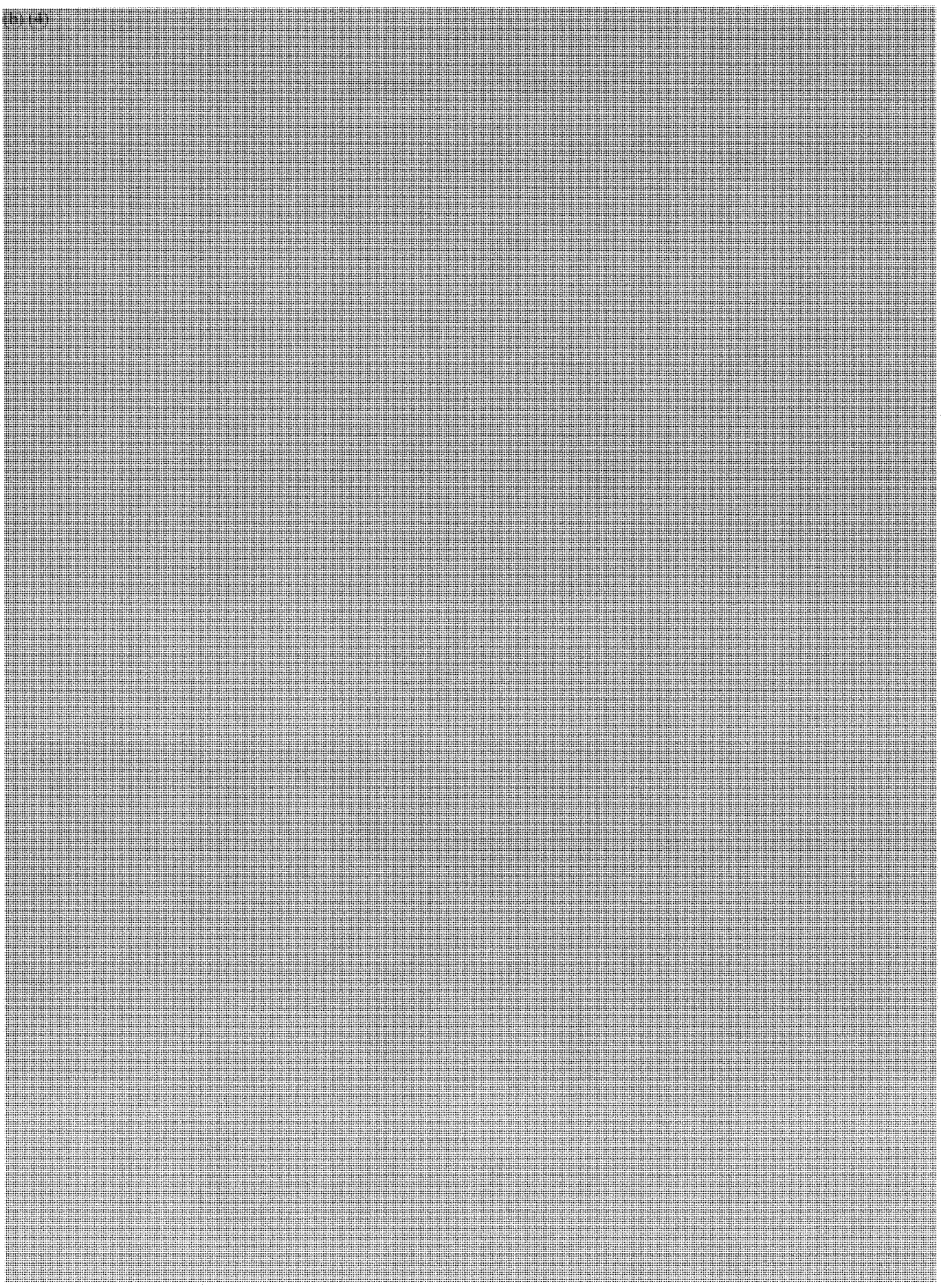
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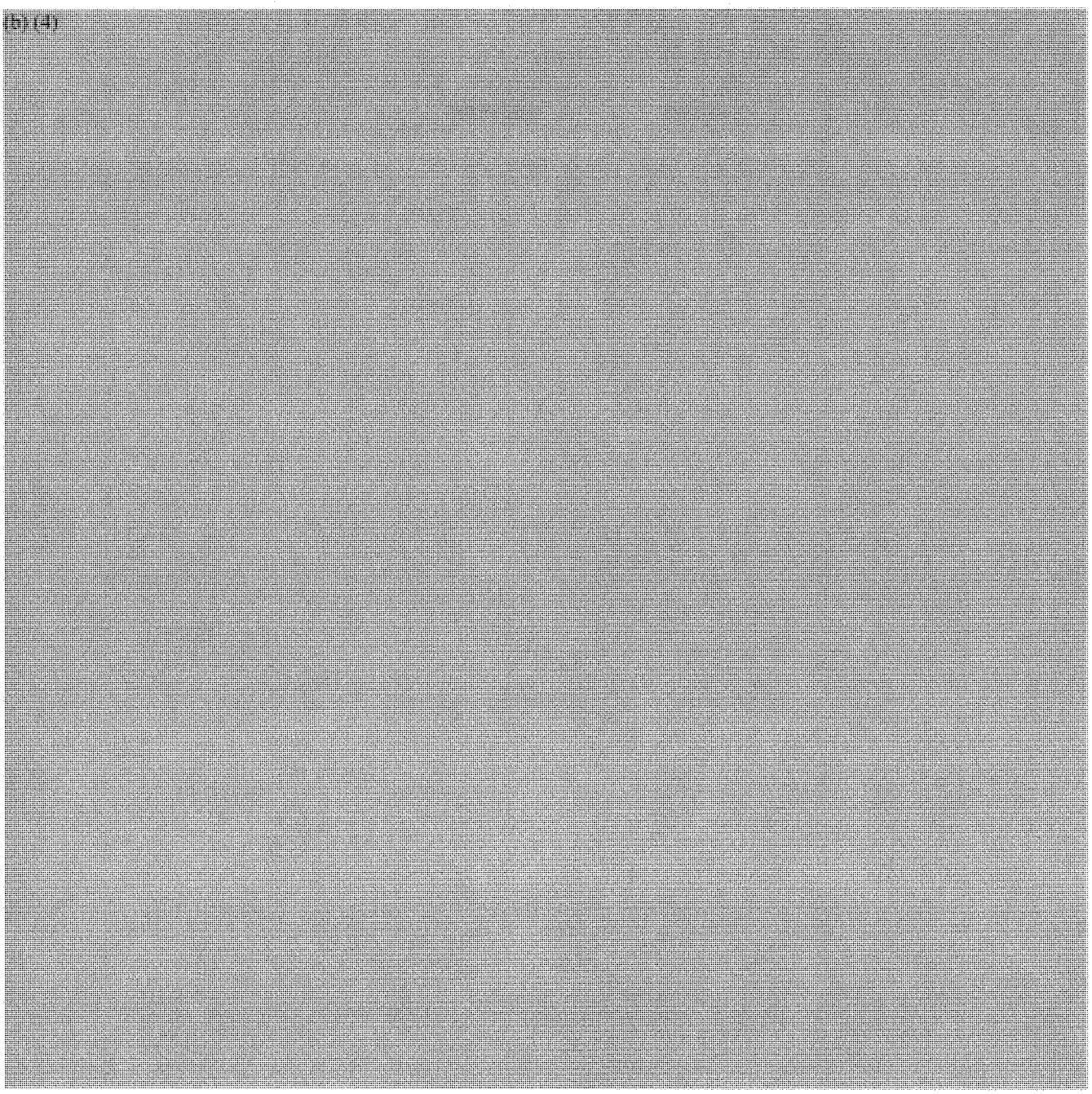
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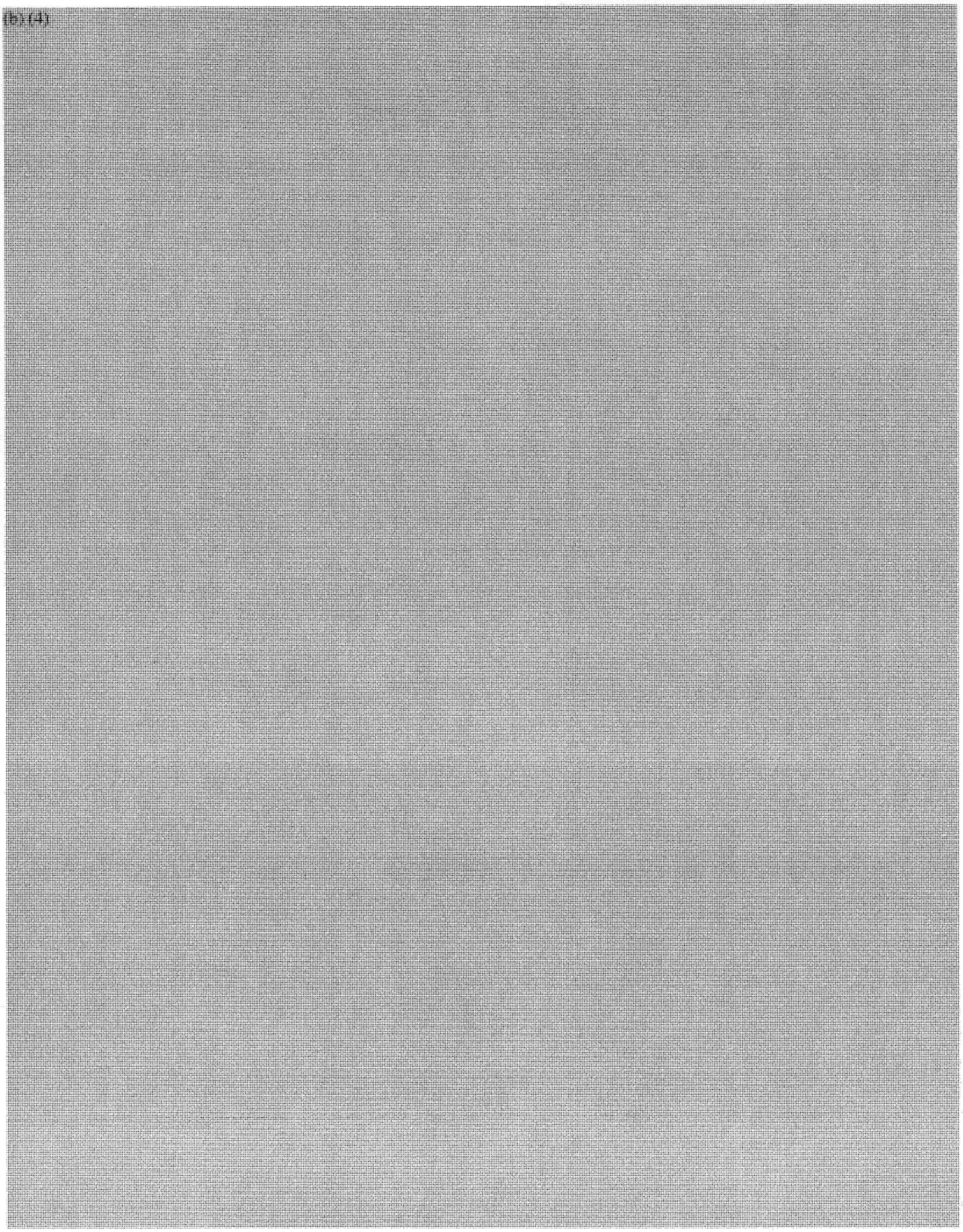
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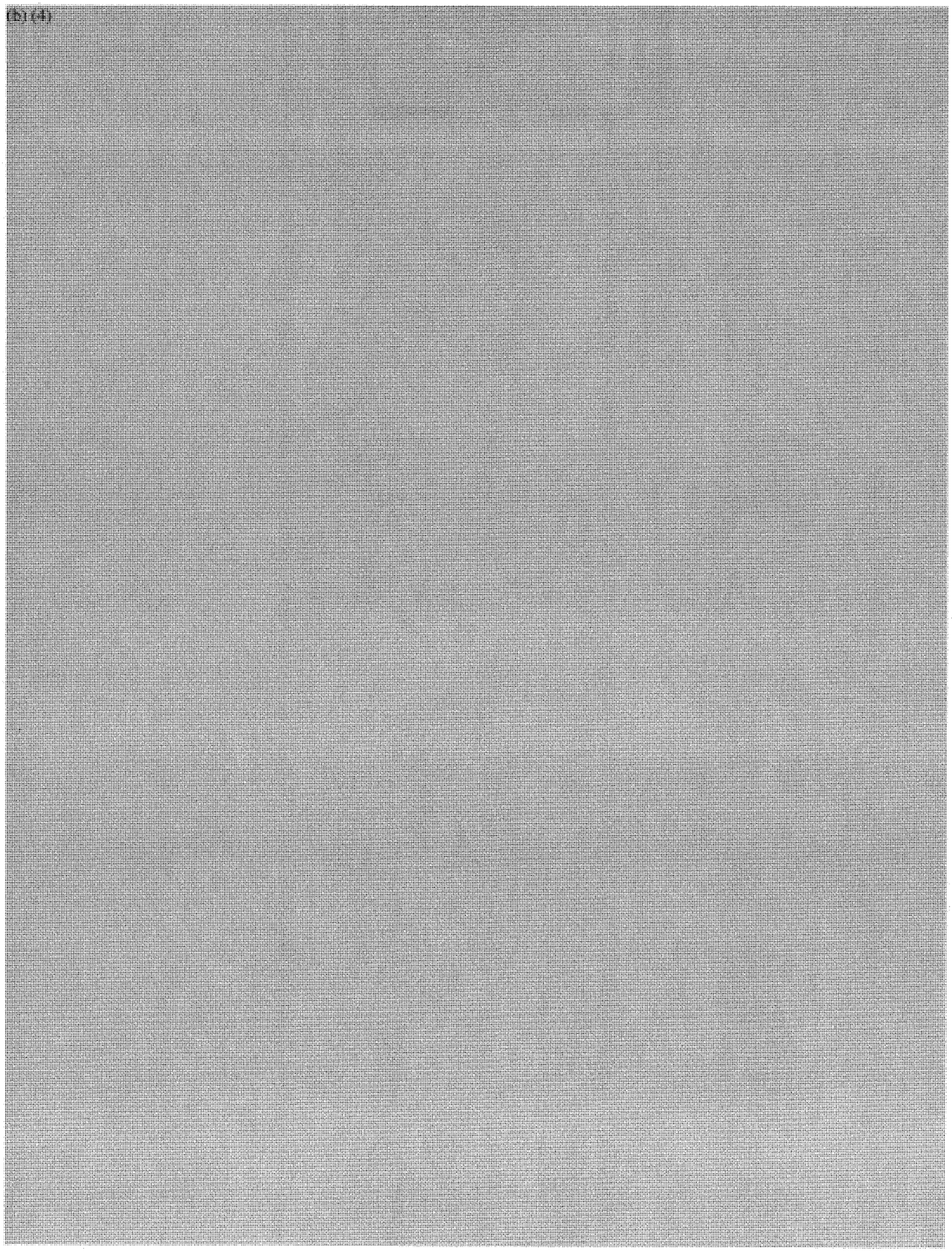
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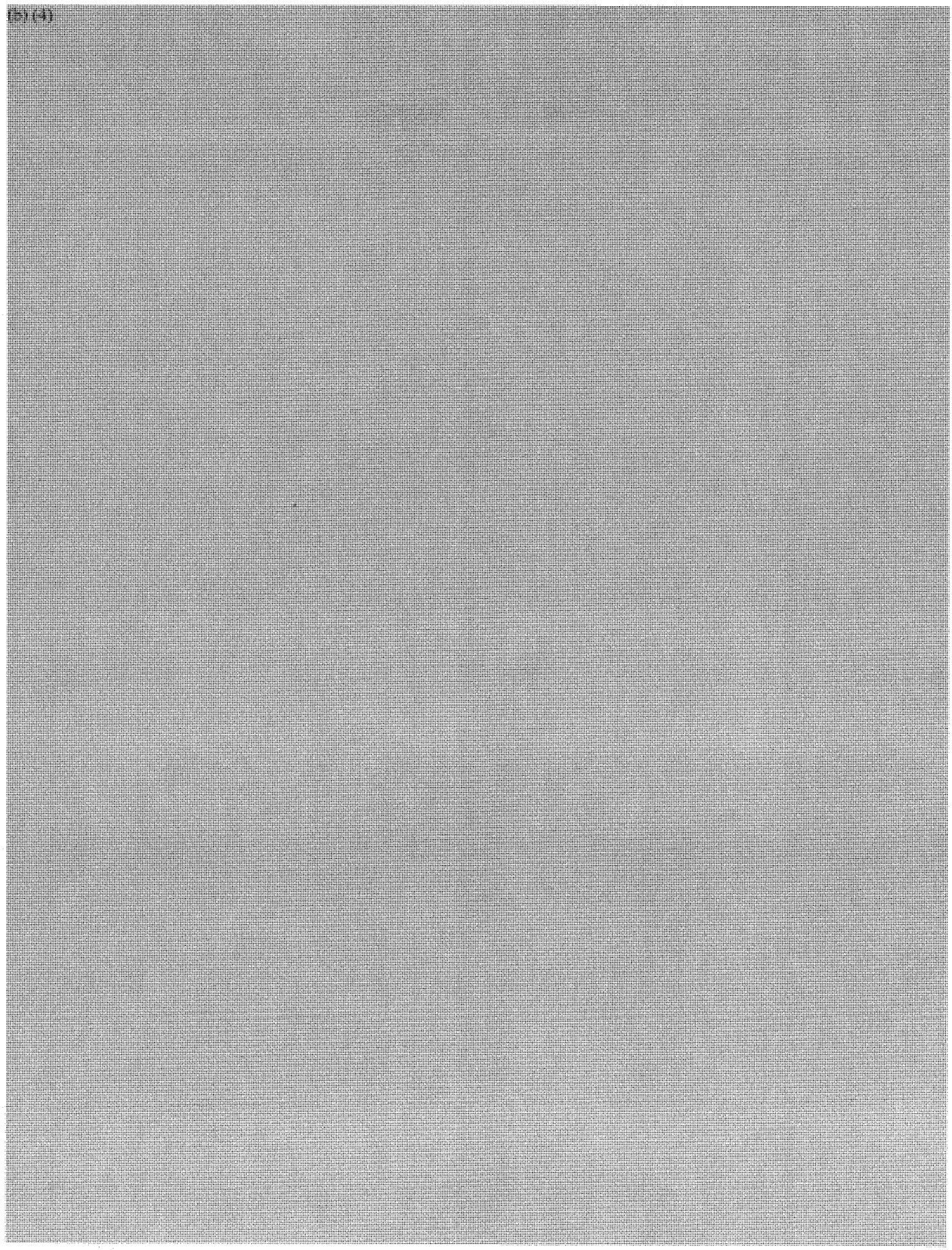
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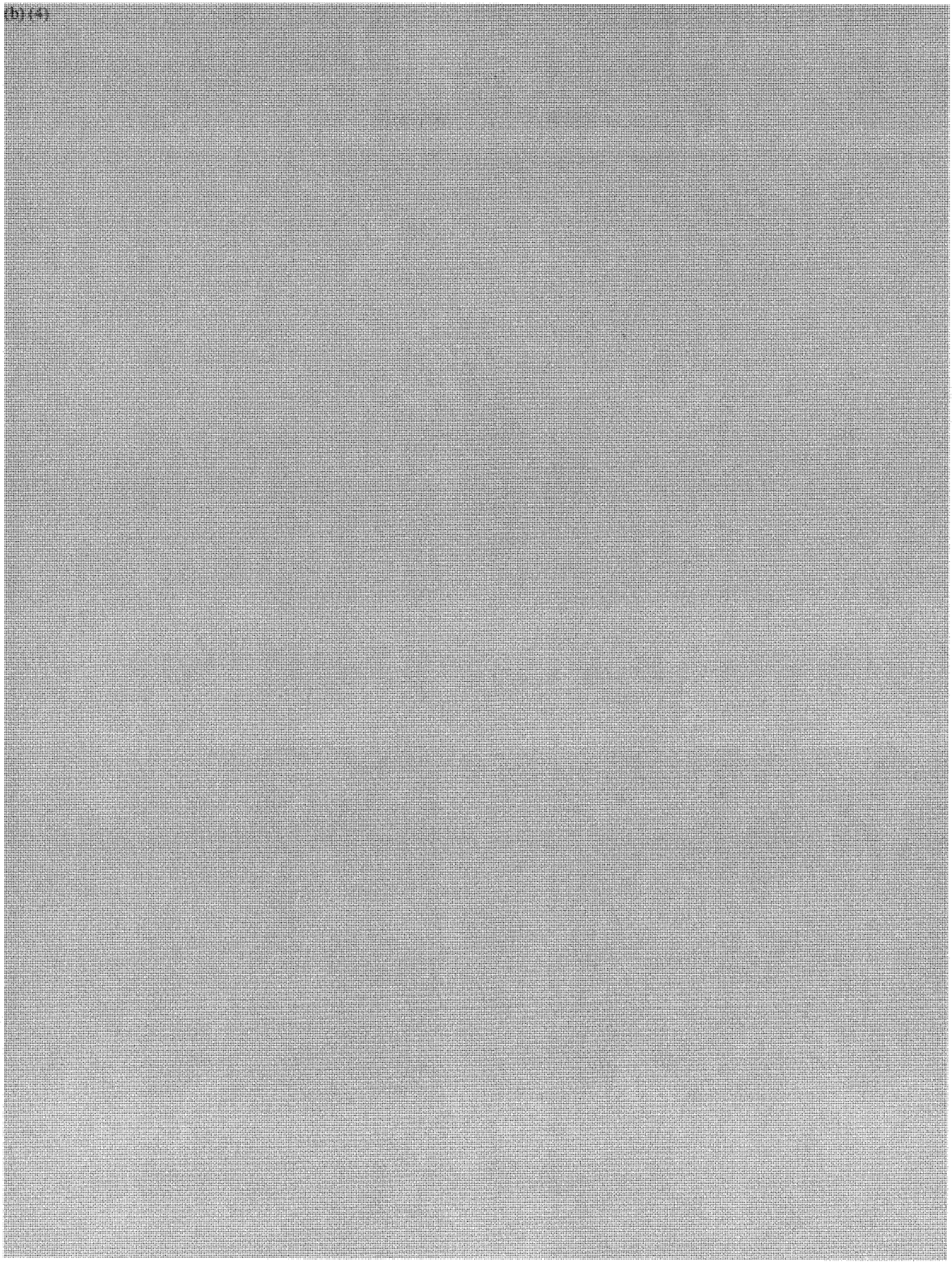
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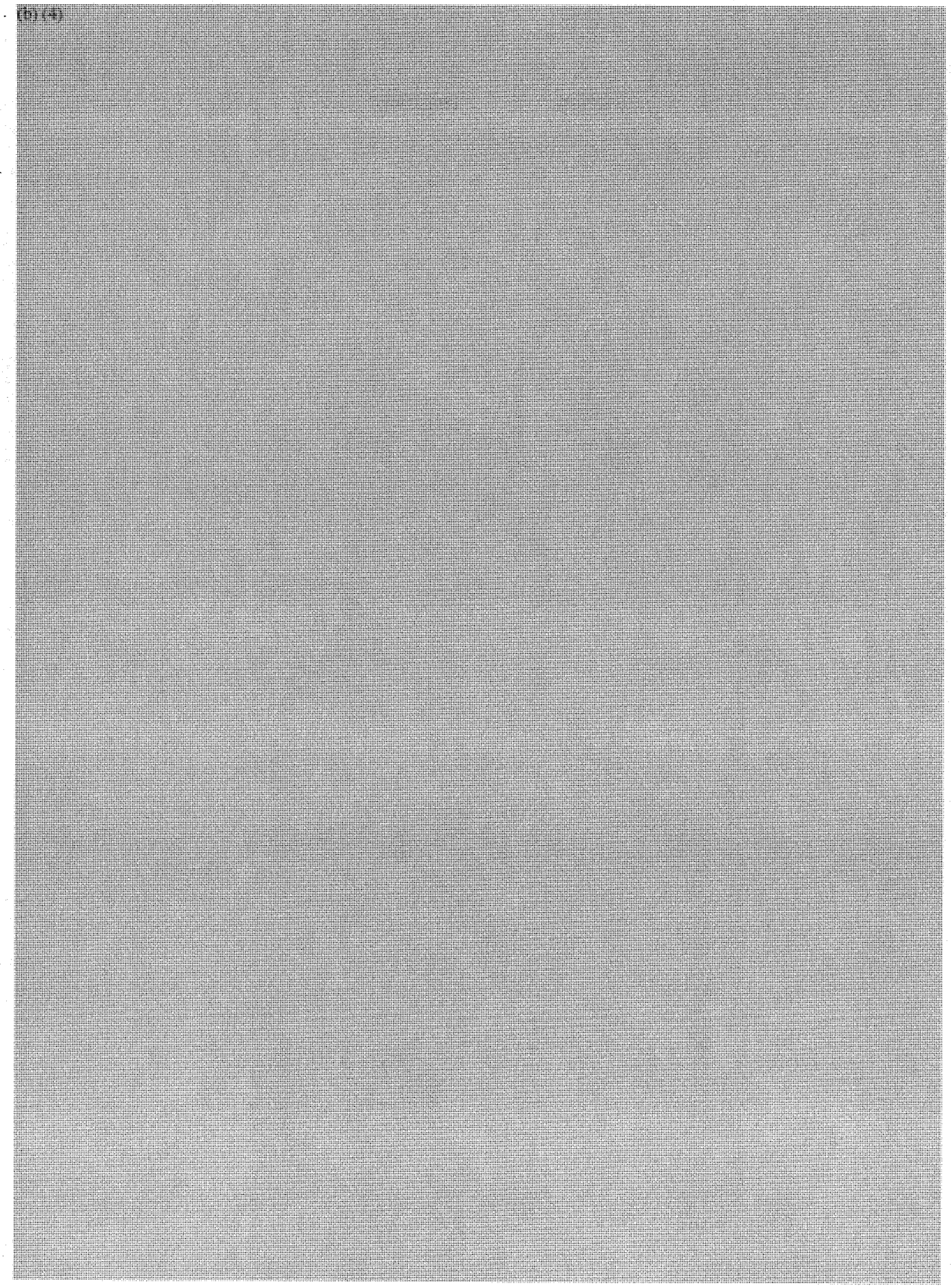
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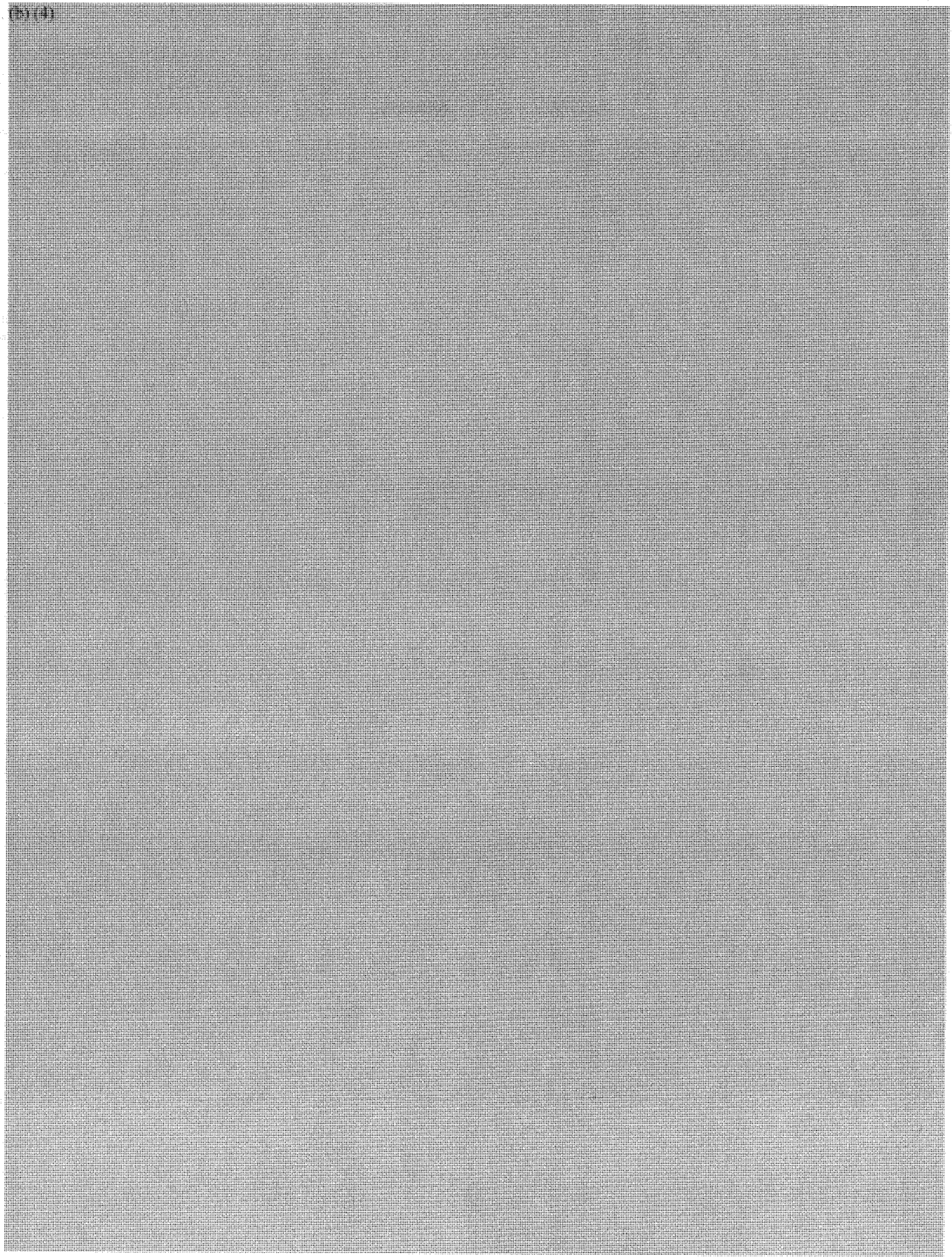


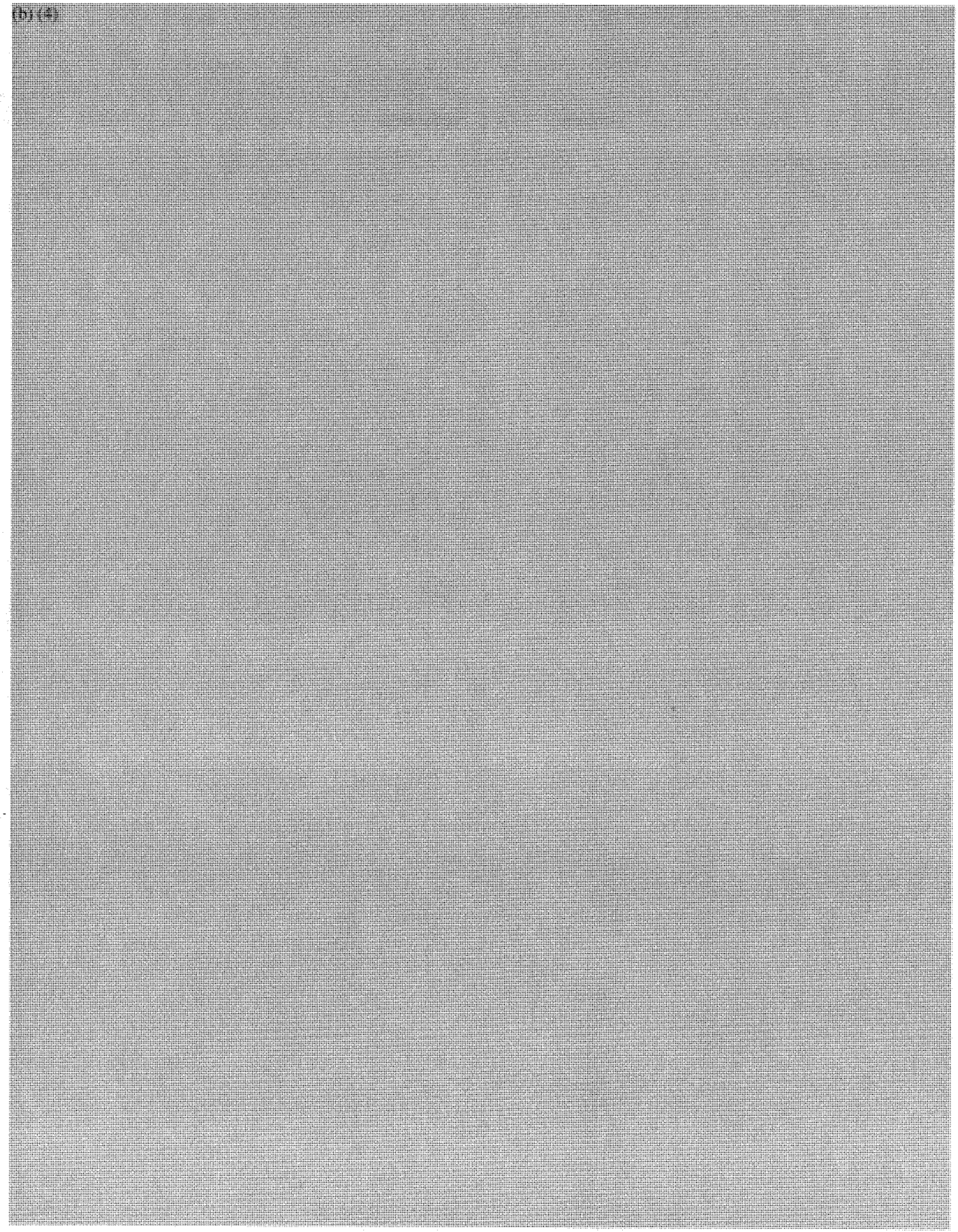
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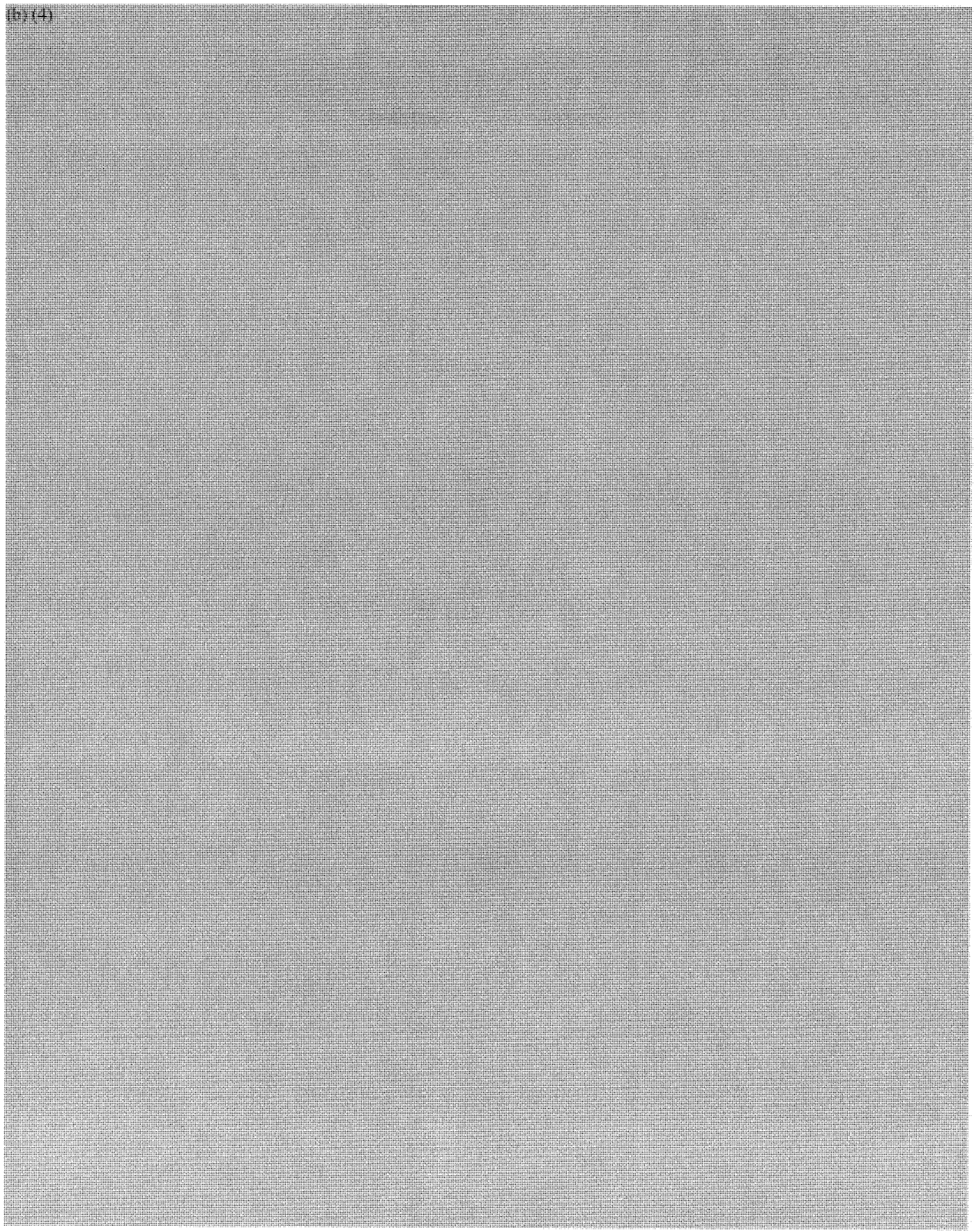
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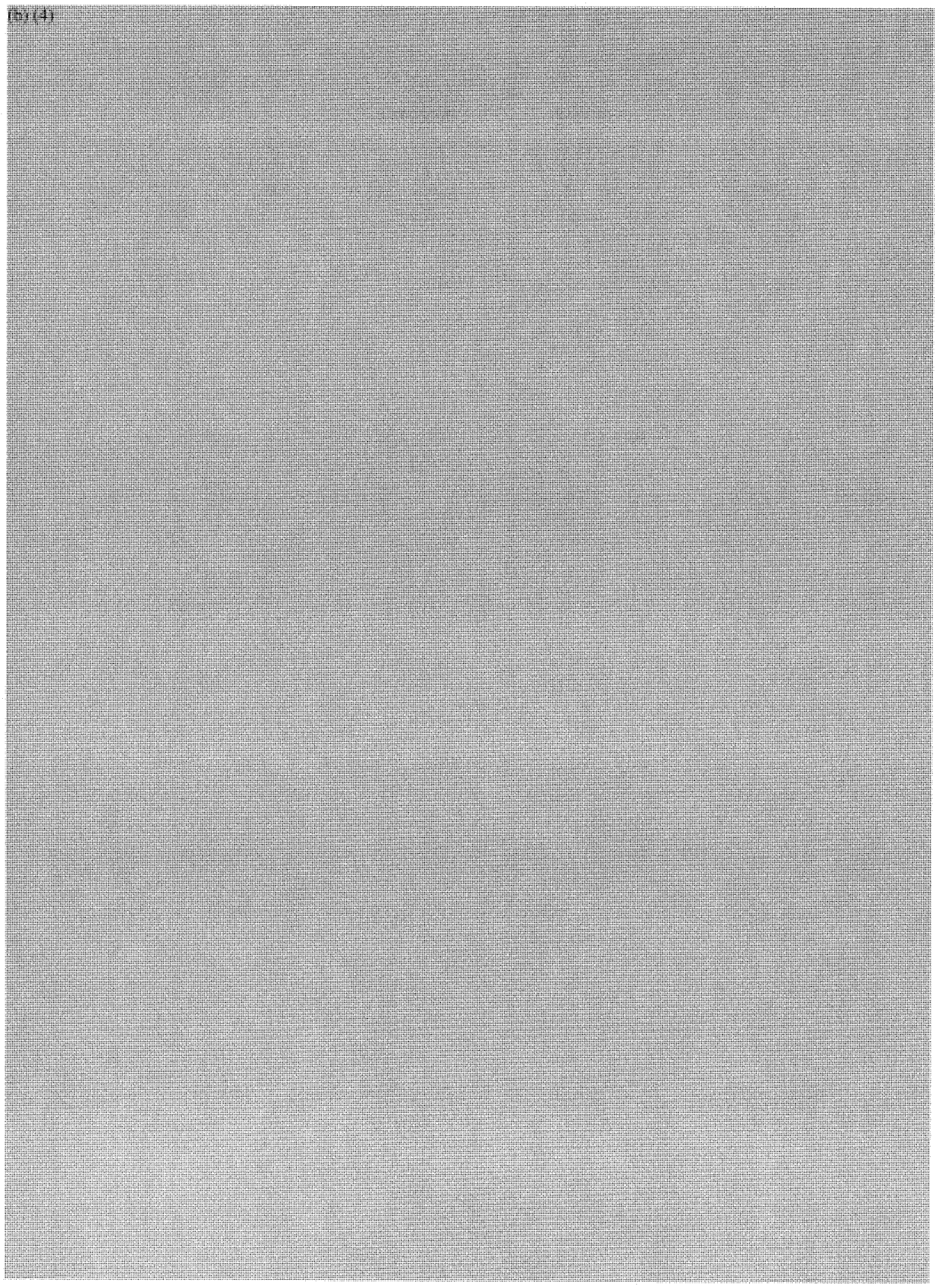


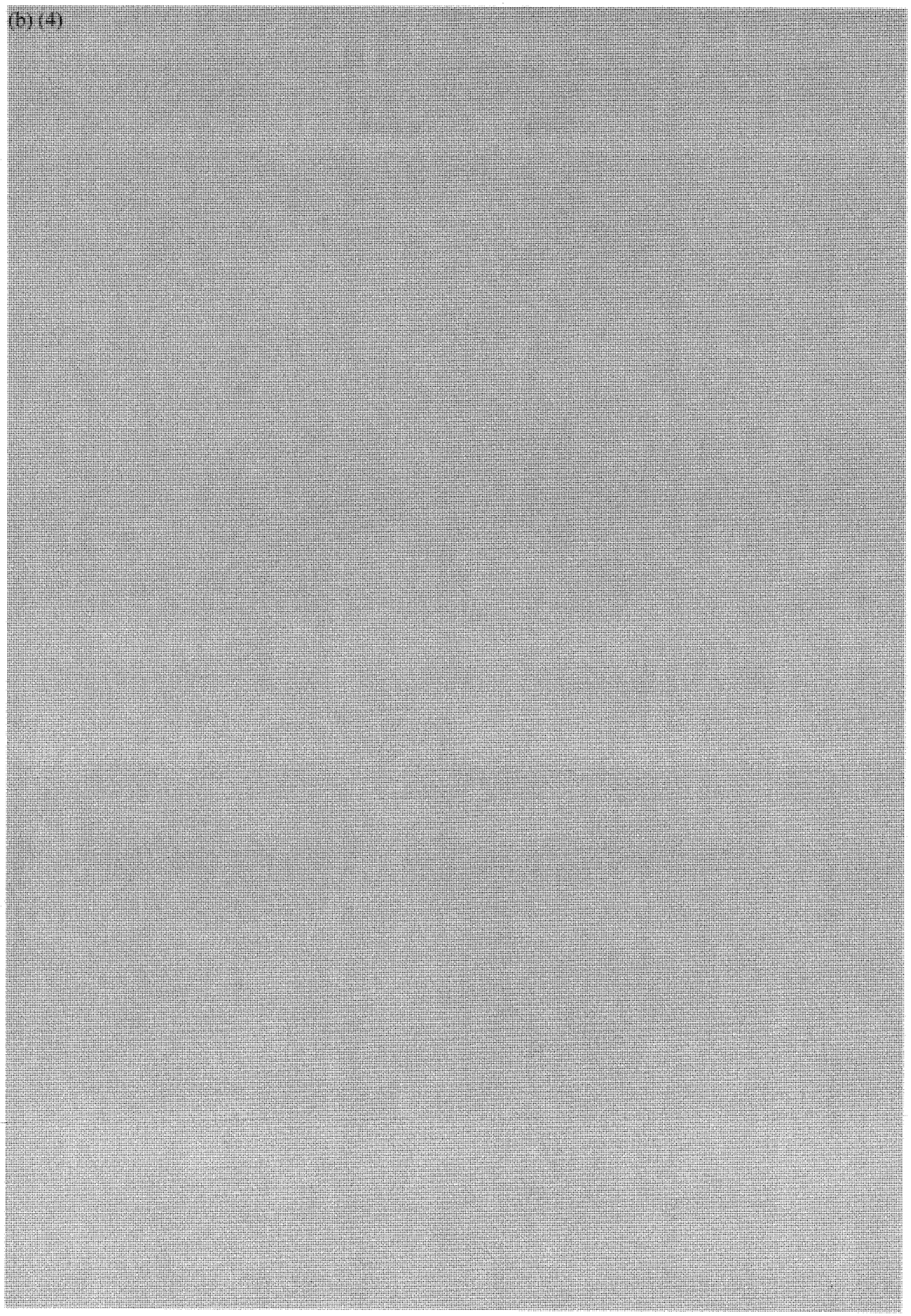

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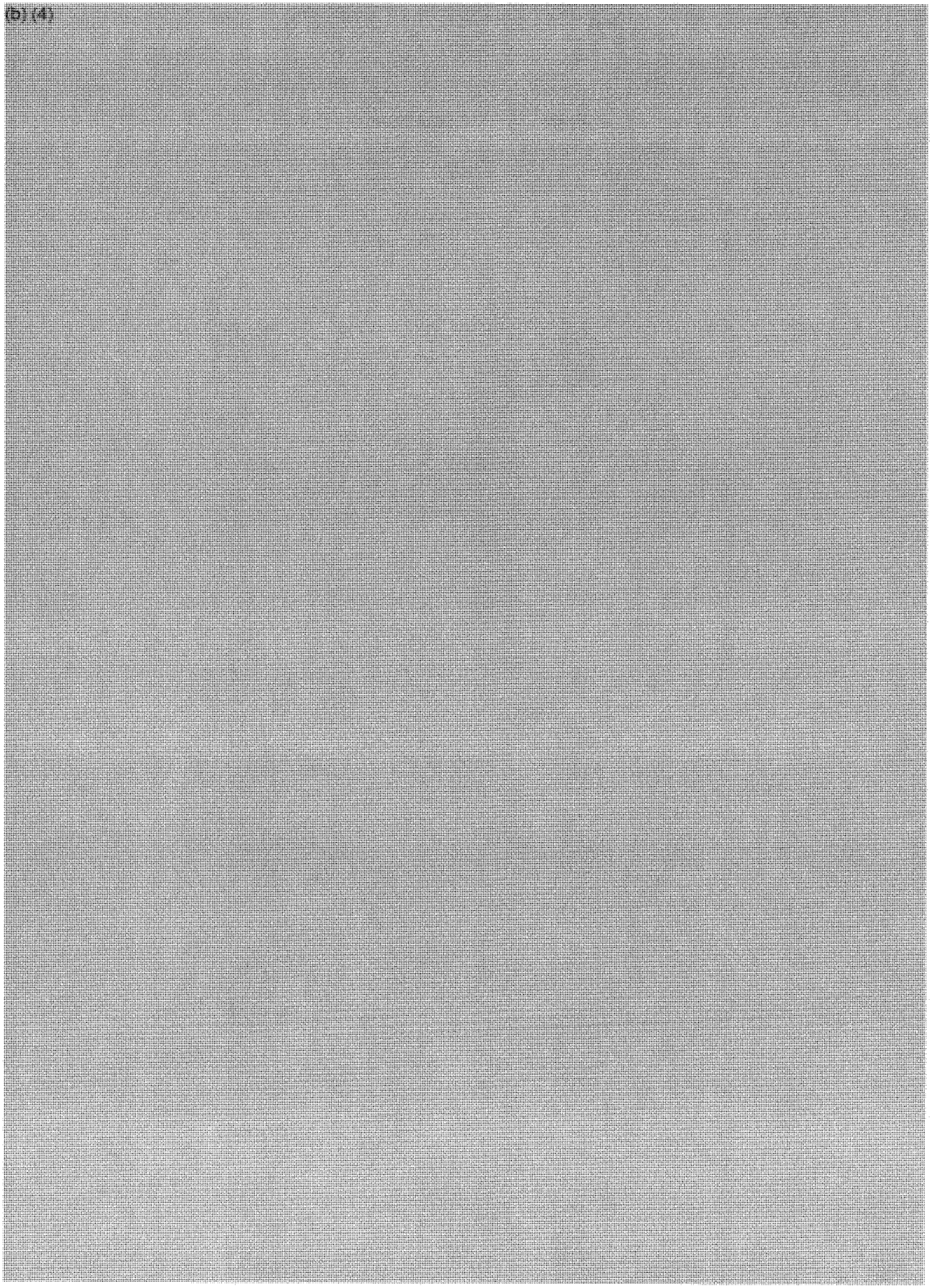


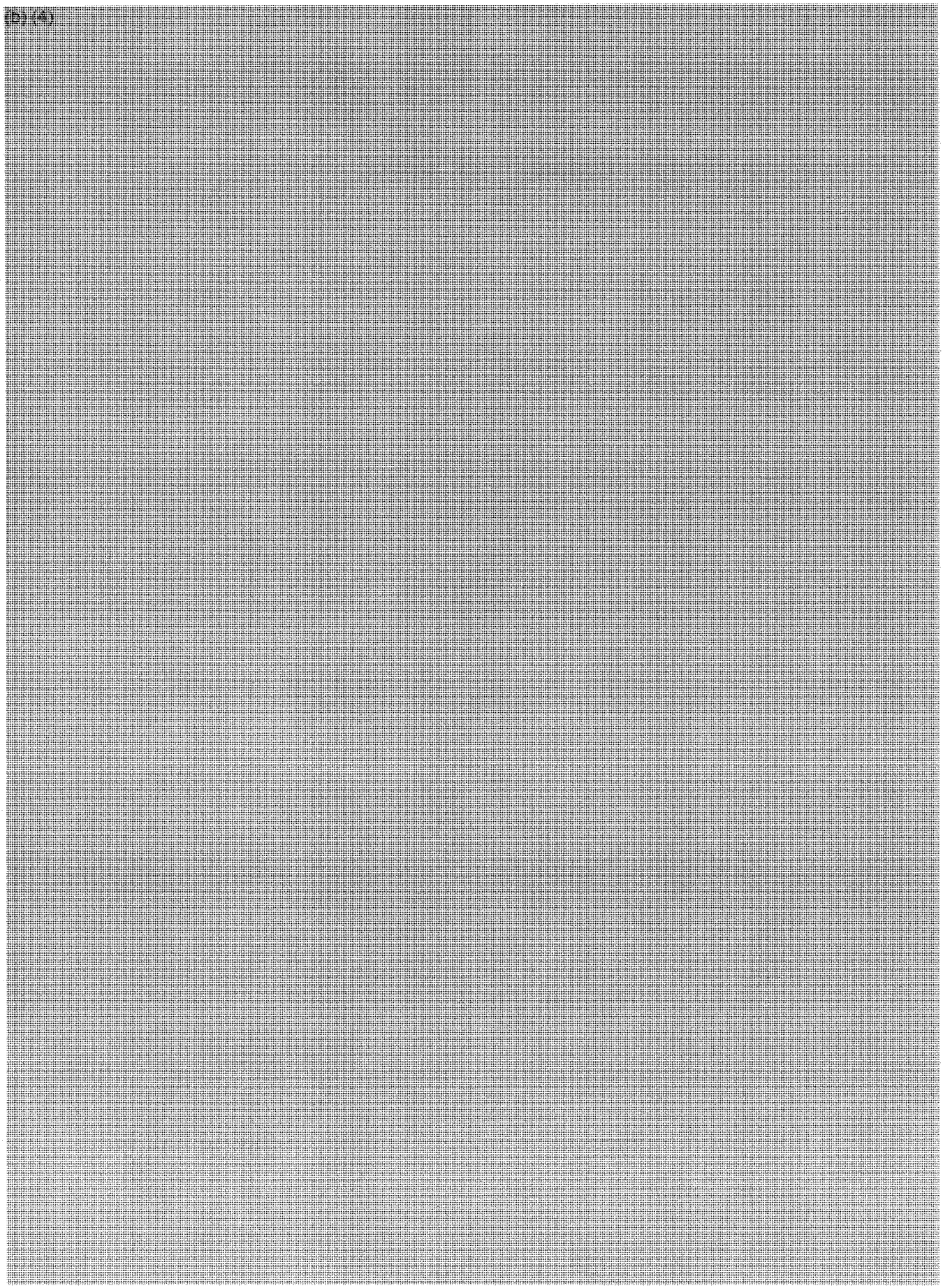
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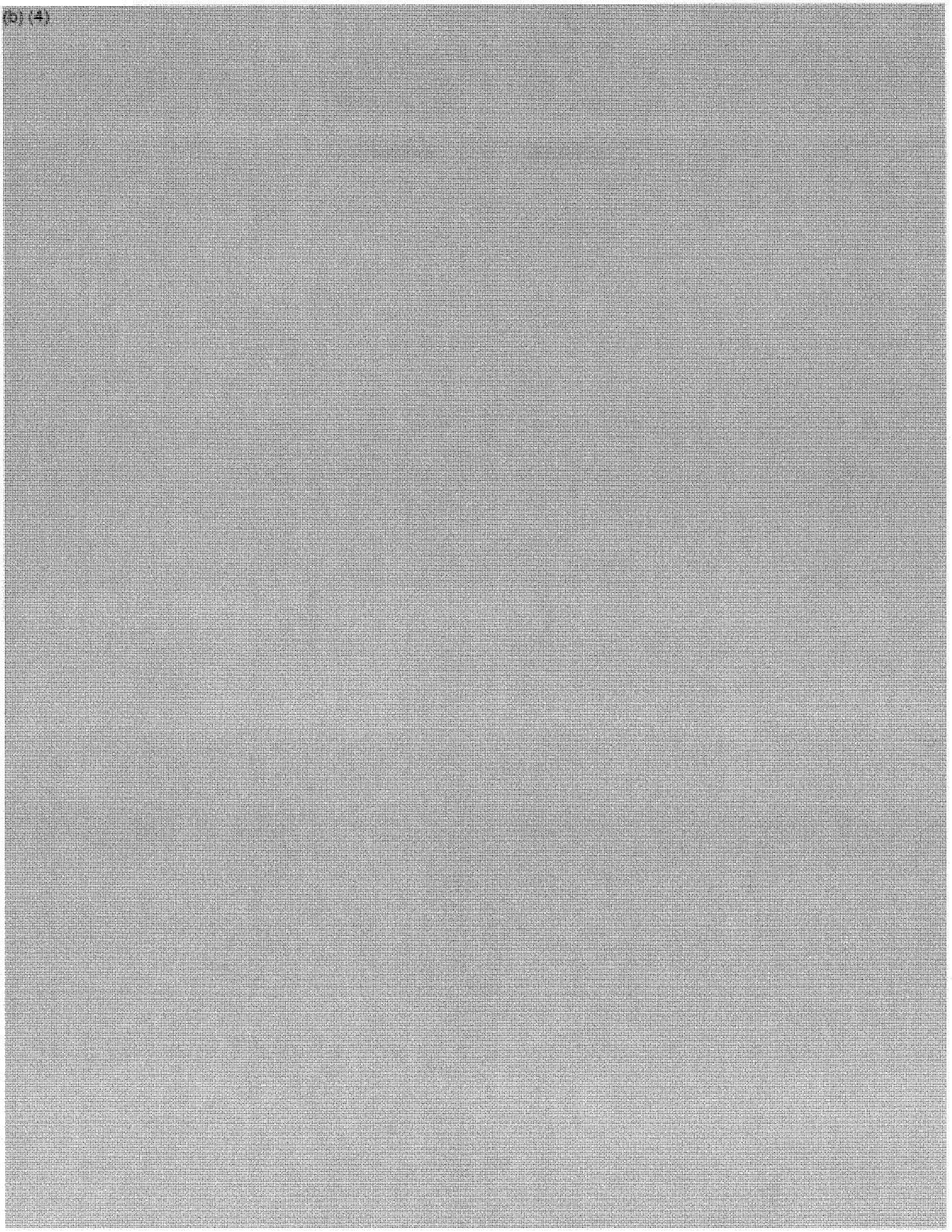

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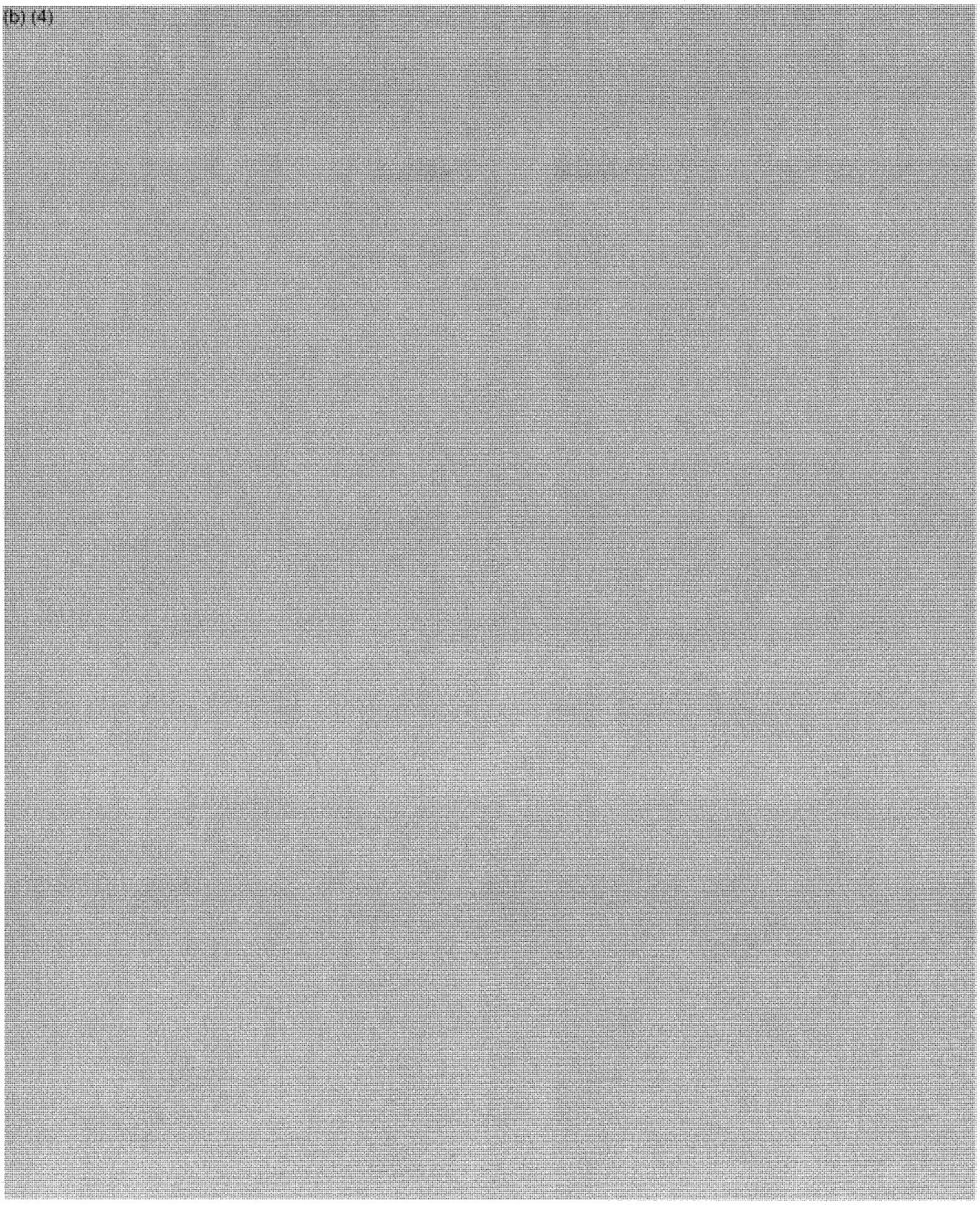


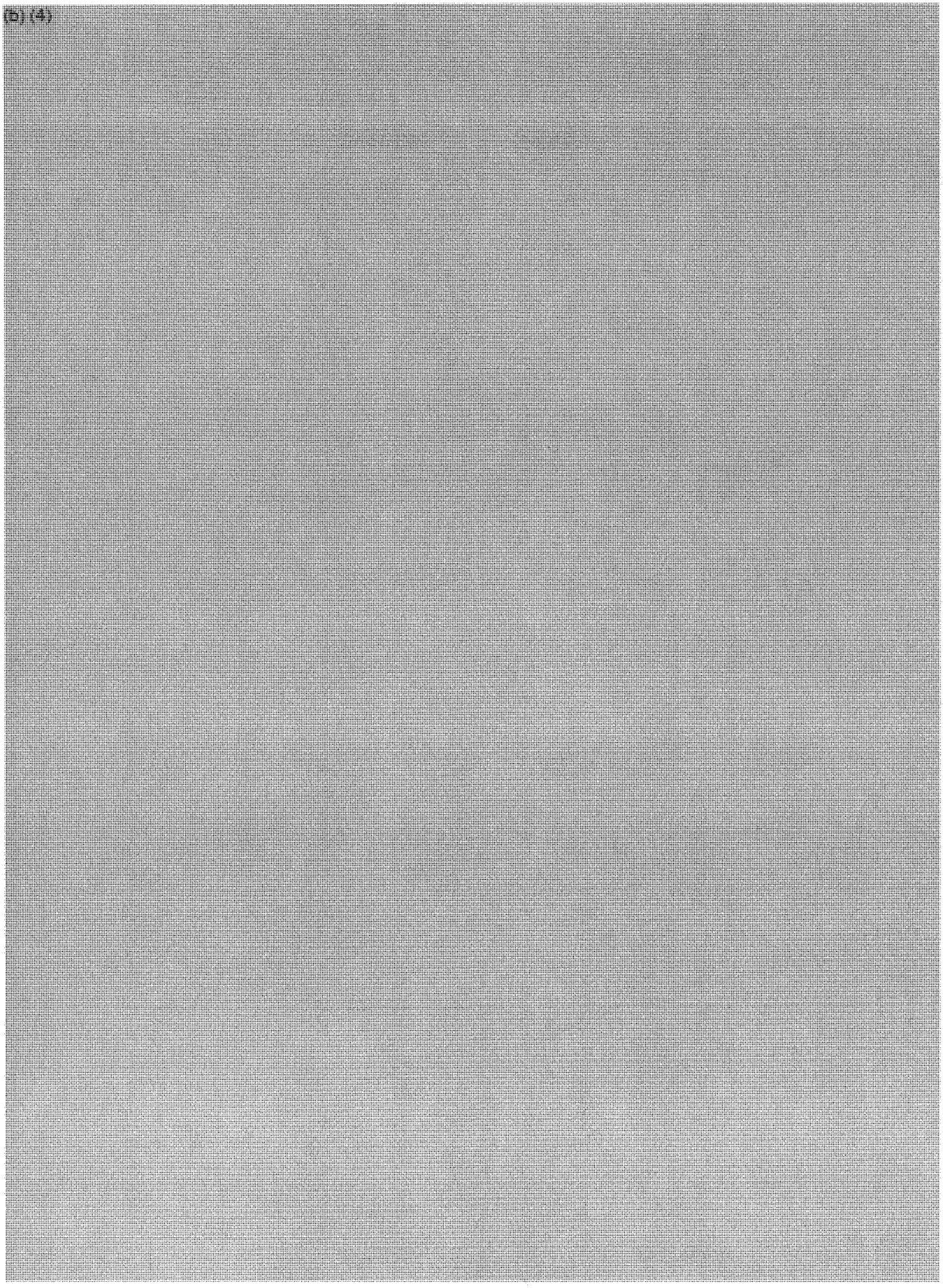

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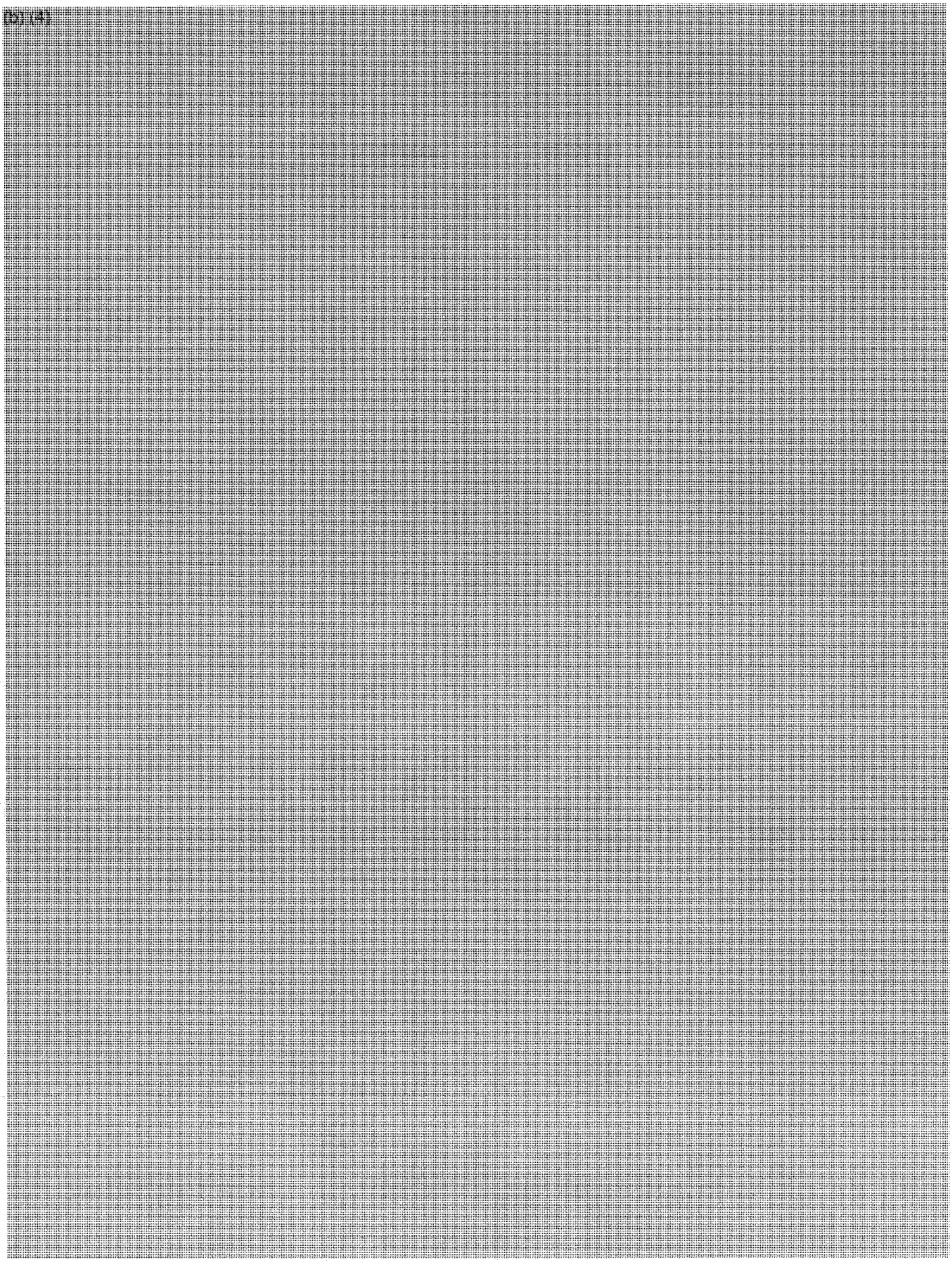


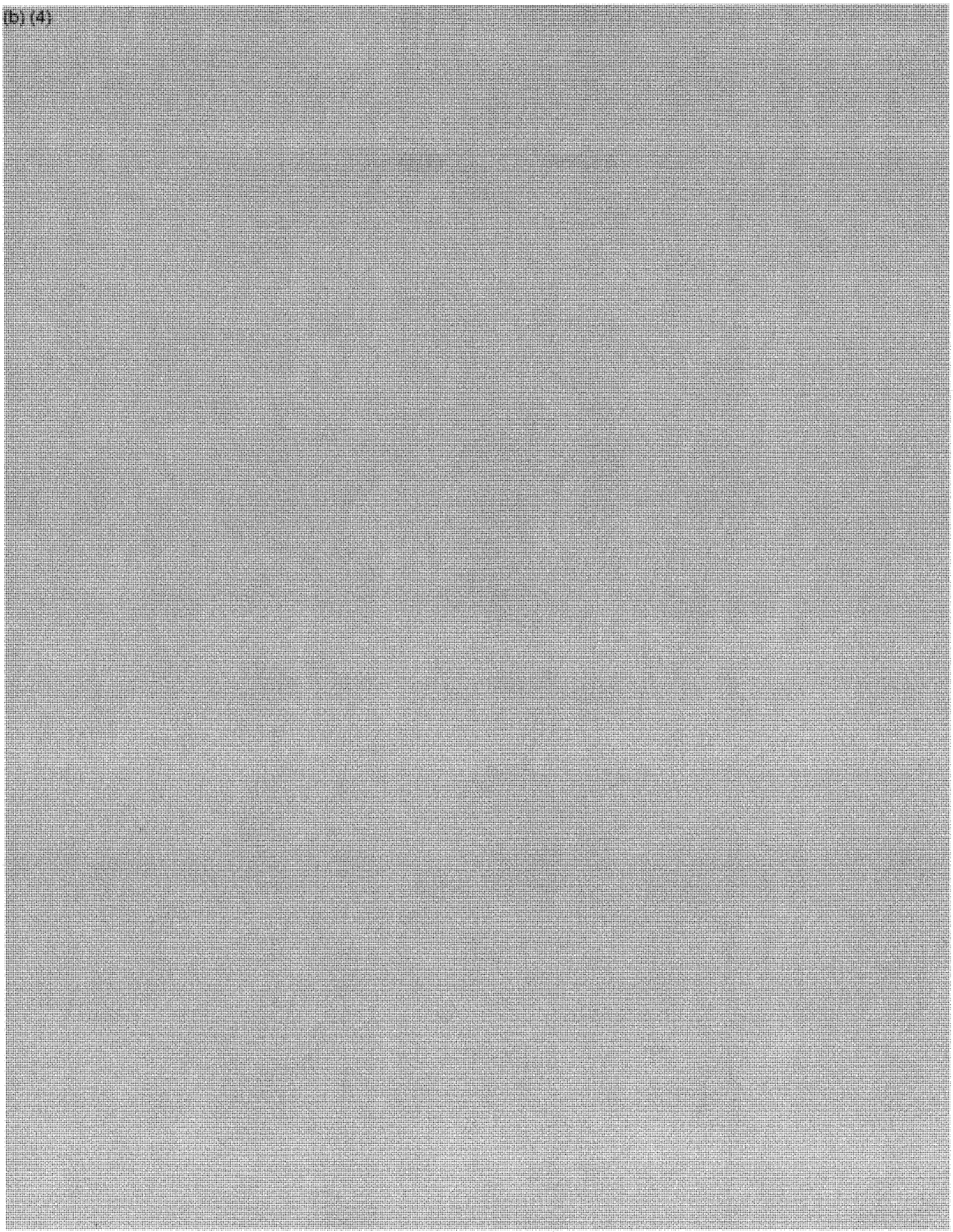
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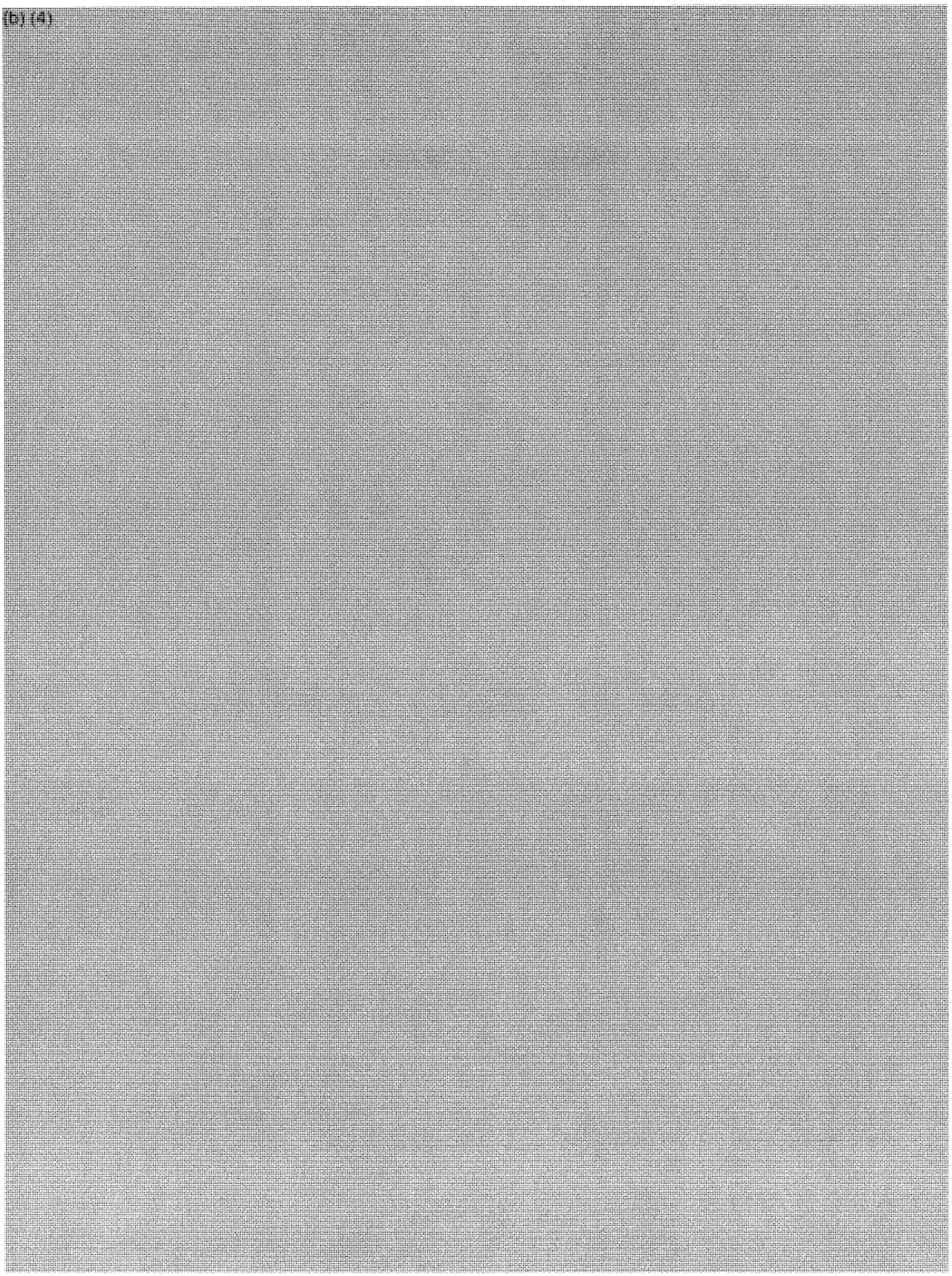



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Curriculum Vitae

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BARRY J. BYRNE

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P.O. Box 100296
Gainesville, FL 32610-0296
(352) 273-5520

Work mail: bbyrne@ufl.edu

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EDUCATION

Denison University Granville, Ohio 1974-1978	B.S.	1978	Chemistry
University of Illinois Chicago, Illinois 1978-1984	M.D. Ph.D.	1984 1984	 Microbiology & Immunology
The Johns Hopkins Hospital Baltimore, Maryland 1984-1987		Resident in Pediatrics	
Johns Hopkins University Baltimore, Maryland 1987-1991		Postdoctoral Fellow, Biological Chemistry Clinical Fellow, Pediatric Cardiology	

HONORS

Chemistry Departmental Fellow, 1976-1978
Denison University, Granville, Ohio

James Scholar, 1983
University of Illinois, Chicago, Illinois

College of Medicine Research Award, 1984
University of Illinois, Chicago, Illinois

Harriet Lane Home Fellowship Award, 1987
Johns Hopkins University, Baltimore, Maryland

Child Health Research Center Grant Awardee, 1991-1992
Johns Hopkins University, Baltimore, Maryland

Clinician Scientist Award, 1994-1996
Johns Hopkins University, Baltimore, Maryland

Univerisity of Florida, Research Professor Award, 2003-2006
University of Florida, Gainesville, Florida

University of Florida, Faculty Research Prize in Clinical Research, 2007
University of Florida, Gainesville, Florida

PROFESSIONAL EXPERIENCE

2006-present	Associate Chair for Research, Department of Pediatrics Medical Director, Congenital Heart Center University of Florida, Gainesville, Florida
2003-present	Virginia Root Sutherland Professor of Cardiology Joint Appointments: Dept. of Radiology, College of Medicine; Dept. of Small Animal Science, College of Veterinary Medicine University of Florida, Gainesville, Florida
2002-present	Professor of Pediatrics and Molecular Genetics & Microbiology Associate Chair for Research Director, Powell Gene Therapy Center University of Florida, Gainesville, Florida
1999-2002	Associate Professor of Pediatrics and Molecular Genetics & Microbiology Co-Director, Powell Gene Therapy Center M.D.- Ph.D. Program Director Pediatric Cardiology Fellowship Program Director University of Florida, Gainesville, Florida
1997-1999	Assistant Professor of Pediatrics and Molecular Genetics & Microbiology Gene Therapy Center and Center for Mammalian Genetics Pediatric Cardiology Fellowship Program Director University of Florida, Gainesville, Florida
1994-1999	Assistant Professor of Pathology Johns Hopkins University, Baltimore, Maryland
1992-1997	Assistant Professor of Pediatrics, Pediatric Cardiology Medical Director, Pediatric Cardiac Transplant Program Johns Hopkins University, Baltimore, Maryland

1987-1991	Postdoctoral Fellow with Dr. Susan Craig, Department of Biological Chemistry and Clinical Fellow, Division of Pediatric Cardiology, Johns Hopkins University.
1984-1987	Intern and Resident in Pediatrics, The Johns Hopkins Hospital, Baltimore, Maryland
1979-1984	Research Assistant and Teaching Assistant, University of Illinois, Chicago, Illinois
1978-1979	Participant in Great Lakes College Assoc. Independent Study in Science, Biology Division, Oak Ridge National Lab, Oak Ridge, Tennessee
1976-1978	Department of Chemistry Fellow and Teaching Assistant, Denison University, Granville, Ohio

MEMBERSHIP AND PROFESSIONAL ACTIVITIES

Board Certification: Pediatrics and Pediatric Cardiology; 1993-present
Medical Licensure: State of Florida; 1999-present
Fellow – American College of Cardiology, 2006 – present
NIH Study Section Chair, Skeletal Muscle Biology, 2006 – 2009.
American Society of Gene Therapy Coordinating Reviewer, 2002-present, Chair 2009.
NIH Study Section Member, Skeletal Muscle Biology, 2001-2008
Society of Regenerative Medicine and Stem Cell Biology- Member, 2000-present
Southern Society for Pediatric Research-Member, 2000-present
Cardiovascular Diseases in the Young – Member, 1997- present
American Society of Cell and Gene Therapy – Program Committee and Member, 1997 - present
American Heart Association Reviewer, 1996-present
Fellow - American Academy of Pediatrics; 1993- present
American Pediatric Society / Society for Pediatric Research; 2000-present
International Society for Heart and Lung Transplantation; 1993-present
Co-Chair, Rare Disease Committee, CTSA Consortium-Child Health Oversight Committee; 2009-

GRANTS and CONTRACTS

ACTIVE

"Gene Therapy Using Viral Vectors for Lung and Cardiovascular Disease"
NIH-P01 HL59412-01 (PI - Proj 4 and Program Co-PI) $1,267,724 (15% effort)

"Transduction of Hepatocytes with Recombinant AAV for Correction of Genetic and Metabolic Abnormalities"
NIH PO1 DK58327-01 08/01/05 – 07/31/11 PI - Byrne $765,000 (15% effort)
Renewal Pending (NICHD)

"Control of Breathing in Glycogen Storage Disease"
R01 HD052682 2/15/07 – 1/31/11 Joint-PI $251,000 (10% effort)
Renewal Pending

"UFCC for Cardiovascular Cell Therapy Research Network"
NHLBI 1/1/11 – 12/31/2015 Co-PI $358,850 (5% effort)

"Phase I/II Trial of AAV-GAA in Pompe Disease" $1,429,722 (10% effort)
NHLBI, GTRP; 06/10 – 05/2012 PI

"Phase I Clincal Study of ZC-701 in Pompe Disease $825,000 (5% effort)
BioMarin/Zystore, 12/2010 – 05/2012 PI

"Magnetic Resonance Imaging and Biomarkers for Muscular Dystrophy"
R01 AR056973-01A1 4/1/2010 – 3/31/2015 Co-I $7,135,744 (5% effort)

"Failed Regeneration in the Muscular Dystrophies: Inflamation, Fibrosis and Fat"
U54 AR052646 - Senator Paul Wellstone Center
NINDS/NHLBI 7/1/10 – 6/30/2015 UF Co-PI $1,239,260 (5% effort)

"Correction of Mitochondrial Dysfunction in a Human iPS Cell Model of Barth Syndrome"
R01HL115274-01
NHLBI 7/1/12 – 6/30/2017 (review pending) Joint PI (Terada) $441,500

RECENT
"Clinical Trials of Gene Therapy for Leber Congenital Amaurosis"
U10 NEI PI-Byrne $ 464,494 (10% effort)

"National Gene Vector Laboratory Toxicology Center"
NIH, 5U42RR016586, 09/30/01 – 08/31/10 PI $4,304,390

"Adeno-Associated Virus-Modified Human Skeletal Myoblast Therapy for Heart Failure"
Bioheart, 7/1/04 – 6/31/11 PI- Byrne PI $185,000

"Pharmacological Chaperone Therapy for Pompe Disease"
Amicus Therapeutics, 9/1/06 – 5/2/11 PI $268,325

"A Randomized, Open-label, Multicenter, Multinational, Dose-Ranging Study of the Safety, Efficacy, Pharmacokinetics, and Pharmacodynamics of Recombinant Human Acid alpha-Glucosidase (rhGAA) Treatment in Patients ≤ 6 Months Old with Infantile-Onset Pompe Disease
Effective Dates: 1/15/2004 – 4/25/2007, Site PI TDC: $367,207

"An Open-Label, Multicenter, Multinational Study of the Safety, Efficacy, Pharmacokinetics, and Pharmacodynamics of Recombinant Human Acid alpha-Glucosidase (rhGAA) Treatment in Patients >6 and <24 months Old with Infantile-Onset Glycogen Storage Disease Type II
Effective Dates: 1/ 1/ 2003 – January 27, 2007, PI TDC: $525,374

"Preclinical Study of Gene Replacement in Muscular Dystrophy"
Muscular Dystrophy Association, PI- Byrne 1/1/02-9/31/06 $2,150,000

"Glycogen Storage Disease: Hepatic Gene Therapy"
R01 DK58236-01 PI - Byrne/Chou 08/1/2000 - 7/31/2003 $300,000

"Preclinical Studies of Enzyme Replacement Therapy for Inherited Cardiomyopathy"
Novazyme Pharmaceuticals, Inc. 9/12/00-4/12/03 $200,000

"Cardiac Muscle Regeneration Using Mesenchymal Stem Cells"
NIST-ATP: Osiris Therapeutics / Byrne 12/1/97 - 11/30/2001 $225,000

"Preclinical Study of Parvovirus Mediated Gene Therapy for Inherited Cardiomyopathy"
AHA-50971B 7/1/2000 – 6/30/2002 $120,000
AHA - Florida Affiliate Grant in Aid

"Induction of Cardiac and Endothelial Allograft Tolerance Using AAV Vectors"
JDFI Center Grant (Atkinson, PI)
9/1/00-8/31/05 Juvenile Diabetes Foundation
Core B (Vector Core) (Muzyczka/Byrne)

PATENTS and APPLICATIONS

1. **7,829,078** Methods of treating anemia using recombinant adeno-associated virus virions; July 15, 2008.
2. **7,704,492** Methods for delivering DNA to muscle cells using recombinant adeno-associated virus virions; July 15, 2008.
3. **7,238,674** Methods for delivering DNA to muscle cells using recombinant adeno-associated virus vectors; March 5, 2002.
4. **7,094,604** Production of pseudotyped recombinant AAV virions, March 11, 2004.
5. **6,783,972** Methods for large-scale production of recombinant AAV vectors; Sept. 22, 1999.
6. **6,660,514** Method of preparing recombinant adeno-associated virus compositions; July 21, 2000.
7. **6,610,290** Adeno-associated virus vectors for the treatment of a cardiomyopathy;
8. **6,461,606** Materials and methods for gene therapy; October 1, 2001.
9. **6,335,011** Methods for delivering DNA to muscle cells using recombinant adeno-associated virus virions to treat lysosomal storage disease; Sept. 28, 1999
10. **6,211,163** Methods for delivering DNA to the bloodstream using recombinant adeno-associated virus vectors; May 10, 1999.
11. **6,146,874** Method of preparing recombinant adeno-associated virus compositions; May 10, 1999.
12. **5,962,313** Adeno-associated virus vectors comprising a gene encoding a lyosomal enzyme; Jan. 16, 1996.
13. **5,858,351** Methods for delivering DNA to muscle cells using recombinant adeno-associated virus vectors; Jan. 16, 1996.
14. **6,083,025** Gene Therapy of Alpha-1 Antitrypsin Deficiency using Skeletal Muscle Delivery of an Adeno-associated Virus Vector; 4/24/98.
15. **UF#-1864** A Method of Purification of Recombinant AAV; 6/98.
16. Scaleable Production of Recombinant AAV using Recombinant Viral Helper Vectors, 1998.

SERVICE ACTIVITES

CTSA – Rare Disease Committee, Co-Chair
CC-CHOC Working group on Core Competency, Chair.
GCRC Scientific Advisory Committee Member
University of Florida Medical School Selection Committee
Associate Editor, *Current Gene Therapy; Cardiology Today*
NIH, Skeletal Muscle Biology Study Section Member and Chair
Director, M.D.- Ph.D. Program

RESEARCH INTERESTS

- Adeno-associated virus mediated gene transfer in the cardiovascular system and striated muscle.
- Cell therapy in cardiovascular disease.

- Gene therapy for muscular dystrophy (Pompe disease and DMD).
- Mechanisms of allograft tolerance in cardiac transplantation.
- Cardiac development.

INVITED LECTURES

Gene Therapy in Cardiomyopathy and Transplantation
Johns Hopkins University, Pediatrics Grand Rounds, 1995.

AAV Vector Biology and Applications in Therapeutic Protein Production
Johns Hopkins University, 1995.

Genetic Therapies in Cardiomyopathy and Transplantation
Case Western Reserve University, Cleveland, OH, 1996.

Cardiac Gene Therapy
4th Asian Congress of Cardiology, Bangkok, Thailand, 1996.

Gene Therapy using DNA Viral Vectors for Cardiomyopathy
IDP Grand Rounds, University of Florida, 1997

Parvovirus-Mediated Gene Therapy
Society for General Microbiology, Warwick, UK, 1997.

AAV Vectors for Inherited Cardiomyopathy
Inter. Gene Therapy Society Meeting, Heracklion, Crete, 1998.

Parvovirus-mediated Gene Therapy in Cardiovascular Disease
Indiana University, Indianapolis, IN, 1999.

NIH-Italian Conference on Genetic and Pharmacological Approaches in Vascular Biology, Milan, Italy, 1999.

Gene Therapy for the Treatment of Lysosomal Storage Diseases
Southern Society of Pediatric Research, February, 1999.

How to make and use AAV vectors
American Heart Association, 1999.

AAV Vectors for Neuromuscular Disease
UCLA Neuromuscular program and Cedars-Sinai, 2002

AAV Vectors for Treatment of Muscular Dystrophy
MDA Symposium, 2004

Clinical Development of AAV Vectors for Muscular Dystrophy
Monaco Meeting on Muscular Dystrophy, 2004

Sustained Correction of Pompe Disease Using AAV Vectors: Effects of Early Gene Transfer on Cardiac and Pulmonary Function
NHLBI Symposium on Fetal Gene Therapy, 2005

Gene Therapy in Pompe Disease: Pathway to Clinical Studies

Myology, Nantes France, 2005

Clinical Development of AAV Vectors for Muscular Dystrophy
Scripps Institute, 2005

Pompe Disease: Lessons from Preclincial Studies and Future Challenges
World LSD Meeting, 2006

Phase I Clinical Trials of rAAV2 and rAAV1-AAT
International Parvovirus Meeting, 2006

AAV SDF1a-Modified Human Skeletal Myoblast Therapy for Heart Failure
Heart Failure Society, Seattle, 2006.

Cardiac Findings and Outcome at One Year in Children Receiving Myozyme
Steps Forward in Pompe Disease, Berlin, 2006

AAV Vectors for Cardiac Gene Therapy
American Heart Association, 2007

Faculty Participant and Invited Speaker
Children's Hospital of Philadelphia, Cardiology2008

Pompe Disease: Bench to Bedside and Back
Lipman Lecture, OHSU, May 22, 2008

7th Annual Gene Therapy Symposium for Heart Lung and Blood Diseases
Plenary Lecture, 2008

Faculty Participant and Invited Speaker
Children's Hospital of Philadelphia, Cardiology2009

AAV Vectors in Neuromuscular Disease
University of Florida
Center for Exercise Science, 2009

Pharmacological Chaperones in LSD Treatment
World Lysosomal Storage Disease Meeting, San Diego, 2009

3rd Annual Anniversary of Darby Clinical Research Institute, Plenary Talk
Medical University of South Carolina, 2009

Pharmacological Chaperones in LSD Treatment
Americal College of Medical Genetics, Tampa, 2009

Novel Biological Therapies for Inherited Disease in Children: Lessons from Animal Models and Clinical Studies
Asian Society for Pediatric Research, 2010

AAV-Mediated Gene Therapy for Pompe: Beyond the Muscle Disease
Cardiology2010, Plenary Talk, Orlando 2010.

AAV Vectors in Neuromuscular Disease: Bench to Bedside
University of Florida, Muscle Biology Seminar Series, 2009

Contemporary Questions in Congenital Heart Disease
Sick Kids, Toronto, Canada, 2009.

NHLBI Symposium on Cardiovascular Regerative Medicine
Bethesda, MD 2009

Novel Biological Therapies for Inherited Disease in Children: Lessons from Animal Models and Clinical Studies
Asian Society for Pediatric Research, 2010

AAV-Mediated Therapy for Pompe: Beyond the Muscle Disease
Cardiology 2010, 13th Update on Pediatric Cardiovascular Disease

Strategies for Treatment of Inherited Cardiomyopathy: Bench to Bedside
Children's Hospital of Pittsburgh, Grand Rounds, 2010

Faculty and Invited Speaker
Cardiology 2011, 14th Update on Pediatric Cardiovascular Disease

Models of Cardiac Metabolic Dysfunction
American Heart Association Invited Symposium, 2011

Treatment Using AAV-Vectors in Lysosomal Storage Disease
MPS III Symposium, University of Pennsylvania, 2011

Patient Registries in Rare Disease
Health Research Alliance Symposium, 2011

Pompe Disease: Lessons from Preclincial Studies and Future Challenges
World LSD Meeting, 2011

NHLBI Cell Therapy Network
Saudi Heart Association, Rhiad Saudi Arabia, 2011

Models of Cardiac Metabolic Dysfunction
NYU Visiting Professor, 2011

Featured Award in Basic Science Invited Lecture
Children's Hospital of Philadelphia, Caridology2012, Orlando 2012.

AAV Vectors in Neuromuscular Disease: Bench to Bedside
University of Florida
Department of Molecular Genetics and Microbiology, 2012

ABSTRACTS

Dhruva, B.R., B.J. Byrne, T. Shenk and K.N. Subramanian. Integration in vitro into simian virus 40 of a sequence that resembles a certain family of interspersed repeated sequences. Cold Spring Harbor 1980 DNA Tumor Virus Meeting. August, p. 107, 1980.

Byrne, B.J., J. Yamaguchi, D.J. Bergsma and K.N. Subramanian. The SV40 Promoter Regions: a) Localization of the early promoter within the 21-bp repeat; and b) the 72-bp repeat exhibits a pronounced host range in its enhancement effect. Cold Spring Harbor 1982 DNA Tumor Virus Meeting. August, p. 13, 1982.

Hartzell, S.W., B.J. Byrne, and K.N. Subramanian. The definition of the boundaries of the SV40 late promoter. ICRF DNA Tumor Virus Meeting, 1983.

Byrne, B.J., Kaczorowski, Y.H., Larson-Kelly, N., and S.W. Craig. Vinculin and Meta-vinculin are alternatively spliced products of a single gene. Society for Pediatric Research, 1990.

Byrne, B.J., Nicholson, K.L., and S.W. Craig. Meta-vinculin is expressed in myocardium of avian embryos with the onset of cardiac activity. ASCB, 1992.

Recchia, F.A., Byrne, B.J., Kass, D.A. Vasorelaxant Effect of Physiologic Arterial Pulsatility in Isolated Vessels. Circulation 90:4 357a, 1994.

Kourtis, A.P., Deyesu, E.E., Hruban R.H., Byrne B.J. Cardiac gene therapy with adeno-associated virus as a means of achieving graft-specific immunosuppression. Mod Pathol 8:33A, 1995.

Pauly, D., D. Johns, E. Deyesu, M. Lowery, J. Lawrence, T. Flotte, B. Byrne, P. Kessler. Acid - glucosidase deficiency: A model system for gene transfer into cardiac muscle. J. Cell. Biochem. Suppl. 21a: 370; 1995.

Kessler, P.D., Matelis, L.A., Wei, S. -K., Silverman, H.S., Flotte, T. R., Kurtzman, G.J., and B.J. Byrne. Sodium Butyrate Greatly Enhances the Efficiency of Viral Transduction in Adult Ventricular Cardiomyocytes by Adeno-associated Viral Vectors. Circulation, (92): I-296; 1995.

Podsakoff G, Carper E, Colosi P, McQuiston S, Chen X, Cao S, Kessler P, Byrne B, Kurtzman. Long-term in vivo gene expression in muscle using AAV vectors. Blood 86 (10) Suppl:1004a; 1995 *Presented American Society of Hematology, 1996.*

Kessler, P.D., Byrne, B.J., Chen, X., Matelis, LA, McQuinston, S, Kurtzman, G, Podsakoff, GM. Gene delivery to skeletal muscle results in the sustained expression and systemic delivery of therapeutic proteins. J. Invest. Med. 44:279a; 1996.

Podsakoff GM, Nakai H, McQuiston SA, Kessler PD, Byrne BJ, Couto LB, Kurtzman GJ. AAV vector-mediated gene delivery to skeletal muscle in vivo results in sustained levels of systemic erythropoietin. Blood 88 (10) Suppl 1: 509-II; 1996.

Byrne, B.J., Brust, S., Chen, X.X., Kessler, P.D., Flotte, T.R. and W. B. Guggino. Recombinant adeno-associated virus in embryonic gene therapy. Weinstein Cardiovascular Development, 1996.

Byrne BJ, Zhang G, Pauly DF, Matelis LA, Chen X, Podsakoff GM, Colosi P, Kurtzman GJ, Guggino WB, & Kessler PD AAV-mediated gene therapy for an inherited form of hypertrophic cardiomyopathy. Circulation 94: I-119; 1996.

Chen X, Kessler PD, Podsakoff GM, Kurtzman GJ, Byrne BJ. Long-term gene expression of adeno-associated virus-mediated gene transfer in mouse skeletal muscle in vivo. Circulation 94: I-43; 1996.

Conway, J., Byrne, B. and G. Hayward. GFP as a marker of transduction in an HSV-1 amplicon gene transfer system. 21st International HSV Workshop, 1996.

Conway, J., Hayward, G., and B.J. Byrne. Recombinant adeno-associated virus replication and packaging is supported by an HSV amplicon expressing *rep* and *cap*. Keystone Symposia, 1997.

Byrne BJ, Pauly DF, Zhang G, Chen X, Guggino WB, Kurtzman GJ, Kessler PD. Gene replacement in acid maltase deficiency using DNA Viral Vectors. Ped Res. 41 (4) Part 2: 19A; 1997

Pauly DP, Byrne BJ, Bayes HS, Kessler PD. Correction of the enzyme deficiency in an hereditary cardiomyopathy through passive transfer of recombinant enzyme. Circulation 96: Suppl. I: I-18; 1997.

Bayes, H, Pauly, D., Johns, D., Lawrence, J., Kessler, P., and B.J. Byrne. Therapeutic Strategy for Lysosomal Storage Disease Based on DNA Viral Vectors. Amer. Soc. Gene Therapy 1st Annual Meeting, May 28-31st, 74a, 1998.

Song, S., Morgan, M., Ellis, T., Poirier, A., Chesnut, K., Wang, J., Brantly, M., Atkinson, M., Byrne, B.J., and TR Flotte. Sustained Secretion of Human Alpha-1 Antitypic from Murine Muscle Transduced with Adeno-associated Virus Vectors., Amer. Soc. Gene Therapy, 1998.

Conway, J., C. M. J. Ap Rhys, I. Zolotukhin, G.S. Hayward and B.J. Byrne, High Titer Recombinant Adeno-Associated Virus Production Utilizing A Replication Defective Recombinant Herpes Virus Expressing Aav-2 Rep And Cap And The Hsv-1 Helper Functions. Cold Spring Harbor Symposium, 1998.

Byrne, B.J., Raben, N., Plotz, P., Fraites, T., and P.D. Kessler., Reconstitution of Acid α–Glucosidase Activity in a Mouse Model of Cardiomyopathy, Pompe Disease. Platform Presentation, American Heart Association, Circulation 98: Suppl. I: I-737, 1998.

Toma C, Byrne BJ, Golub J, Gruber PJ, Murry CE Pittenger MF, Kessler PD. Efficient myogenic conversion of human mesenchymal stem cells with forced expression of MyoD. Circulation 100: Suppl. I: 1-164, 1999.

Pauly D, Fraites T, Schlessing, Cloutier D, Kessler PD, Byrne BJ. Correction and Transfer of Enzyme Activity Using Adenovirus encoding Human and Murine Acid a-glucosidase. Amer. Soc. Gene Therapy 2nd Annual Meeting, p 178a, June 9-13, 1999.

Toma C, Pittenger M, Byrne BJ, Kessler PD. Adult Human Mesenchymal Cells Differentiate to a Striated Muscle Phenotype following Arterial Delivery to the Murine Heart. Circulation 102: Suppl. II: II-683, 2000.

Fraites TJ, Schlessing MR, Owens KM, Cloutier DA, Zolotukhin I, Raben N, Plotz PH, Kessler PD, Byrne BJ. Recombinant adeno-associated virus mediated correction of murine acid a-glucosidase deficiency. Molecular Ther 1: Part 2 of 2; S254, 2000.

Cresawn,KO, Porvasnik,SL, Raben,R, Plotz, PR and BJ Byrne. Inhibition of Humoral Immunity in Liver-Targeted Gene Therapy for Glycogen Storage Disease Type II. American Society of Gene Therapy 5th Annual Meeting, June 5-9, 2002. Molecular Ther., Vol 5, (5) Part 2 of 2; S342, May 2002.

Schleissing, MR, Porvasnik, SL and BJ Byrne. Delivery of Recombinant Adeno-Associated Virus Encoding Human Acid Alpha-Glucosidase through *Intra-Uterine* Injection in a Murine Model of Pompe Disease. American Society of Gene Therapy 5th Annual Meeting, June 5-9, 2002. Molecular Ther., Vol 5, (5) Part 2 of 2; S362, May 2002.

Mah, Cathryn; Cresawn, Kerry O; DeRuisseau, Lara R; Fuller, David; Byrne, Barry J: Correction of Respiratory Function by Recombinant AAV1 Mediated Gene Therapy ina Murine Model of glycogen Storage Disease Type II. Poster Session, Gene Therapy Approaches to Pulmonary Disease. American Society of Gene Therapy 8th Annual Meeting, June 1-5, 2005, St. Louis, MO.

Pacak, Christina A; Mah, Cathryn; Gaidosh, Gabriel; Lewis, Melissa; Torres, Raquel; Campbell, Kevin; Walter, Glenn A; Byrne, Barry J: Development of AAV-Mediated Gene Therapy for Murine Models of Genetic Diseases Affecting the Heart. American Society of Gene Therapy 8th Annual Meeting, June 1-5, 2005, St. Louis, MO

Kohlbrenner, Erik; Aslanidi, George; Nash, Kevin; Shklayev, Stanislav; Campbell-Thompson, Martha; Byrne, Barry J; Snyder, Richard O; Muzyczka, Nicholas; Warrington, Kenneth H; and Zolotukhin; Sergei: Successful Production of Pseudotyped Mosaic rAAV Vectors Using a Modified Baculovirus Expression System. American Society of Gene Therapy 8th Annual Meeting, June 1-5, 2005, St. Louis, MO

Young-Kook, Choi; Zolotukhin, Irene; Byrne, Barry J; and Song, Sihong: Effect of DNA-PKcs on AAV Replication. Poster Session: AAV Vectors: Vector Biology. American Society of Gene Therapy 8th Annual Meeting, June 1-5, 2005, St. Louis, MO

DeRuisseau, Lara R; Mah, Cathryn S; Farites, Thomas J; Fuller, David D; and Byrne, Barry J: Recombinant AAV1-Mediated Treatment of CNS Glycogen Accumulation in Mouse Model of Glycogen Storage Disease Type II. American Society of Gene Therapy 8th Annual Meeting, June 1-5, 2005, St. Louis, MO

Cresawn, Kerry O; Mah, Cathryn S; Fraites, Thomas J; Lewis, Melissa A; zolotukhin, Irene; and Byrne, Barry J: Sustained Correction of Glycogen Storage Disease Type II by rAAV1 Vector-Medlated Gene Therapy. Poster Session: Inborn Errors of Metabolism: Liver and Pancreatic Diseases. American Society of Gene Therapy 8th Annual Meeting, June 1-5, 2005, St. Louis, MO

Cresawn, Kerry O; Mah, Cathryn S; Zolotukhin, Irene; Lewis, Melissa A; and Byrne, Barry J: Comparison of rAAV Serotype, Promotor, and Treatment Age for the Correction of Glycogen Storage Disease Type II. Poster Session: Inborn Errors of Metabolism: Liver and Pancreatic Diseases. American Society of Gene Therapy 8th Annual Meeting, June 1-5, 2005, St. Louis, MO

Brantly, Mark L; Humphries Margaret; Song, Sihong; Conlon, Thomas; Poirier, Amy; Byrne, Barry J; Snyder, Richard, and Flotte, Terence R: Phase I Clinical Trial of Recombinant Adeno-Associated Virus (rAAV)-Alpha-1 Antitrypsin Vectors. American Society of Gene Therapy 8th Annual Meeting, June 1-5, 2005, St. Louis, MO

Porvasnik, Stacy L; Onal, Tankut; Sakai, Yoshi; Torres, Raquel; Walter, Glenn A; Byrne, Barry J; and Spencer, Carolyn T: Gene Therapy in a Rat Model of Pulmonary Hypertension. American Society of Gene Therapy 8th Annual Meeting, June 1-5, 2005, St. Louis, MO

Simon, Greg; Wasserfall, Clive; Byrne, Barry; and Atkinson, Mark: Prevention of Type 1 Diabetes in the NOD Mouse. The 8th Meeting of the Immunology of Diabetes Society (IDS-8). October 6-9, 2005.

Pacak, C.A., C. Mah, B. Thattaliyath, M.A. Lewis, S. Germain, and B.J. Byrne (2006). The AAV9 Capsid Preferentially Transduces Cardiac Tissue and demonstrates unique behavior In Vivo. XIth Parvovirus Workshop. Les Diablerets, Switzerland.

Pacak, C., C. Mah, B. Thattaliyath, M. Lewis, S. Germain, G. Walter, and B.J. Byrne (2006). AAV9-Mediated Gene Delivery Corrects the Cardiac Phenotype in a Mouse Model of Pompe Disease. 5th Annual Gene Therapy Symposium for Heart, Lung, and Blood Diseases. Sonoma, California.

Mah, C., C.A. Pacak, K.O. Cresawn, L.R. DeRuisseau, S. Gremain, M.A. Lewis, D.D. Fuller, and B.J. Byrne (2006). Physiological Correction of Pompe Disease using Adeno-Associated Serotype 1 Vectors. XIth Parvovirus Workshop. Les Diablerets, Switzerland. Oral Presentation.

Pacak, C.A., C. Mah, K.O. Cresawn, M.A. Lewis, S. Germain, and B.J. Byrne (2006). rAAV2/9 Mediated Gene Delivery of Acid a-Glucosidase Corrects the Cardiac Phenotype in a Mouse Model of Pompe Disease. The American Society of Gene Therapy 9th Annual Meeting, Baltimore, Maryland.

Mah, C., L.R. DeRuisseau, C.A. Pacak, M.A. Lewis, D.D. Fuller, and B.J. Byrne (2006). Correction of Ventilation in Glycogen Storage Disease Type II Mice and Gel-Mediated Delivery of Adeno-Associated Virus Serotype 1 Vectors. The American Society of Gene Therapy 9th Annual Meeting, Baltimore, Maryland.

DeRuisseau, L.R., C. Mah, D.D. Fuller, and B.J. Byrne (2006). Neural Deficits Contribute to respiratory Insufficiency in Pompe Disease: A Therapeutic Approach with AAV1. The American Society of Gene Therapy 9th Annual Meeting, Baltimore, Maryland.

Mah, C., C.A. Pacak, K.O. Cresawn, L.R. DeRuisseau, S. Germain, M.A. Lewis, D.D. Fuller, and B.J. Byrne (2006). Physiological Correction of Glycogen Storage Disease Type II using Adeno-Associated Virus Serotype 1 Vectors. The American Society of Gene Therapy 9th Annual Meeting, Baltimore, Maryland. Oral Presentation.

DeRuisseau, L.R., C. Mah, B.J. Byrne, and D.D. Fuller (2006). Neural Control of Breathing: Disease and Plasticity (2006). Experimental Biology Meeting Abstracts. The FASEB Journal, 20, Abstract #750.

CA Pacak, G Gaidosh, S Germain, M Lewis, GA. Walter, BJ Byrne (2006). Muscle Specific Delivery of the Alpha Sarcoglycan Gene Provides Functional and Morphological Correction of Limb Girdle Muscular Dystrophy Type 2D, Pediatric Science Days, 2006.

CA Pacak, C Mah, K Cresawn, M Lewis, S Germain, B Byrne (2006). rAAV2/9 Mediated Gene Delivery of Acid α-Glucosidase Corrects the Cardiac Phenotype in a Mouse Model of Pompe Disease. American Society of Gene Therapy: (Oral Presentation – June 2006, Baltimore MD)

CA. Pacak, C Mah, B Thattaliyath, MA. Lewis, S Germain, BJ Byrne (2006). The AAV9 Capsid Preferentially Transduces Cardiac Tissue and Demonstrates Unique Behavior In Vivo. Parvovirus Workshop: (Oral Presentation – Aug. 2006, Les Diablerets, Switzerland)

Polyak, S., A. Acosta, S. Porvasnik, T. Conlon, A. Mach, J.F. Valentine, B.J. Byrne, and C. Mah. (2007). Identification of new AAV vector pseudotypes suitable for small intestine and colon gene transfer. Crohn's and Colitis Foundation National Research and Clinical Conference/6th Annual Advances in the Inflammatory Bowel Diseases. Aventura, Florida. Oral Presentation.

Pacak, C.A., C. Mah, B. Thattaliyath, M.A. Lewis, S. Germain, G.A. Walter, and B.J. Byrne. (2007). The AAV9 Capsid Preferentially Transduces Cardiac Tissue and demonstrates unique behavior In Vivo. The American Society of Gene Therapy 10th Annual Meeting. Seattle, Washington.

Correia, C.E., D.A. Weinstein, J. Verstegen, A. Specht, J.Y. Chou, B.J. Byrne, and C. Mah. (2008). Early Administration of rAAV2/8 Vector Mediates short-term Correction of a Canine Model of Glycogen Storage Disease Type Ia. The American Society of Gene Therapy 11th Annual Meeting. Boston, Massachusetts.

DJ Falk, CS Mah, DA Cloutier, MA Lewis, DD Fuller, and BJ Byrne (2009). Rapid rAAV-mediated Improvement of Respiratory Function in an Animal Model of Pompe Disease. 12th Annual ASGT meeting, San Diego, May 2009.

Correia, C., D. Weinstein, L. Fiske, J. Verstegen, A. Specht, M. Struck, H. Ramirez, K. Onclin-Verstegen, S. Porvasnik, J. Chou, B. Byrne, and C. Mah. (2009). Administration of rAAV2/8 and rAAV2/1 vectors mediates sustained correction of a canine model of glycogen storage disease type Ia. The American Society of Gene Therapy 12th Annual Meeting. San Diego, California.

Falk, D.J., C.S. Mah, D.A. Cloutier, D.D. Fuller, and B.J. Byrne (2009). Rapid rAAV-Mediated Improvement of Respiratory Function in an Animal Model of Pompe Disease. The American Society of Gene Therapy 12th Annual Meeting. San Diego, California.

DJ Falk, MS Soustek, CS Mah, DA Cloutier, SA Germain, and BJ Byrne (2010). Systemic Delivery of AAV2/9 Vectors Improve Cardiac Function in Pompe Disease. 13th Annual ASGCT meeting, Washington DC, May 2010.

DJ Falk, MS Soustek, CS Mah, DA Cloutier, SA Germain, JS Kelley, KE Erger, TJ Conlon, N Clement, and BJ Byrne (2010). Acid Alpha-Glucosidase Delivery Using Adeno-Associated Virus-2/9 in Adult Animals Improves Respiratory and Cardiac Function in Pompe Disease. 2nd Conference on Clinical Research for Rare Diseases, Bethesda, MD, September 2010.

DJ Falk, MS Soustek, CS Mah, DA Cloutier, SA Germain, JS Kelley, KE Erger, TJ Conlon, N Clement, and BJ Byrne (2010). Systemic delivery of AAV9 augments cardiac and respiratory function in a murine model of Pompe disease. 10th Annual Gene Therapy Symposium; Sonoma, CA, November 2010.

DJ Falk, M.S. Soustek, C.S. Mah, D.A. Cloutier, S.A. Germain, and B.J. Byrne (2010). Systemic Delivery of AAV2/9 Vectors Improve Cardiac Function in Pompe Disease. The American Society of Gene and Cell Therapy 13th Annual Meeting. Washington, D.C. Oral Presentation.

DJ Falk, MS Soustek, CS Mah, DA Cloutier, SA Germain, JS Kelley, KE Erger, TJ Conlon, N Clement, and BJ Byrne (2011). Next generation treatment of Pompe disease using systemic gene transfer with AAV9. 7th Annual World Lysosomal Storage Disease Symposium; Las Vegas, NV. Molecular Genetics and Metabolism, 2011.

PUBLICATIONS

Bergsma, D.J., D.M. Olive, S.W. Hartzell, B.J. Byrne and K.N. Subramanian. Cyclization of linear chimeric plasmids in vitro by a novel end-to-end joining reaction or by intramolecular recombination: one of the products contains a 147-bp perfect palindrome stable in Escherichia coli. Gene, 20:157-167, 1982.

Byrne, B.J., M.S. Davis, J. Yamaguchi, D.J. Bergsma and K.N. Subramanian. Definition of the simian virus 40 early promoter region and demonstration of a host range bias in the enhancement effect of the simian virus 40 72-bp repeat. Proc. Natl. Acad. Sci USA, 80:721-725, 1983.

Hartzell, S.W., B.J. Byrne and K.N. Subramanian. Mapping of the late promoter of simian virus 40. Proc. Natl. Acad. Sci. USA, 81:23-27, 1984.

Hartzell, S.W., B.J. Byrne and K.N. Subramanian. The simian virus 40 minimal origin and the 72-base pair repeat are required simultaneously for efficient induction of late gene expression with large tumor antigen. Proc. Natl. Acad. Sci. USA, 81:6335-6339, 1984.

Byrne, B.J.: The early transcriptional control region of simian virus 40. Ph.D. Thesis, University of Illinois, 1984.

Byrne, B.J., Kaczorowski, Y.H., Coutu, M.D., and S.W. Craig. Chicken vinculin and meta-vinculin are derived from a single gene by alternative splicing of a 207-base pair exon unique to meta-vinculin. J. Biol. Chem., 267(18):12845-12850, 1992.

Grenier, M.A, and B.J. Byrne, Abdominal Pain as a Presenting Symptom of Supraventricular Tachycardia, Clin. Pediatrics, 43(7):380-81, 1995.

Recchia, F.A., Senzaki, H., Saeki, A., Byrne, B.J., and D.A. Kass, Pulse pressure-related changes in coronary flow in vivo are modulated by nitric oxide and adenosine. Circ. Res., 79(4): 849-856, 1996.

Kessler, P.D., Podsakoff, G.M., Chen, X., McQuiston, S., Colosi, P., Matelis, L.A, Kurtzman, G., and B.J. Byrne. Gene delivery to skeletal muscle results in sustained expression and systemic delivery of a therapeutic protein, Proc. Nat. Acad. Sci. USA, 93: 14082-14087, 1996.

Conway, J.E., Zolotukhin, S., Muzyczka, N., Hayward, G., and B.J. Byrne., Recombinant adeno-associated virus replication and packaging is entirely supported by an HSV amplicon expressing *rep* and *cap*. J. Vir., 71(11):8780-8789, 1997.

Georgakopoulos, D., Mitzner, W., Chen, C-H, Byrne, B.J., Millar, H.D., Hare, J.M., Kass, D.A. In Vivo Murine Left Ventricular Pressure-Volume Relations by Miniturized Impedance-Micromanometry. Amer. J. Phys. 274(4 Pt 2): H1416-H1422, 1997.

Pauly, D.F., Johns, D.C., Metalis, L.A., Lawrence, J.H., Byrne, B.J., and P.D. Kessler, Complete correction of acid α-glucosidase deficiency in Pompe's disease fibroblasts in vitro and lysosomally targeted expression in neonatal cardiac and skeletal muscle, Gene Therapy, 5(4): 473-480, 1998.

Raben, N., Nagaraju, K., Lee, E., Kessler, P.D., Byrne, B.J, Lee, L., LaMarca, M., King, C., Ward, J., Sauer, B., Plotz, P., Targeted disruption of the acid maltase gene in mice causes an illness with the critical features of both infantile and adult human glycogen storage disease type II., J. Biol. Chem., 273(30):19086-19092 , 1998.

Harrison, R., Byrne, B.J. and L Tung, Electroporation as a method of gene transfer in cardiac tissue., FEBS Letters, 435(1):1-5 , 1998.

Song, S., Morgan, M., Ellis, T., Poirier, A., Chesnut, K., Wang, J., Brantly, M., Atkinson, M., Byrne, B.J., and TR Flotte, Sustained Secretion of Human Alpha-1 Antitrypsin from Murine Muscle Transduced with Adeno-associated Virus Vectors, Proc. Natl. Acad. Sci., 24;95(24):14384-8, 1998.

Kessler, P.D., and B.J. Byrne, Myoblast Cell grafting into Heart Muscle: Cellular Biology and Potential Applications, Ann. Rev. Phys., 61:219-242, 1999.

Recchia, F.A., Byrne, B.J., and D.A. Kass, Sustained vascular dilation induced by increased pulsatile perfusion of porcine carotid arteries *in vitro*., Acata Phys. Scand., 166:15-21, 1999.

Zolotukhin, S., Byrne, B.J., Mason, E., Zolotukhin, I., Potter, M., Chesnut, K., Summorford, C., Samulski, J., and Muzyczka, N., Recombinant Adeno-associated Virus Purification Using Novel Methods Improves Infectious Titer and Yield. Gene Therapy., Jun;(6)6: 973-985, 1999.

Conway J.C., apRhys, C., Zolotukhin, I, Zolotukhin, S., Muzyczka, N., Hayward G and B.J. Byrne. High-titer recombinant adeno-associated virus production utilizing a recombinant herpes simplex virus type I vector expressing aav-2 rep and cap. Gene Therapy, Jun;6(6):986-993, 1999.

Asfour B, Byrne BJ, Baba HA, Hammel D, Hruban RH, Weyand M, Deng M, Scheld HH. Effective gene transfer in the rat myocardium via adenovirus vectors using a coronary recirculation model. Thorac Cardiovasc Surg. Oct;47(5):311-6., 1999.

Asfour B, Hare JM, Kohl T, Baba HA, Kass DA, Chen K, Tjan TD, Hammel D, Weyand M, Hruban RH, Scheld HH, Byrne BJ. A simple new model of physiologically working heterotopic rat heart transplantation provides hemodynamic performance equivalent to that of an orthotopic heart. J Heart Lung Transplant, Oct;18(10):927-36., 1999.

Miller, J.W., Urbinati, C.R., Teng- Umnuay, P., Stenberg, M.J., Byrne, B.J., Thornton, C.A., Swanson, M.S. Recruitment of human muscleblind proteins to (CUG)(n) expansions associated with myotonic dystrophy. EMBO J. Sep 1;19(17):4439-4448., 2000.

Peng X, Recchia FA, Byrne BJ, Wittstein IS, Ziegelstein RC, Kass DA. In vitro system to study realistic pulsatile flow and stretch signaling in cultured vascular cells. Am J Physiol Cell Physiol. Sep; 279(3):C797-C805., 2000.

Xu, L., Daly, T., Gao, C., Flotte, T.R., Song, S., Byrne, B.J., Sands, M.S. and K.P. Ponder. The CMV-β-actin promoter directs higher expression from an AAV vector in the liver than the

CMV or EF1α promoter and results in therapeutic levels of human factor X in mice. Molecular Ther., 12(5) 563-573, 2001.

Pauly, DF, Fraites, TJ, Bayes, HS, Huie, ML, Hirschhorn, R, Plotz, PH, Raben, N, PD Kessler, and Byrne, BJ. Interceliuar transfer of the virally-derived precursor form of acid alpha-glucosidase corrects the enzyme deficiency in the inherited cardioskeletal myopathy, Pompe disease. Human Gene Therapy, 20(5): 12:527-38, 2001.

Raben, N. Lu, N., Nagaraju, K., Rivera, Y., Lee, Y., Yan, B., Byrne, B., Meikle,PJ., Umapathysivam, K., Hopwood, JJ, and P. H. Plotz. Conditional tissue-specific expression of the acid alpha-glucosidase (GAA) gene in the GAA knockout mice: implications for therapy. Human Mol. Gen, 10:19, 2039-2047, 2001.

Toma, C, Pittenger, MF, Cahill, K, Byrne, BJ and Kessler, PD. Human Mesenchymal Stem Cells Differentiate to a Cardiomyocyte-like Phenotype in the Adult Murine Heart. Circulation, 105: 93-98, Jan. 2002.

Kapturczak, M, Zolotukhin, S, Cross, J, Pileggi, A, Molano, RD, Jorgensen, M, Byrne, B, Flotte, TR, Ellis,T, Inverardi, L, Ricordi, C, Nick, H, Atkinson, M and A. Agarwal.Transduction of Human and Mouse Pancreatic Islet Cells Using a Bicistronic Recombinant Adeno-associated Viral Vector. Molecular Ther., Vol.5 (2) 1-7, Feb 2002.

Raben, N, Plotz, P, and Byrne, BJ. Acid α-glucosidase Deficiency (Glycogenosis type II, Pompe Disease), Cur Molec. Med., 2(2):195-216, March 2002.

Fraites, TJ, Schleissing, MR, Shanely,RA, Cloutier, DA, Zolotukhin, I, Pauly, DF, Raben, N, Plotz, PH, Powers, SK, Kessler, PD, and Byrne, BJ. Correction of the Enzymatic and Functional Deficits in a Model of Pompe Disease Using Adeno-associated virus vectors. Molecular Ther., Vol 5, (5) 571-578, May 2002.

Donahue, P.K., Hoke, T., Bawa, P.K., Mitchell, R., Pathak, A., Rowe, P.C., Byrne, B.J. Oxygen saturation as a screening test for Critical Congenital Heart Disease. Pediatric Cardiology, 23:403-409, 2002.

Grant MB, May WS, Caballero S, Brown GA, Guthrie SM, Mames RN, Byrne BJ, Vaught T, Spoerri PE, Peck AB, Scott EW. Adult hematopoietic stem cells provide functional hemangioblast activity during retinal neovascularization. Nat Med. 8(6):607-12, June 2002.

Mah, C, Fraites, TJ, Zolotukhin, I, Song, S., Flotte, TR, Batich, C and BJ Byrne. Improved method of recombinant AAV2 delivery for systemic targeted gene therapy. Molecular Ther., Vol 6, (1)106-12, July 2002

Mah, C, Byrne, BJ and Flotte, TR., Virus-based gene delivery systems. Clin Pharmacokinet. 2002;41(12):901-11. 2002.

Sun MS, Pan CJ, Shieh JJ, Ghosh A, Chen LY, Mansfield BC, Ward JM, Byrne BJ, Chou JY Sustained hepatic and renal glucose-6-phosphatase expression corrects glycogen storage disease type Ia in mice. Hum Mol Genet. 1;11(18):2155-64, Sep 2002.

Zolotukhin, S., Potter, M., Zolotukhin,I. Sakai,Y, Loiler, S., Fraites, TJ, Chido,V., Phillipsberg, T, Muzyczka, N, Hauswirth, W, Flotte, TR, Byrne, BJ and Richard O. Snyder. Production and Purification of Serotype 1, 2 and 5 Recombinant Adeno-Associated Viral Vectors. Methods 28(2):158-67, Oct.2002

Asfour B, Baba HA, Scheld HH, Hruban RH, Hammel D, Byrne BJ. Uniform Long-Term Gene Expression using Adeno-Associated Virus (AAV) by Ex Vivo Recirculation in Rat-Cardiac Isografts.Thorac Cardiovasc Surg. 50(6):347-50, Dec 2002.

Marques,E.T., Jr., Chikhlikar,P., de Arruda,L.B., Leao,I.C., Lu,Y., Wong,J., Chen,J.S., Byrne,B., and August,J.T. HIV-1 p55Gag encoded in the lysosome-associated membrane protein-1 as a DNA plasmid vaccine chimera is highly expressed, traffics to the major histocompatibility class II compartment, and elicits enhanced immune responses. J. Biol. Chem. 278, 37926-37936, 2003.

Cahill KS, Toma C, Pittenger MF, Kessler PD, Byrne BJ. Cell therapy in the heart: cell production, transplantation, and applications. Methods Mol Biol., 219:73-81, 2003.

Mah, C, Zolotukhin, I, Sarkar, R, Schleissing, MR, Xiao, X, Kazazian, HH, Byrne, BJ, Treatment of a Mouse Model of Hemophilia A using AAV Vectors Expressing Murine Factor VIII, Human Gene Therapy, 14:143-152, Jan.20, 2003.

Mah C, Sarkar R, Zolotukhin I, Schleissing M, Xiao X, Kazazian HH, Byrne BJ.Dual Vectors Expressing Murine Factor VIII Result in Sustained Correction of Hemophilia A Mice. Hum Gene Ther, Jan 20;14(2):143-52, Jan. 2003.

Post H, Kajstura J, Lei B, Sessa WC, Byrne B, Anversa P, Hintze TH, Recchia FA. Adeno-associated virus mediated gene delivery into coronary microvessels of chronically instrumented dogs. J Appl Physiol., 95(4);1688-94, Oct. 2003.

Cahill,K.S., Gaidosh,G., Huard,J., Silver,X., Byrne,B.J., and Walter,G.A. Noninvasive monitoring and tracking of muscle stem cell transplants. Transplantation 78, 1626-1633, 2004.

Chikhlikar,P., Barros de,A.L., Agrawal,S., Byrne,B., Guggino,W., August,J.T., and Marques,E.T., Jr. Inverted terminal repeat sequences of adeno-associated virus enhance the antibody and CD8(+) responses to a HIV-1 p55Gag/LAMP DNA vaccine chimera. Virology 323, 220-232, 2004.

Flotte TR, Brantly ML, Spencer LT, Byrne BJ, Spencer CT, Baker DJ, Humphries M. Phase I trial of intramuscular injection of a recombinant adeno-associated virus alpha 1-antitrypsin (rAAV2-CB-hAAT) gene vector to AAT-deficient adults. Hum Gene Ther.;15(1):93-128, Jan 2004.

Mah C, Fraites TJ Jr, Cresawn KO, Zolotukhin I, Lewis MA, Byrne BJ. A new method for recombinant adeno-associated virus vector delivery to murine diaphragm. Mol Ther.;9(3):458-63, Mar 2004.

Rucker M, Fraites TJ Jr, Porvasnik SL, Lewis MA, Zolotukhin I, Cloutier DA, Byrne BJ. Rescue of enzyme deficiency in embryonic diaphragm in a mouse model of metabolic myopathy: Pompe disease. Development. 131(12):3007-19, 2004.

Cahill KS, Gaidosh G, Huard J, Silver X, Byrne BJ, Walter GA. Noninvasive monitoring and tracking of muscle stem cell transplants.Transplantation. 15;78(11):1626-33. Dec 2004.

Cresawn KO, Fraites TJ, Wasserfall C, Atkinson M, Lewis M,Porvasnik S, Liu C, Mah C, Byrne BJ. Impact of Humoral Immune Response on Distribution and Efficacy of Recombinant

Adeno-Associated Virus-Derived Acid α-glucosidase in a Model of Glycogen Storage Disease Type II. Hum Gene Ther.: 16 (1): Jan., 2005.

Mohiuddin, I., Loiler, S., Zolotukhin, I, Byrne, B. J.,. Flotte, T.R., and Snyder, R.O. Herpesvirus-based Infectious Titering of Recombinant Adeno-associated Viral Vectors. Mol. Ther.: 11:320-326, 2005.

Walker MC, Mandell TC, Crawford PC, Simon GG, Cahill KS, Fernandes PJ, MacLeod JN, Byrne BJ, Levy JK: Expression of erythropoietin in cats treated with a recombinant adeno-associated viral vector. AJVR 66(3):450-456, Mar 2005.

Lane MD, Nam H-J, Padron E, Gurda-Whitaker B, Kohlbrenner E, Aslanidi G, Byrne B, McKenna R, Muzyczka N, Zolotukhin S, and Agbandje-McKenna M. Production, purification, crystallization and preliminary X-ray analysis of adeno-associated virus serotype 8. Acta Cryst F61:558-561, 2005.

Mah C, Cresawn KO, Fraites TJ, Pacak CA, Lewis MA, Zolotukhin I, Byrne BJ. Sustained correction of glycogen storage disease type II using adeno-associated virus serotype 1 vectors. Gene Ther. 2005 May 26;

Lane MD, Nam HJ, Padron E, Gurda-Whitaker B, Kohlbrenner E, Aslanidi G, Byrne B, McKenna R, Muzyczka N, Zolotukhin S, Agbandje-McKenna M. Production, purification, crystallization and preliminary X-ray analysis of adeno-associated virus serotype 8. Acta Crystallograph Sect F Struct Biol Cryst Commun. 2005 Jun 1;61(Pt 6):558-61. Epub 2005 Jun 1.

Spencer CT, Byrne BJ, Gewitz MH, Wechsler SB, Kao AC, Gerstenfeld EP, Merliss AD, Carboni MP, Bryant RM. Ventricular arrhythmia in the X-linked cardiomyopathy Barth syndrome. Pediatr Cardiol. 2005 Sep-Oct;26(5):632-7.

Kohlbrenner E, Aslanidi G, Nash K, Shklyaev S, Campbell-Thompson M, Byrne BJ, Snyder RO, Muzyczka N, Warrington KH Jr, Zolotukhin S. Successful production of pseudotyped rAAV vectors using a modified baculovirus expression system. Mol Ther. 2005 Dec;12(6):1217-25. Epub 2005 Oct 6.

Ghosh A, Allamarvdasht M, Pan CJ, Sun MS, Mansfield BC, Byrne BJ, Chou JY. Long-term correction of murine glycogen storage disease type Ia by recombinant adeno-associated virus-1-mediated gene transfer. Gene Ther. 2006 Feb;13(4):321-9.

Mohiuddin I, Loiler S, Zolotukhin I, Byrne BJ, Flotte TR, Snyder RO. Herpesvirus-based infectious titering of recombinant adeno-associated viral vectors. Mol Ther. 2005 Feb;11(2):320-6.

Howell RR, Byrne B, Darras BT, Kishnani P, Nicolino M, van der Ploeg A. Diagnostic challenges for Pompe disease: An under-recognized cause of floppy baby syndrome. Genet Med. 2006 May;8(5):289-296.

Kishnani PS, Steiner RD, Bali D, Berger K, Byrne BJ, Case L, Crowley JF, Downs S, Howell RR, Kravitz RM, Mackey J, Marsden D, Martins AM, Millington DS, Nicolino M, O'grady G, Patterson MC, Rapoport DM, Slonim A, Spencer CT, Tifft CJ, Watson MS; ACMG Work Group on Management of Pompe Disease. Pompe Disease Diagnosis and Management Guideline. Genet Med. 2006 May;8(5):267-288.

Brantly, M.L., Spencer,L.T., Humphries,M., Conlon,T.J., Spencer,C.T., Poirier,A., Garlington,W., Baker,D., Song,S., Berns,K.I., Muzyczka,N., Snyder,R.O., Byrne,B.J., and Flotte,T.R.

(2006). Phase I trial of intramuscular injection of a recombinant adeno-associated virus serotype 2 alphal-antitrypsin (AAT) vector in AAT-deficient adults. Hum. Gene Ther. 17, 1177-1186.

Kishnani, P.S., Corzo,D., Nicolino,M., Byrne,B., Mandel,H., Hwu,W.L., Leslie,N., Levine,J., Spencer,C., McDonald,M., Li,J., Dumontier,J., Halberthal,M., Chien,Y.H., Hopkin,R., Vijayaraghavan,S., Gruskin,D., Bartholomew,D., der Ploeg,A.V., Clancy,J.P., Parini,R., Morin,G., Beck,M., De la Gastine,G.S., Jokic,M., Thurberg,B., Richards,S., Bali,D., Davison,M., Worden,M.A., Chen,Y.T., and Wraith,J.E. (2006). Recombinant human acid alpha-glucosidase. Major Clinical Benefits in Infantile-Onset Pompe Disease. Neurology 2007;68:99-109.

Pacak CA, Mah CS, Thattaliyath BD, Conlon TJ, Lewis MA, Cloutier DE, Zolotukhin I, Byrne BJ, Tarantal AF; Recombinant Adeno-Associated Virus Serotype 9 Leads to Preferential Cardiac Transduction in Vivo. Circ Res. 2006 Aug 18;99(4):e3-9. Epub 2006 Jul 27. PMID: 16873720

Spencer, CT; Bryant, RM; Day, J; Gonzalez, IL; Colan, SD; Thompson, WR; Berthy, J; Redfearn, SP; Byrne, BJ; Cardiac and Clinical Phenotype in Barth Syndrome. Pediatrics 2006 *118*, e337-e346.

Polyak, S., Mah,C., Porvasnik,S., Herlihy,J.D., Campbell-Thompson,M., Byrne,B.J., and Valentine,J.F. (2007). Gene Delivery to Intestinal Epithelial Cells In vitro and In vivo with Recombinant Adeno-Associated Virus Types 1, 2 and 5. Dig. Dis. Sci.

Nam, H.J., Lane,M.D., Padron,E., Gurda,B., McKenna,R., Kohlbrenner,E., Aslanidi,G., Byrne,B., Muzyczka,N., Zolotukhin,S., and gbandje-McKenna,M. (2007). Structure of adeno-associated virus serotype 8, a gene therapy vector. J. Virol. 81, 12260-12271.

Pacak, C.A., Walter,G.A., Gaidosh,G., Bryant,N., Lewis,M.A., Germain,S., Mah,C.S., Campbell,K.P., and Byrne,B.J. (2007). Long-term skeletal muscle protection after gene transfer in a mouse model of LGMD-2D. Mol. Ther. 15, 1775-1781.

Mah, C., Pacak,C.A., Cresawn,K.O., Deruisseau,L.R., Germain,S., Lewis,M.A., Cloutier,D.A., Fuller,D.D., and Byrne,B.J. (2007). Physiological Correction of Pompe Disease by Systemic Delivery of Adeno-associated Virus Serotype 1 Vectors. Mol. Ther. 15, 501-507.

Flotte,T.R., Conlon,T.J., Poirier,A., Campbell-Thompson,M., and Byrne,B.J. (2007). Preclinical characterization of a recombinant adeno-associated virus type 1-pseudotyped vector demonstrates dose-dependent injection site inflammation and dissemination of vector genomes to distant sites. Hum. Gene Ther. 18, 245-256.

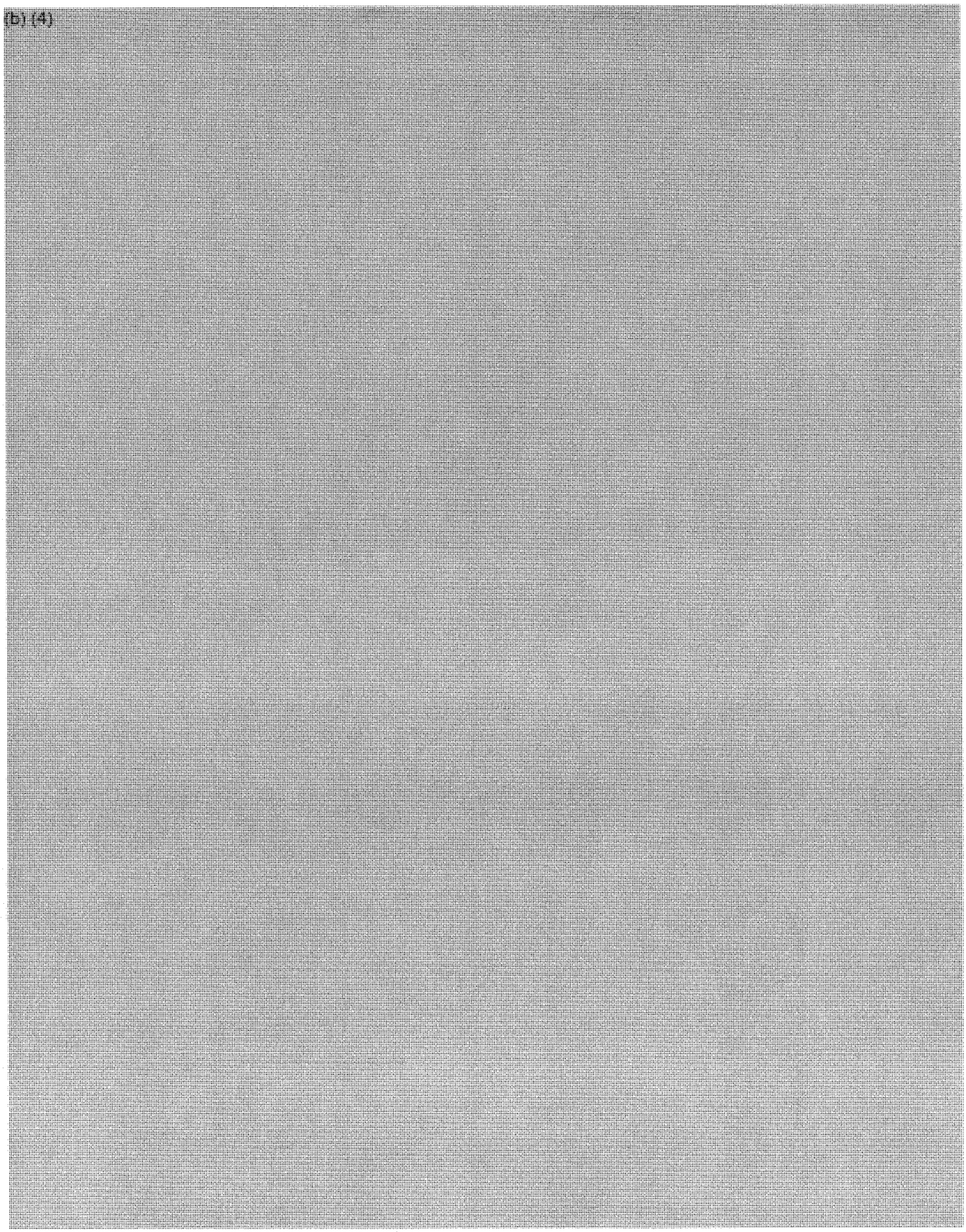
Andino, L.M., Takeda,M., Kasahara,H., Jakymiw,A., Byrne,B.J., and Lewin,A.S. (2008). AAV-mediated knockdown of phospholamban leads to improved contractility and calcium handling in cardiomyocytes. J. Gene Med. 10, 132-142.

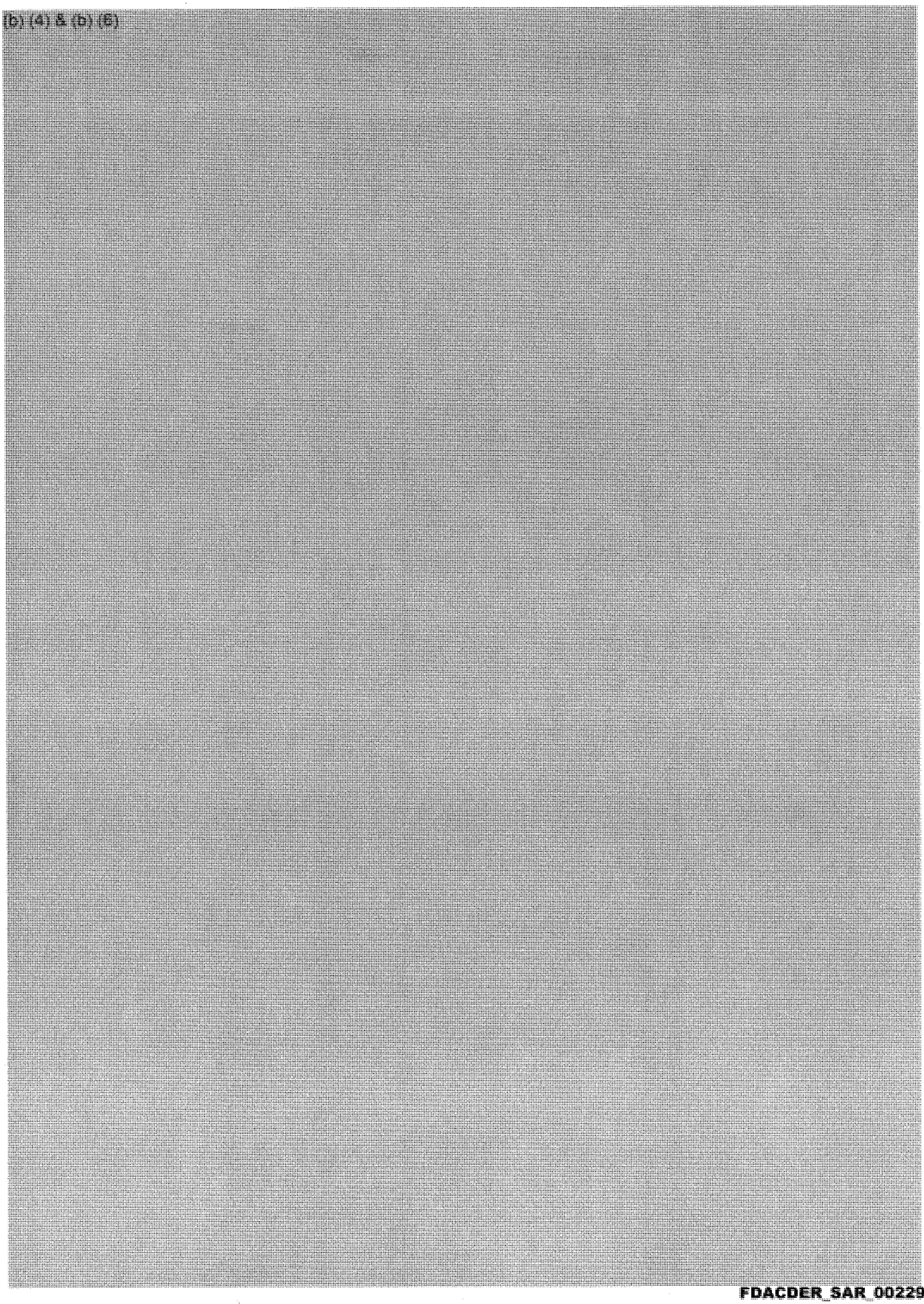
Flotte TR, Goetzmann J, Caridi J, Paolillo J, Conlon TJ, Potter M, Mueller C, Byrne BJ. Apparently nonspecific enzyme elevations after portal vein delivery of recombinant adeno-associated virus serotype 2 vector in hepatitis C virus-infected chimpanzees. Hum Gene Ther. 2008 Jul;19(7):681-9.

Pacak CA, Conlon T, Mah CS, Byrne BJ. Relative persistence of AAV serotype 1 vector genomes in dystrophic muscle. Genet Vaccines Ther. 2008 Oct 15;6:14.

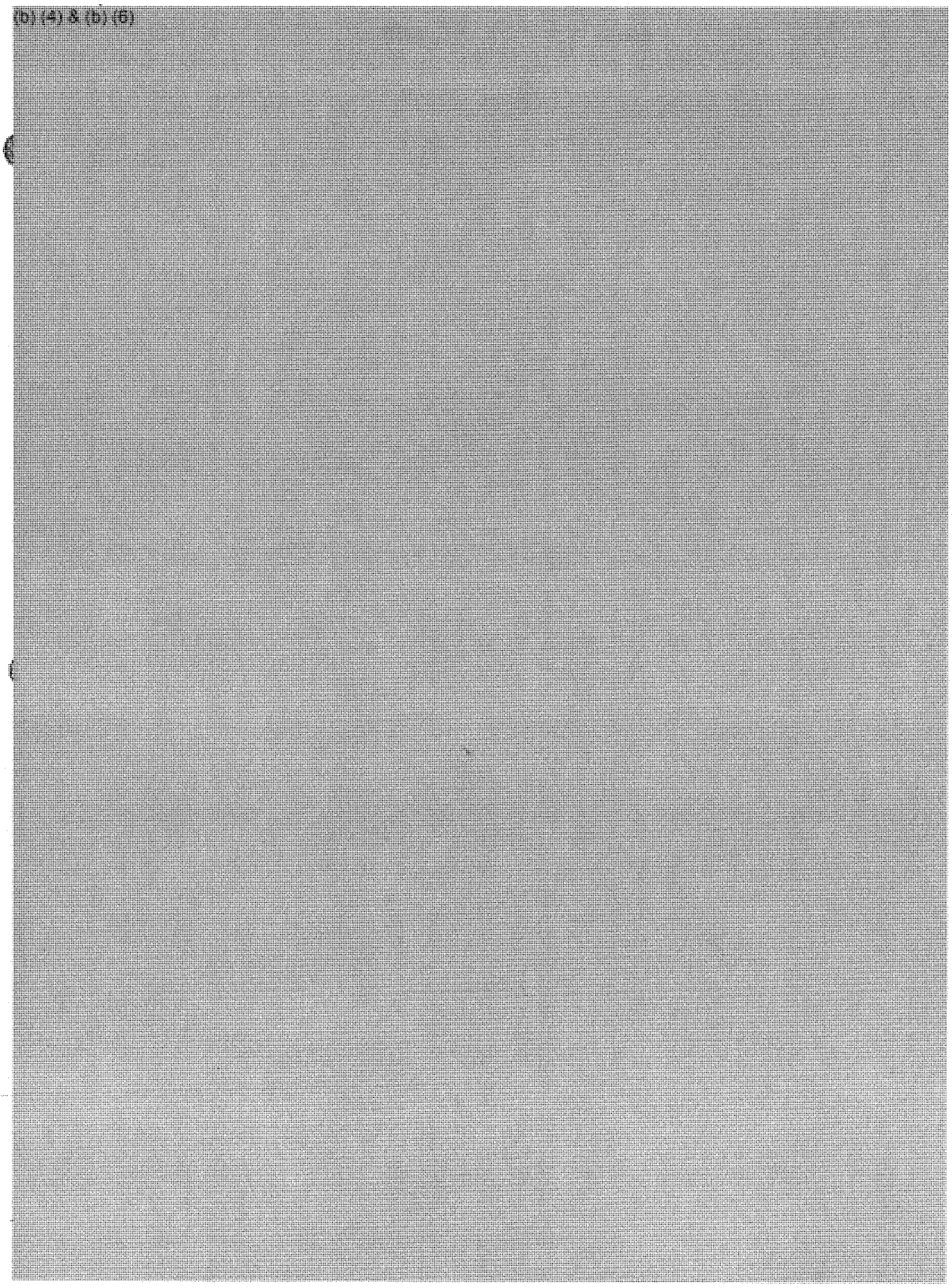
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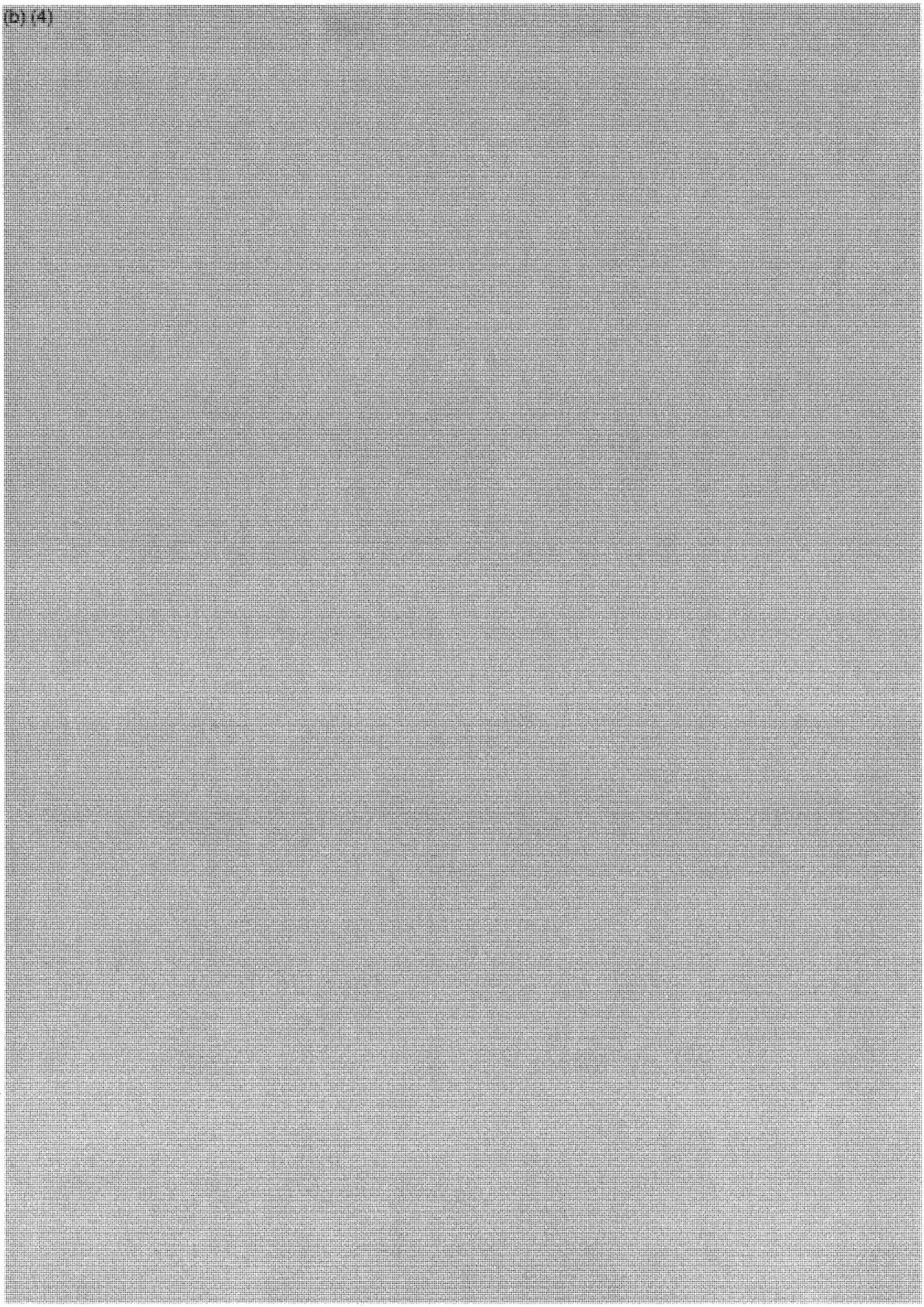

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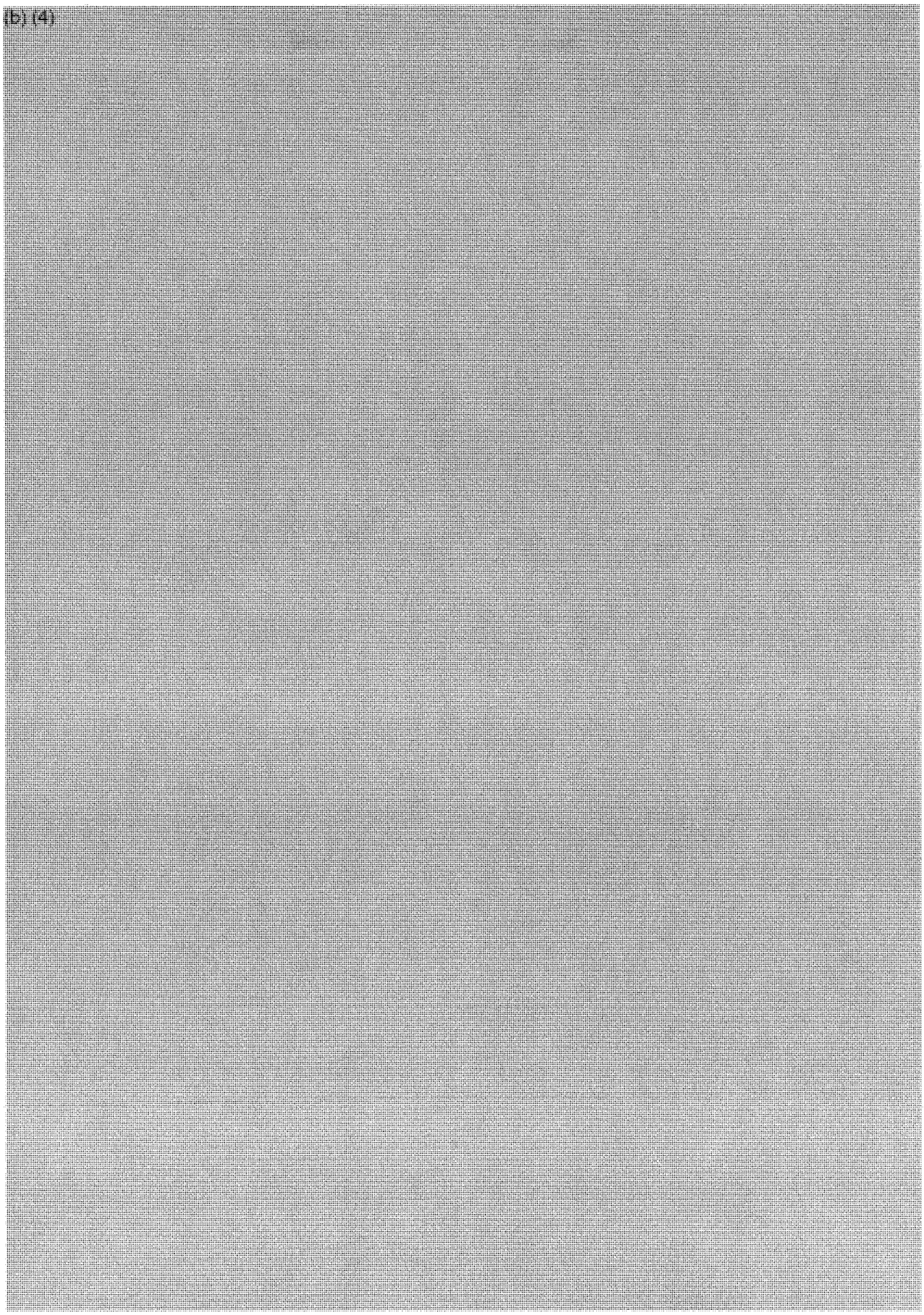

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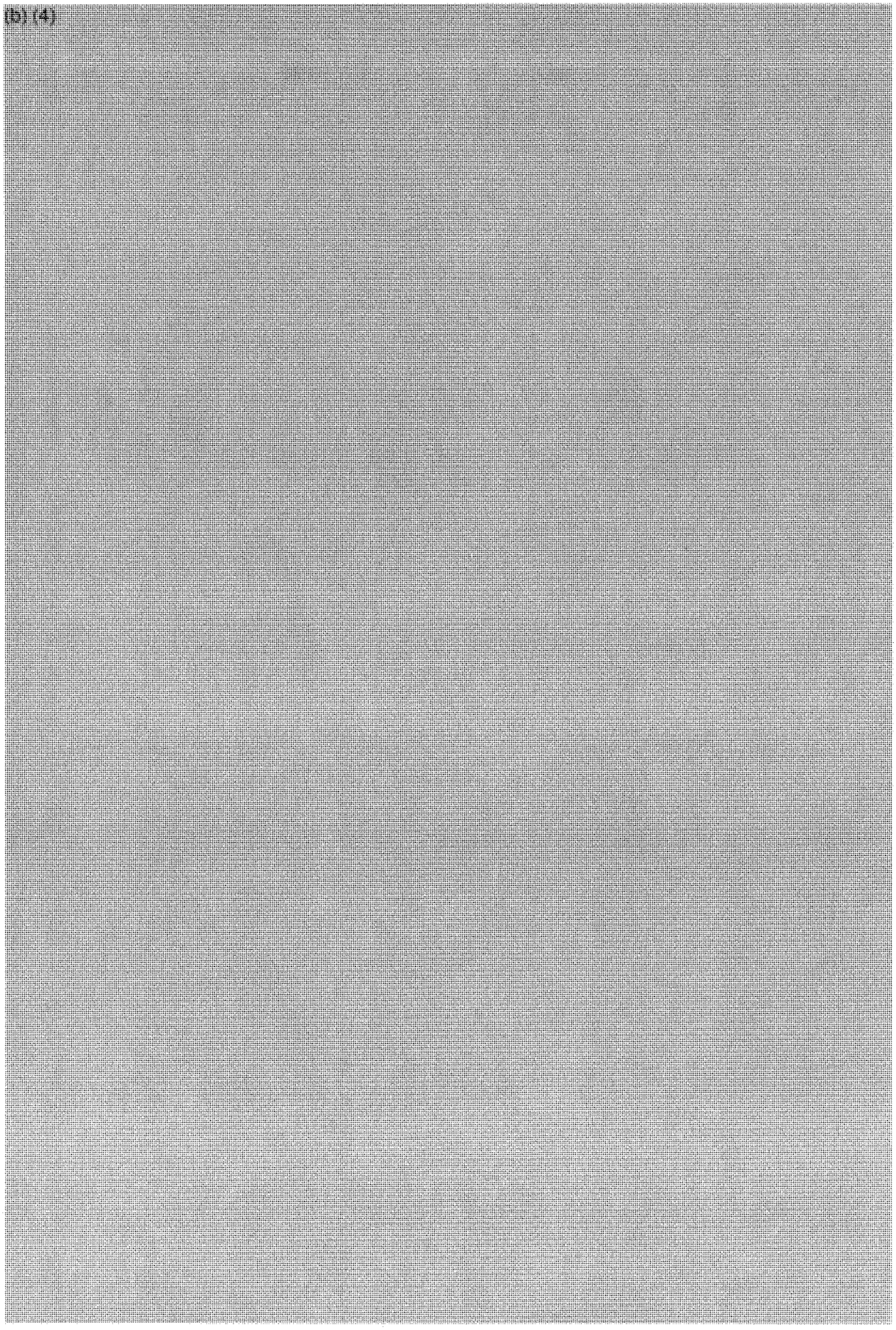
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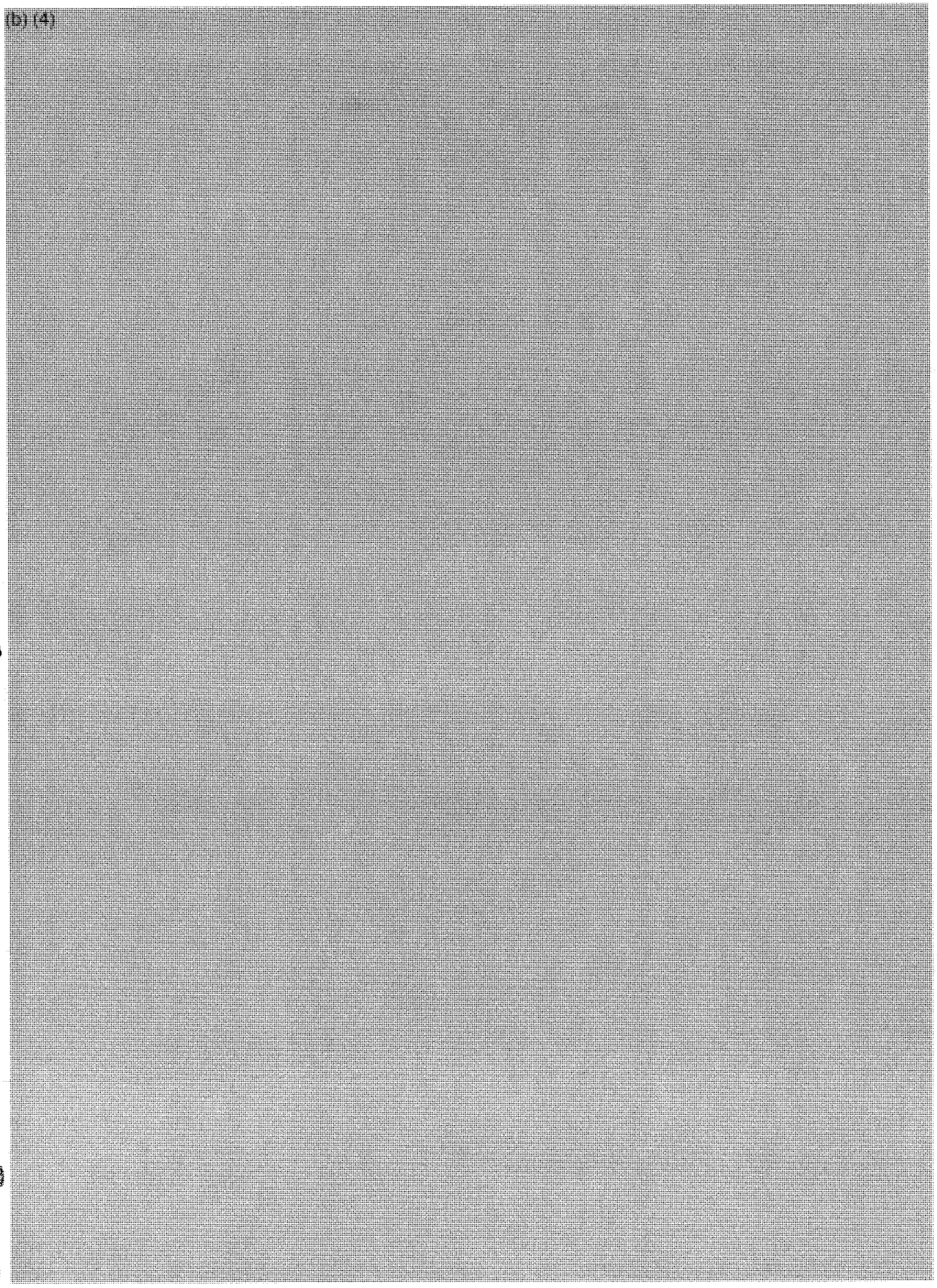


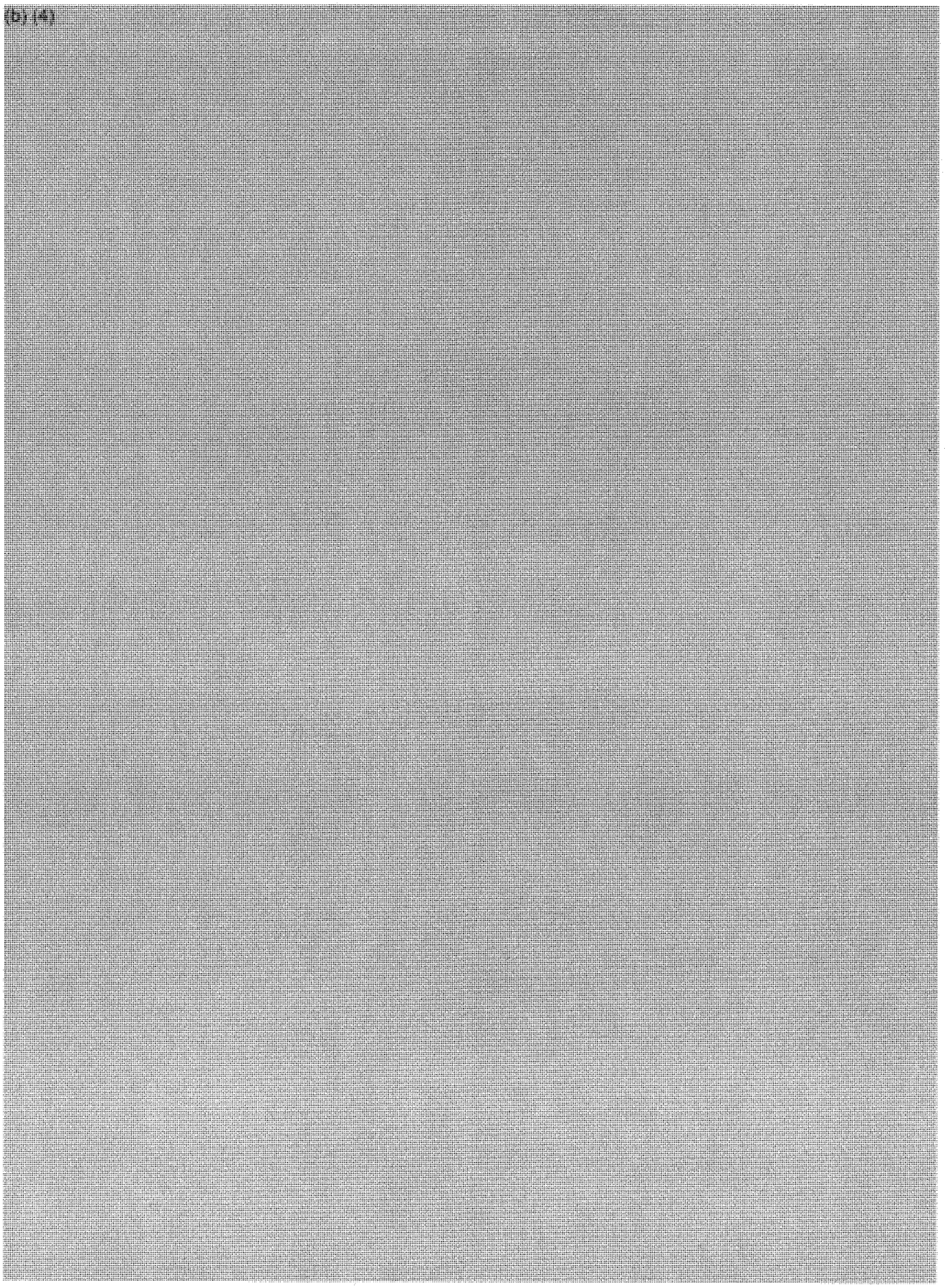
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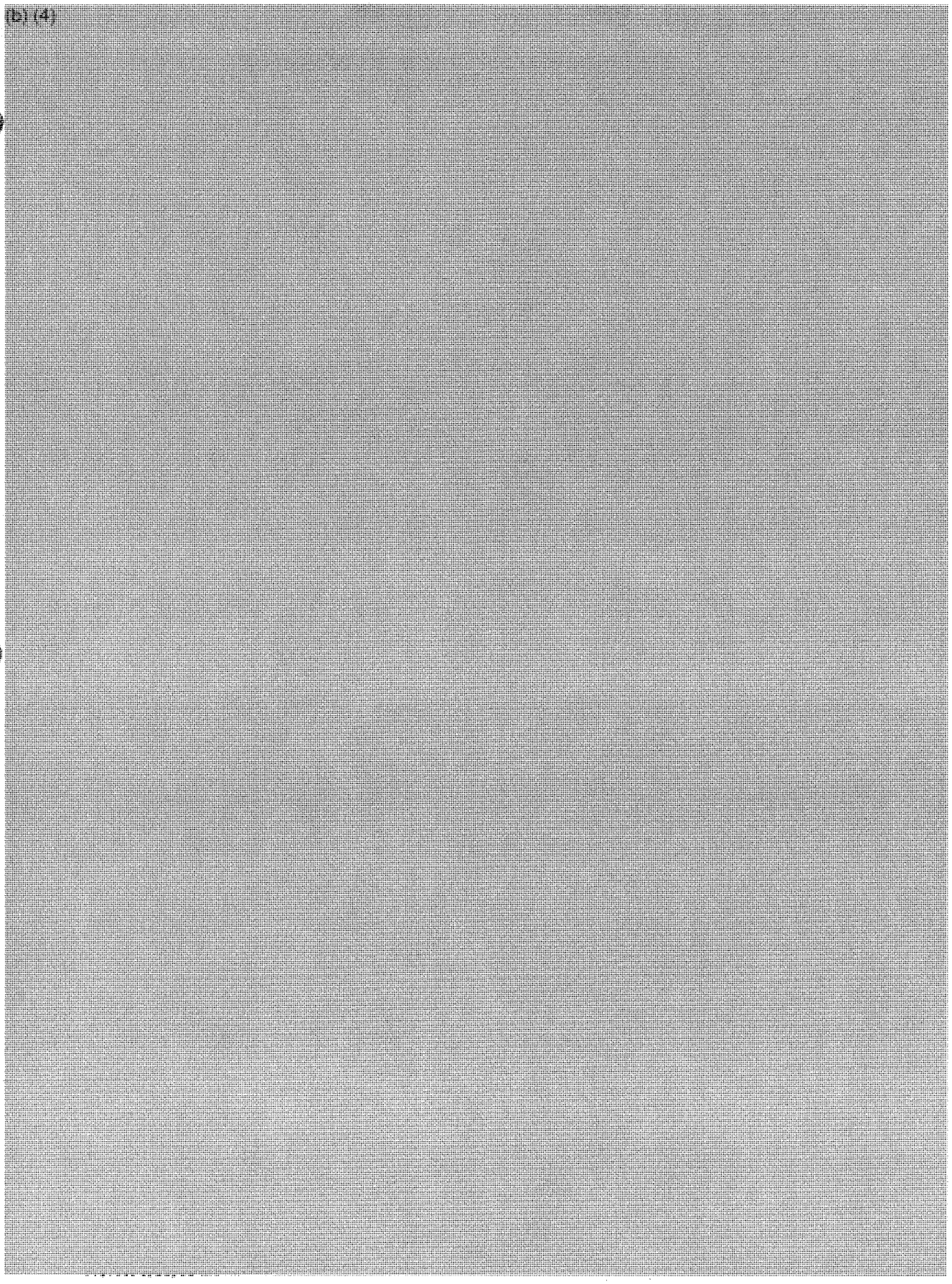



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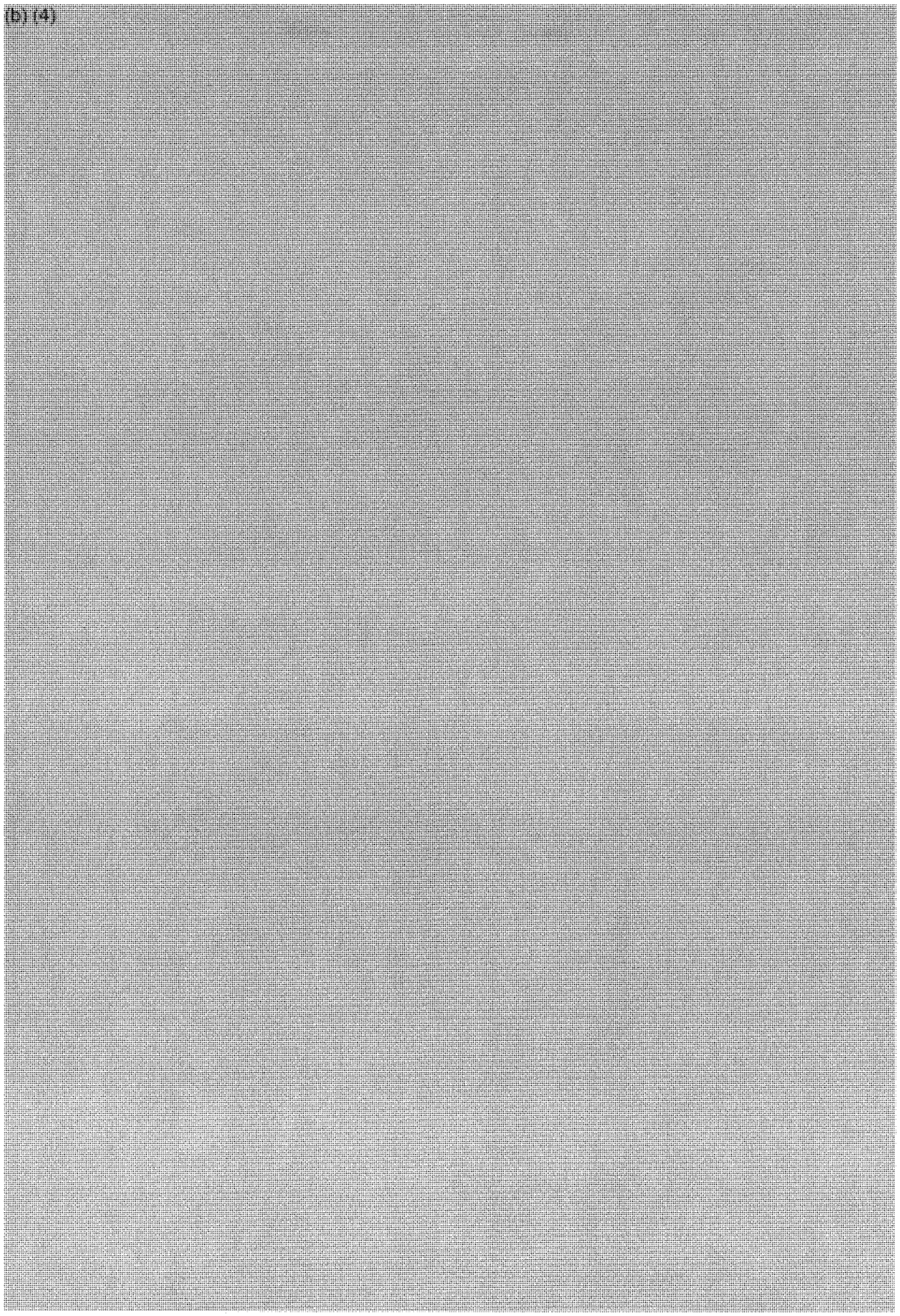

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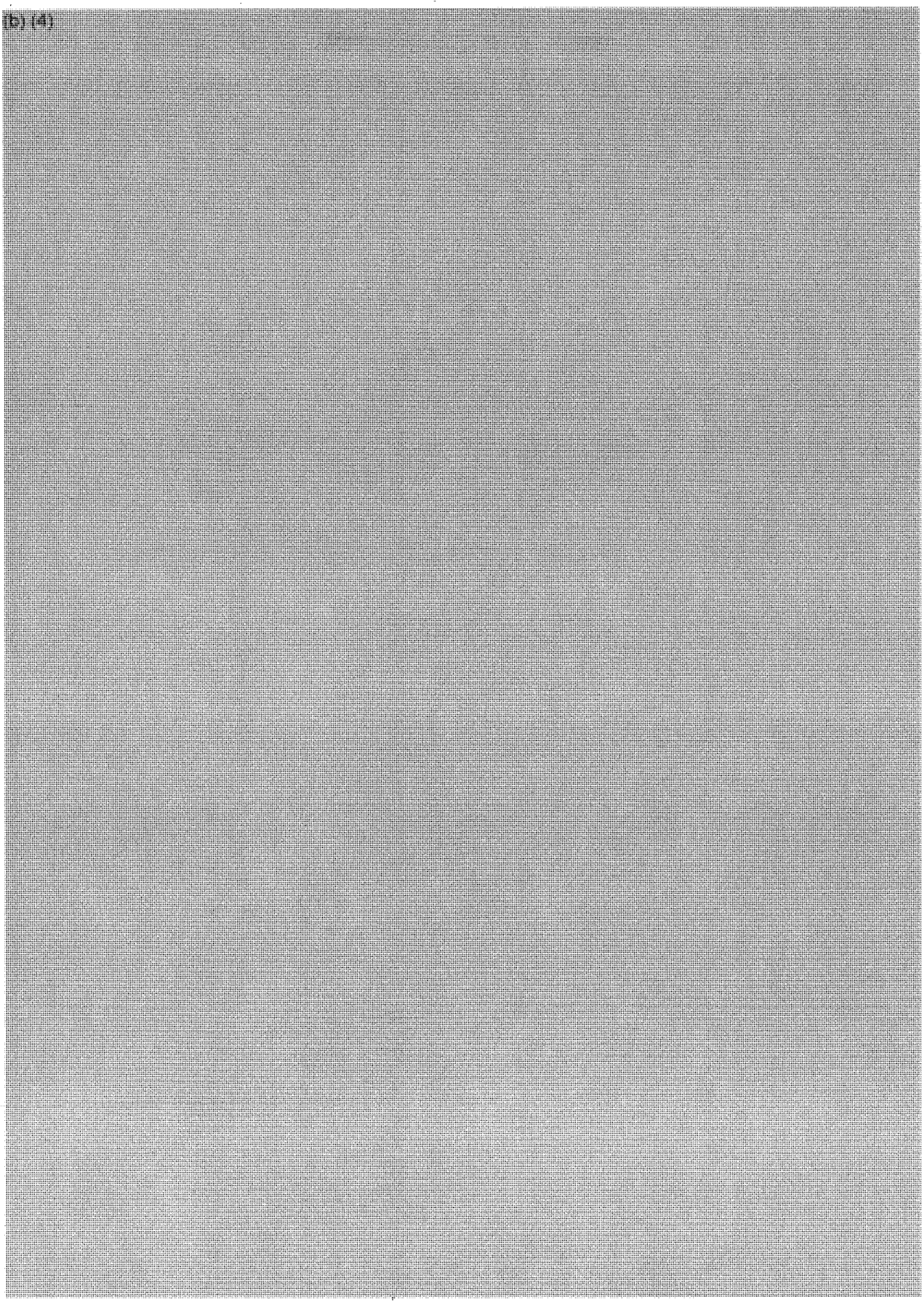

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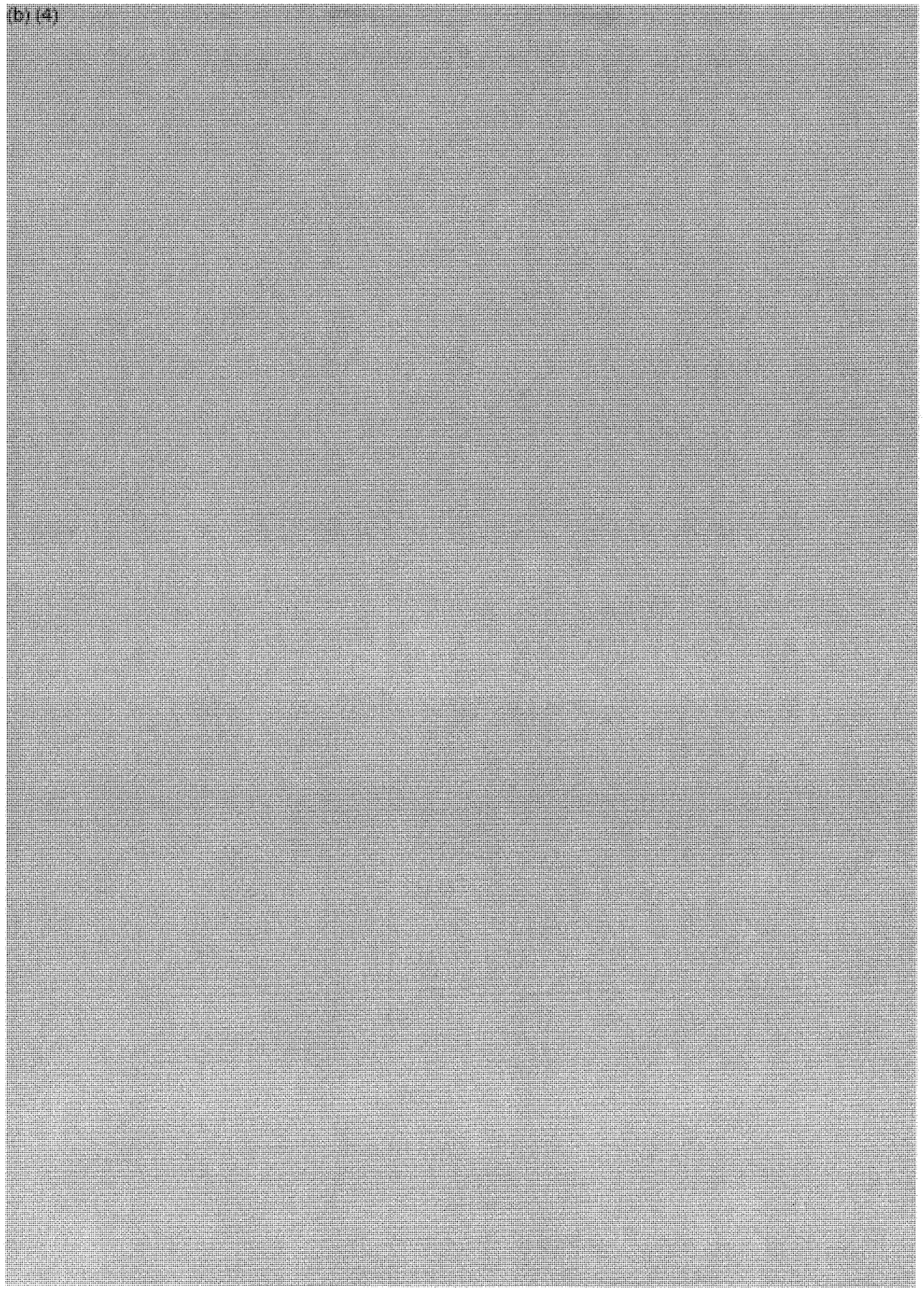

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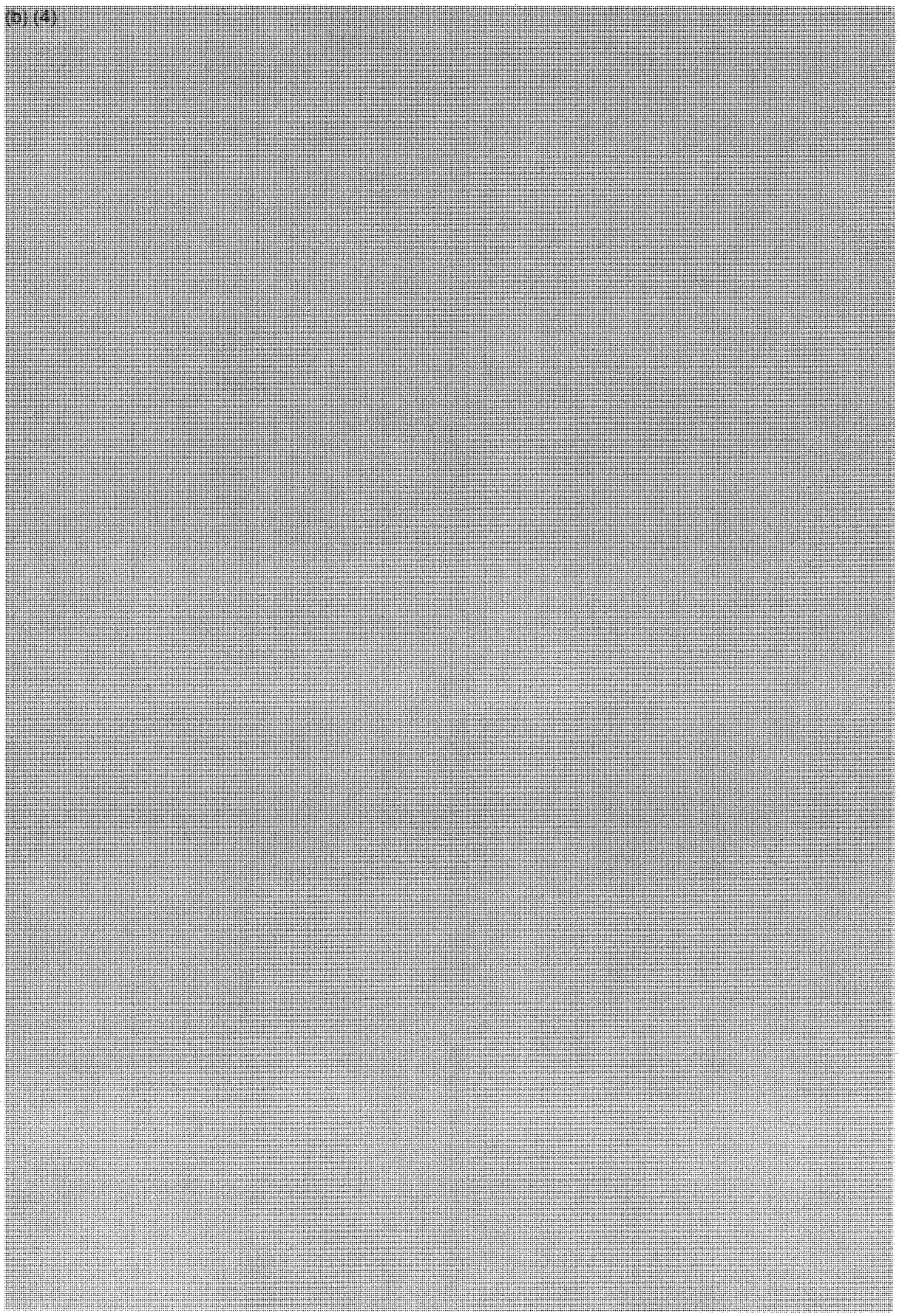
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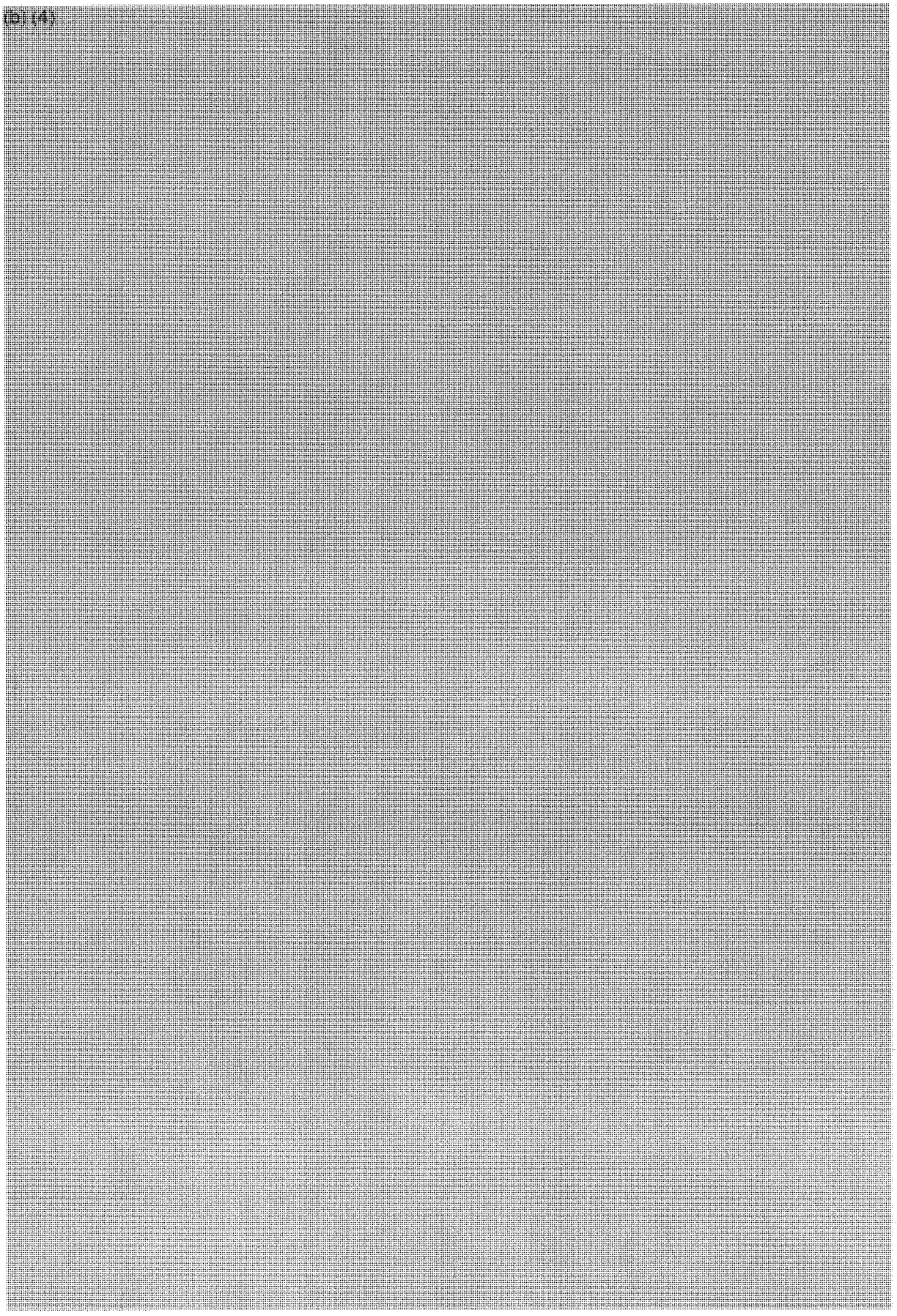

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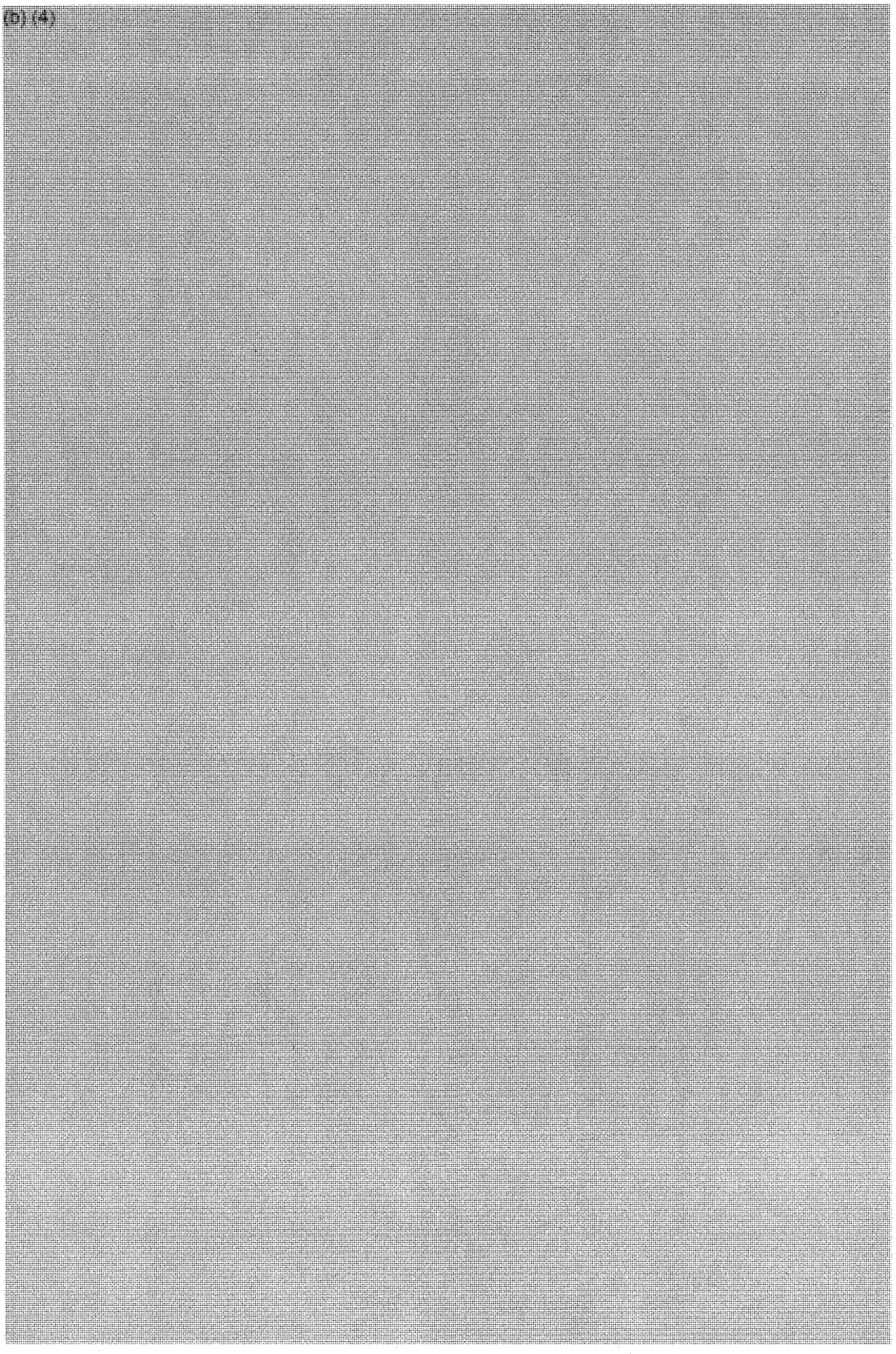
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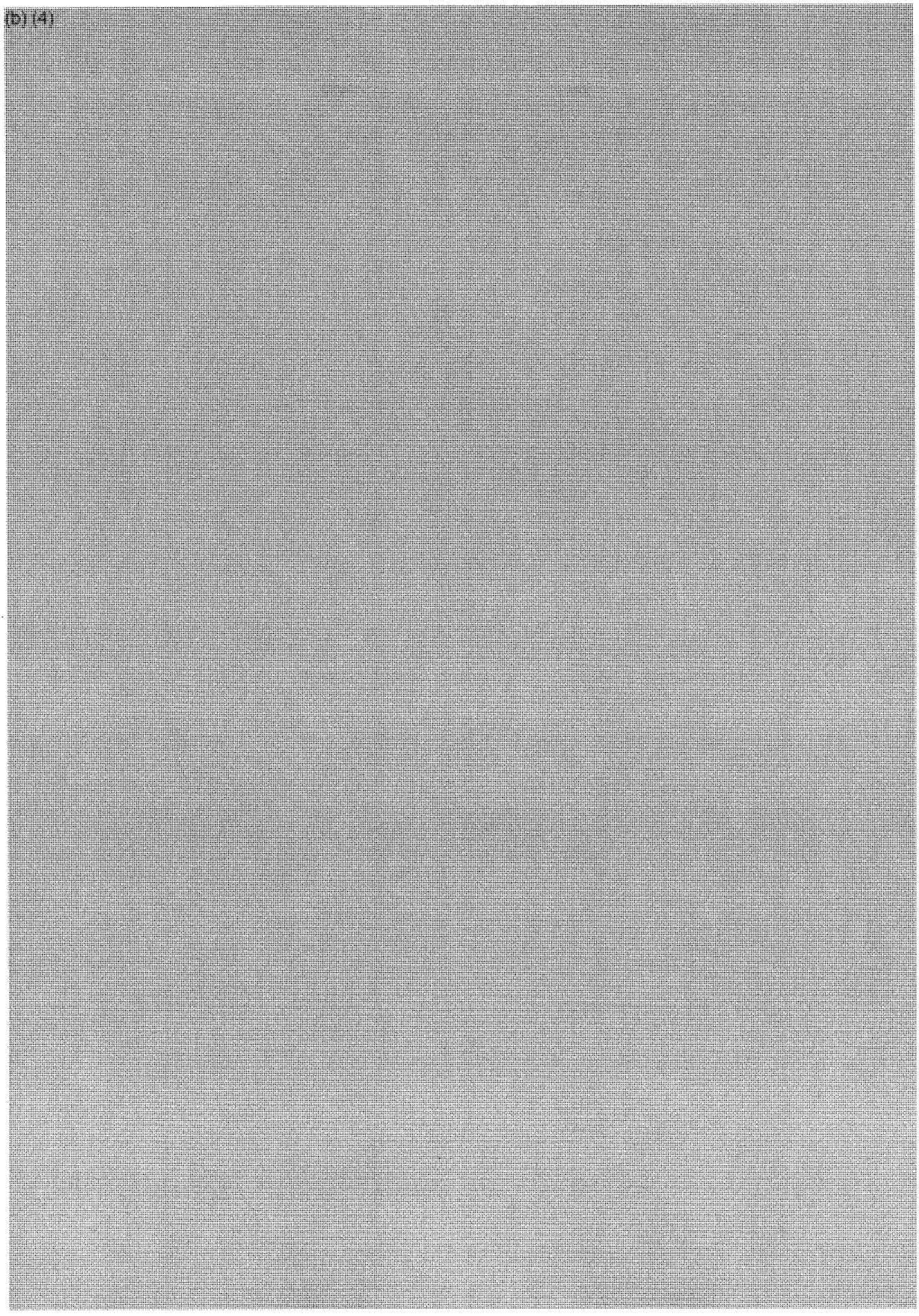
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Curriculum Vitae

NAME: Peter Thomas Heydemann

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EDUCATION:

1970	B.A. ---Yale University
1974	M.D. ---University of Illinois

POSTGRADUATE TRAINING:

1978-1981	Residency/Fellowship in Neurology/Child Neurology, University of Chicago, Chicago, Illinois
1977-1978	Chief Resident in Pediatrics, Children's Memorial Hospital, Chicago, Illinois
1974-1977	Internship and Residency in Pediatrics, Children's Memorial Hospital, Chicago, Illinois

APPOINTMENTS:

1994----->	Associate Professor of Pediatrics and Neurology Director, Section of Pediatric Neurology Co-Director, Rush Muscular Dystrophy Clinic Rush College of Medicine RUSH Medical Center, Chicago, Illinois
1986-1994	Assistant Professor of Pediatrics and Neurology Director , Section of Pediatric Neurology Co-director Rush Muscular Dystrophy Clinic Rush College of Medicine Rush Presbyterian St. Lukes Medical Center, Chicago, Illinois
1982-1986	Co-director Muscular Dystrophy Program, Michael Reese Hospital and Medical Center, Chicago, Illinois Director Spina Bifida Program, Michael Reese Hospital and Medical Center
1981-1986	Assistant Professor of Pediatrics and Neurology, University of Chicago, Chicago, Illinois Attending Physician, Departments of Pediatrics, Neurology, and Rehabilitative Medicine, Michael Reese Hospital and Medical Center, Chicago, Illinois
1981	Instructor in Neuroanatomy, University of Chicago, Chicago, Illinois
1977-1978	Instructor in Pediatrics, Northwestern University, Chicago, Illinois

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HOSPITAL STAFF APPOINTMENTS:

Rush-Presbyterian-St. Lukes Medical Center 1986-present.
Community Hospital Munster, Indiana 1984-present (consulting).
Copley Hospital, Aurora, IL. 1987-present (consulting).
Grant Hospital 1988-1993 (resigned).
Michael Reese Hospital and Medical Center 1981-86 (resigned).
Children's Memorial Hospital 1979-81 (resigned).

SOCIETIES:

American Academy of Neurology
Child Neurology Society
Professors of Child Neurology
Illinois State Medical Society

COMMITTEES:

Sotos Syndrome Medical Advisory Board 2006 →
Community Support Services Bd of Directors (Brookfield, IL) 2004 →
Vice President for Programs, Chair Programs Committee
Examiner, American Board of Psychiatry and Neurology 1993 →
Reviewer, Clinical Neuropharmacology 2001
AdHoc Reviewer American Journal of NeuroRadiology 1993
Child Neurology Society, Junior Membership Committee, 1982-1985
Child Neurology Credentials Committee 1996-1998

HOSPITAL AND DEPARTMENTAL COMMITTEES:

Rush Pharmacy & Therapeutics Committee 2005 →
Rush Dept of Pediatrics: Residency Selection Committee, 1986-1991, 2003→
Pediatric and Radiology Sedation Committees 1990------->1998
Rush Faculty Senate 1988----->1996
Rush Department of Pediatrics Apppointments and Promotions1986-1996
Rush Department of Pediatrics PICU Quality of Care Committee 1986-1992
Director of Student Education, Michael Reese Hospital Department of Pediatrics 1985-1986
Residency Selection Committee, Michael Reese Hospital, Department of Pediatrics 1982-1986
Ethics Committee, University of Chicago/Michael Reese Departments of Pediatrics 1984-1986 (departmental representative)
Quality of Care Committee, Michael Reese Hospital Department of Pediatrics 1983-1986
Chicago Pediatric Intensive Care Group 1983-1985
Chicago Neuromuscular Diseases Group 1984-86, 2004→

CERTIFICATION:

1979 Diplomate American Board of Pediatrics

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LICENSURE: 1975 Illinois 1976 California 1984 Indiana

PUBLICATIONS:

ABSTRACTS:

Heydemann, P. and Huttenlocher, P., "Synaptogenesis, Synaptic Density, and the Effect of Cortisol in Reaggregated Mouse Cerebral Isocortex: A Model for

FDACDER_SAR_0022917

Evaluating Drug Effects on Synaptic Development," Annals of Neurology 12: 2, 1982.

Kraus, N., Heydemann, P., and Ozdamar, O., "The Effects of Hydrocephalus on the Auditory Brainstem Response," Annals of Neurology 14: 3, 376-77, 1983.

Venkatasubramanian, P.N., Barany, M., Siegel, I.M., Wilbur, A.C., Zwicky, G.S., Heydemann, P.T., "Quantitation of Phosphate Metabolites in Human Leg of Neuromuscular Diseases in vivo," Society of Magnetic Resonance in Medicine, 7th meeting, August 20, 1988.

Glantz, R., Wright, R., Heydemann,P., Hahn,Y. & Siegel, I., "Ventriculomegaly in Pediatric Myotonic Dystrophy: Management Implications," Neurology 38, no. 3, suppl 1, page 293, March 1988.

Pierre-Louis, S., Bergen, D., Koch-Weser, M., Heydemann, P., "Impaired response time during paroxysmal delta activity," Journal of Clinical Neurophysiology 6, 4, p. 338, 1989.

Chamlin, S., Chez, M., Heydemann, P., Van Slyke, P., "Prednisone therapy in Landau-Kleffner Syndrome: Improved speech performance and correlating EEG changes," Annals of Neurology 32: 3, p. 476, 1992.

Swisher, C. , Heydemann, P., Boyer, K., McLeod, R., Roizen, N., Mets, M., Patel, D.,Stein, M. , Stein, L., et al. "Neurological Function in Treated Congenital Toxoplasmosis ", Annals of Neurology 32: 3, p. 448, 1992.

Korenblit, A., Heiliczer, J., Heydemann, P., Schwartz, M., "Hemolytic Uremic Syndrome Response to Gamma-globulin Infusion resulting in Thrombocytosis followed by a Cerebral Infarct in a Child with Down Syndrome," Blood 80 (10 Suppl 1), 1992.

ARTICLES:

Huttenlocher, P. and Heydemann, P., "Fine Structure of Cortical Tubers in Tuberous Sclerosis - A Golgi Study," Annals of Neurology 16: 595-602, 1984.

Kraus, N., Ozdamar, O., Heydemann, P., Reed, N., and Stein, L., "Auditory Brainstem Responses in Hydrocephalic Patients," EEG and Clinical Neurophysiology 59:310-317,1984.

FDACDER_SAR_0022918

Babikian, V., Heydemann, P., and Swisher, C., "Extrapyramidal Movements in Tuberculous Meningitis - A Clue for Early Diagnosis," Clinical Pediatrics, Feb. 1985.

Fox, A., Kazacos, KR, Gould, N., Heydemann, P., Thomas, C., and Boyer, K., "Fatal Eosinophilic Meningoencephalitis and Visceral Larva Migrans Caused by the Raccoon Ascarid Baylisascaris procyonis," New England Journal of Medicine 312:1619-1623, 1985.

Bergen, D., Rayman, L., Heydemann, P., "Bilateral Todd Paralysis after Focal Seizure", Epilepsia 33 (6): 1101-5, Dec 1992.

Poddar, S., Gitelis, S., Heydemann, P., Piasecki, P., "Bilateral predominant radial nerve crutch palsy ---- a case report," Clinical Orthopedics and Related Research 297, p245-246, Dec.1993.

McAuley, J., Boyer, K., Patel, D., Mets, M., Swisher, C., Roizen,N., Wolters, C., Stein, L., Stein, M., Schey, W., Remington, J., Meier, P., Johnson, D., Heydemann, P., Holfels, E., Withers, S., Mack, D., Brown, C., Patton, D., and McLeod, R., "Early and Longitudinal Evaluations of Treated Infants and Children and Untreated Historical Patients with Congenital Toxoplasmosis: The Chicago Collaborative Treatment Trial," Clinical Infectious Diseases 18, 38-72, 1994.

Swisher, C., Boyer, K., McLeod, R., et al. (Heydemann), "Congenital Toxoplasmosis," Seminars in Pediatric Neurology, vol 1, no. 1, 4-25, Sept. 1994.

Roizen, N., Swisher, C. Stein, M., et al. [Heydemann], Outcomes in Treated Congenital Toxoplasmosis, Pediatrics 95, 1, 11-20, Jan. 1995.

Swoboda, KJ, Soong, BW, McKenna , C, Brunt, ERP, Litt, M, Bale, JFJr, Ashizawa, T, Bennett, LB, Bowcock, AM, Roach, ES, Gerson, D, Matsuura, T, Heydemann, PT, Nespeca, MP, Jankovic, J,Leppert, M, Ptacek, LJ, "Paroxysmal kinesigenic dyskinesia and infantile convulsions: Clinical and linkage studies," Neurology 55, 2, July 25, 2000.

Brown CA, Lanning RW, McKinney KQ, Salvino AR, Cherniske E, Crowe CA, Darras BT, Gominak S, Greenberg CR, Grosmann C, Heydemann P, Mendell JR, Pober BR, Sasaki T, Shapiro F, Simpson DA, Suchowersky O, Spence JE, Novel and recurrent mutations in lamin A/C in patients with Emery-Dreifuss muscular dystrophy, Am J Med Genet 102(4):359-67, Sep 1, 2001.

Pranzatelli MR, Tate ED, Wheeler BA, Bass N, Gold, AP, Griebel ML, Gumbinas M, Heydemann PT, Holt PJ, Jacob P, Kotagal S, Minarcik CJ, Schub HS, "Screening for autoantibodies in children with opsoclonus-myoclonus-ataxia," Pediatric Neurology 27, 5, 384-387, 2002.

FDACDER_SAR_0022919

Arenson, N, Heydemann PT, Late onset Krabbe Disease Mimicking ADEM, Pediatric Neurology 33, 3, 208-210, 2005

McLeod R, Boyer K, Karrison T, Kasza K, Swisher C, Roizen N, Jalbrzikowski J, Remington J, **Heydemann P**, Noble AG, Mets M, Holfels E, Withers S, Latkany P, Meier P; Toxoplasmosis Study Group, Outcome of treatment for congenital toxoplasmosis, 1981-2004: the National Collaborative Chicago Based Congenital Toxoplasmosis Study, Clin Infect Dis 15;42(10):1383-94, May 2006.

Roizen N, Kazka K, Karrison T, Mets M, Noble AG, Boyer KM, Swisher C, Meier P, Remington J, Jalbrzikowski J, McLeod R, Kipp M, Robiah P, Chamot D, Estes R, Cezar S, Mack D, Pfiffner L, Stein M, Danis B, Patel D, Hopkins J, Holfels E, Stein L, Withers S, Cameron A, Perkins J, **Heydemann P**, Impact of visual impairment on measures of cognitive function for children with congenital toxoplasmosis: Implications for compensatory intervention strategies. Pediatrics 118(2):e 379-90, August 2006.

Jamieson SE, Peixoto-Rangel AL, Hargrave AC, Roubaix LA, Mui EJ, Boulter NR, Miller EN, Fuller SJ, Wiley JS, Castellucci L, Boyer K, Peixe RG, Kirisits MJ, Elias Lde S, Coyne JJ, Correa-Oliveira R, Sautter M, Smith NC, Lees MP, Swisher CN, **Heydemann P**, Noble AG, Patel D, Bardo D, Burrowes D, McLone D, Roizen N, Withers S, Bahia-Oliveira LM, McLeod R, Blackwell JM, Evidence for associations between the purinergic receptor P2X(7) (P2RX7) and toxoplasmosis. Genes Immun. 2010 Jul;11(5):374-83. (Epub 2010 Jun 10.)

Boyer K, Hill D, Mui E, Wroblewski K, Karrison T, Dubey JP, Sautter M, Noble AG, Withers S, Swisher C, **Heydemann** P, Hosten T, Babiarz J, Lee D, Meier P, McLeod R; Toxoplasmosis Study Group, Unrecognized ingestion of Toxoplasma gondii oocysts leads to congenital toxoplasmosis and causes epidemics in North America. Clin Infect Dis. 2011 Dec;53(11):1081-9. (Epub 2011 Oct 21.)

CHAPTERS:
Heydemann, P., "Breath-holding Spells," pp847-849, chapter in Dershewitz,R., ed., Ambulatory Pediatric Care, J. B. Lipincott, Philadephia, 1988.

Heydemann, P., "Syncope in Childhood and Adolesence," pp768-772 in Dershewitz, R., ed., Ambulatory Pediatric Care, J. B. Lipincott, Philadelphia, 1988.

Heydemann, P., "Breath-holding Spells," chapter in Dershewitz,R., ed., Ambulatory Pediatric Care, J. B. Lipincott, Philadephia, 2nd ed., 1993.

Heydemann, P., "Syncope in Childhood and Adolesence," in

FDACDER_SAR_0022920

Dershewitz, R., ed., Ambulatory Pediatric Care, J. B. Lipincott, Philadelphia, 2nd ed., 1993.

Heydemann, P. "Muscular Dystrophy and Related Myopathies," in Burg, FD, et al editors, Current Pediatric Therapy , 15 th edition, 1996.

Heydemann, P. "Paroxysmal non-epileptiform disorders," in Dershewitz, R., ed., Ambulatory Pediatric Care, J. B. Lipincott, Philadelphia, 3rd ed., 1999.

Heydemann, P. "Meningismus," in Dershewitz, R., ed., Ambulatory Pediatric Care, J. B. Lipincott, Philadelphia, 3rd ed., 1999.

Heydemann, P. "Myopathy," in Stockman JA and Lohr JA eds., Essence of Pediatrics, 1st ed., 2001.

Heydemann, P. "Hypotonia in Infancy" in Reuter-Rice K and Bolick B, Pediatric Acute Care: A Guide for Interprofessional Practice, Jones & Bartlett 1st ed, 2012.

Heydemann, P. "Muscular Dystrophy" in Reuter-Rice K and Bolick B, Pediatric Acute Care: A Guide for Interprofessional Practice, Jones & Bartlett 1st ed, 2012.

REVIEWS: American Journal of Neuroradiology, anonymous review, 1995. (call ed.)

PRESENTATIONS: Research Presentations (National and International)

Heydemann, P. and Huttenlocher, P., "Synaptogenesis in Mouse Cerebral Cortex and the Effect of Steroids on in vitro Synaptogenesis in Reaggregated Mouse Isocortex," Child Neurology Society, Salt Lake City, October 7, 1982.

Heydemann, P., Kraus, N., and Ozdamar, O., "Hydrocephalus and the Auditory Brainstem Response," Child Neurology Society, Williamsburg, Virginia, October 15, 1983.

Heydemann, P., Swisher, C.,Boyer, K., McLeod, R., and the Toxoplasmosis Study Group, "Neurological Function in Treated Congenital Toxoplasmosis ", 7th International Congress of Pediatric Neurology, Buenos Aires, Argentina , November 12, 1992.

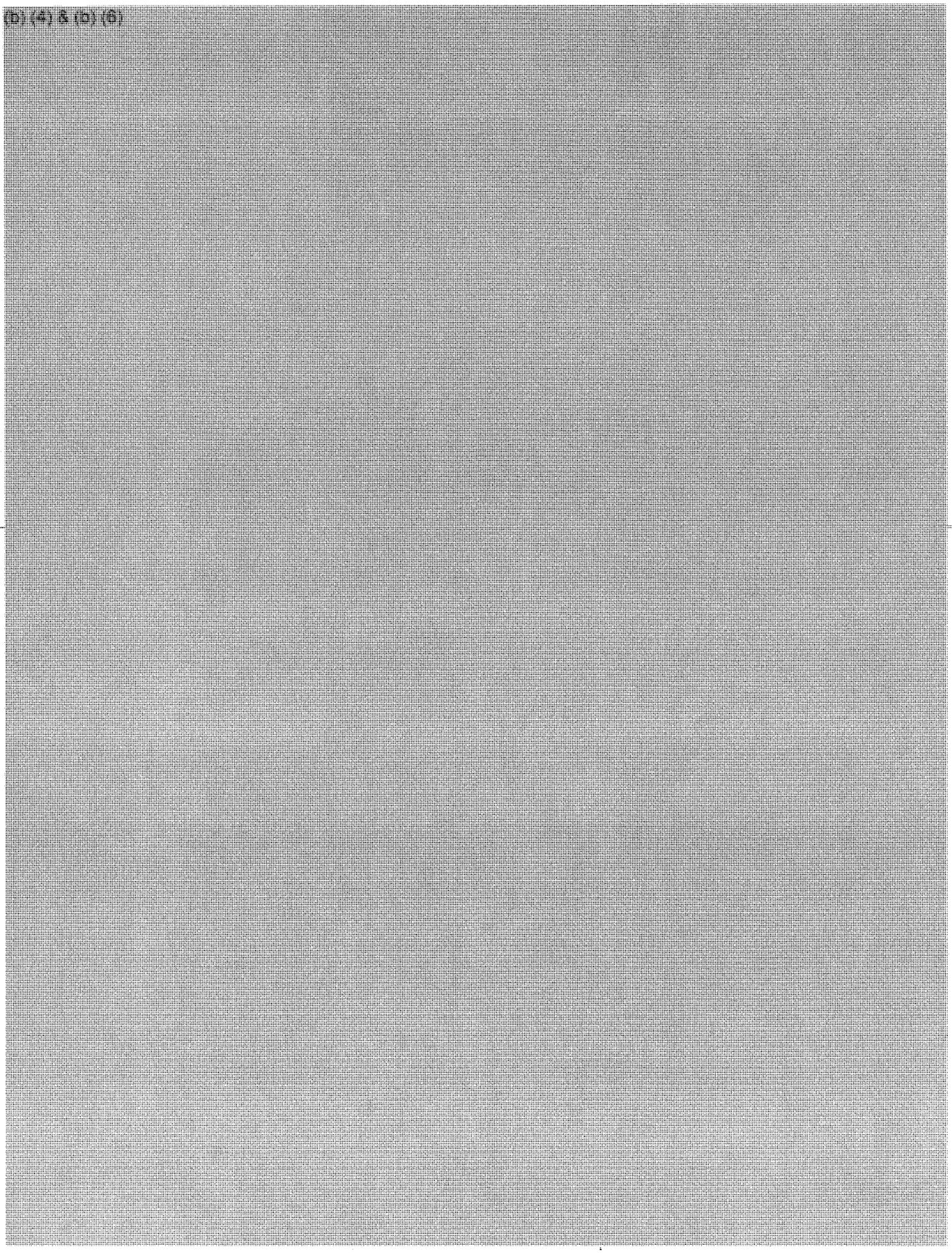
LECTURE TOPICS in 2007-2011:
Pediatric Headaches
Pediatric Seizure disorders
Congenital Muscular Dystrophies
Update on the Childhood Muscular Dystrophies

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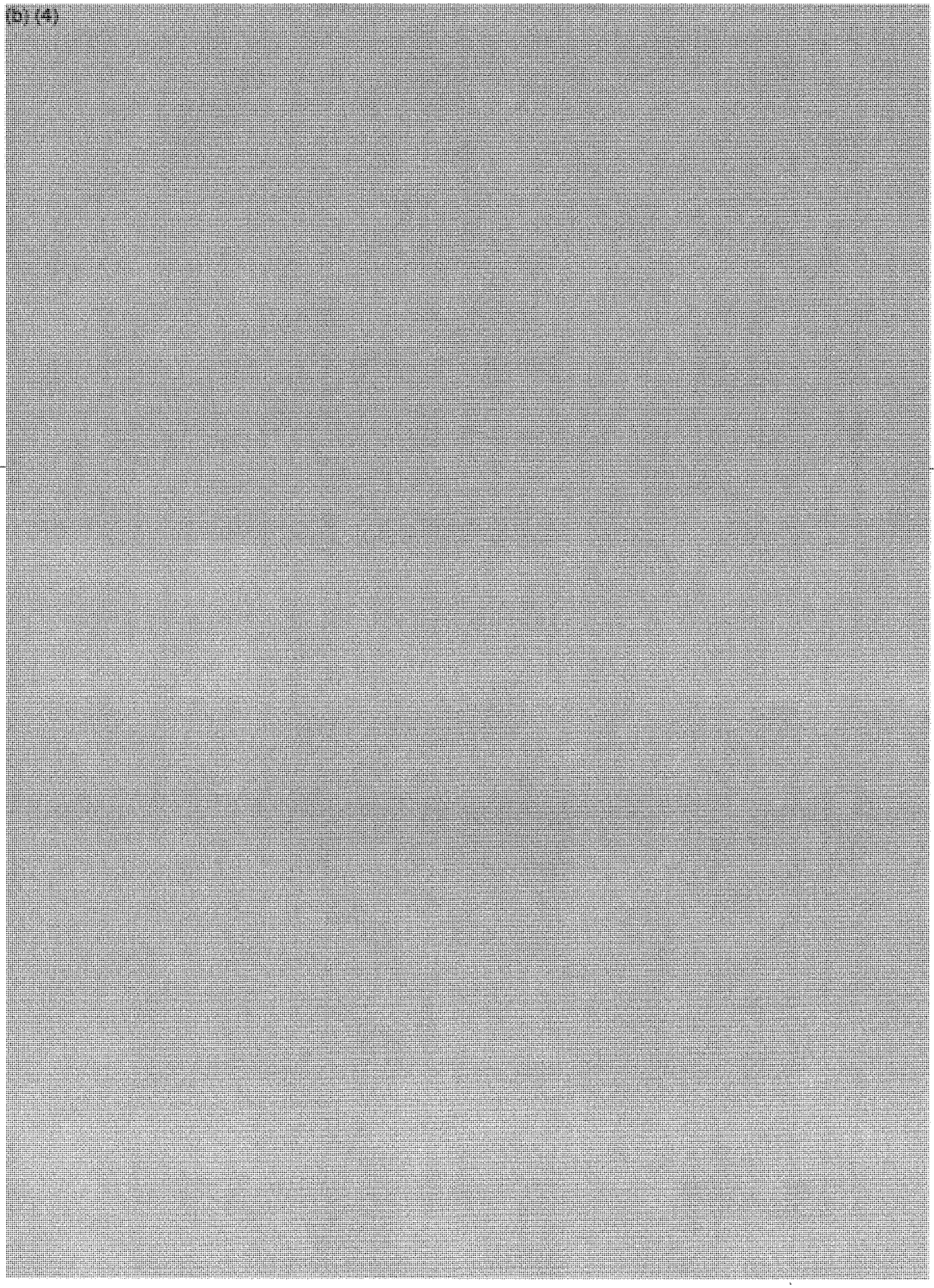
Tourette Syndrome
Neonatal Hypoxic Ischemic Encephalopathy
Febrile Seizures
Childhood NeuroMuscular Disorders
Duchenne Muscular Dystrophy

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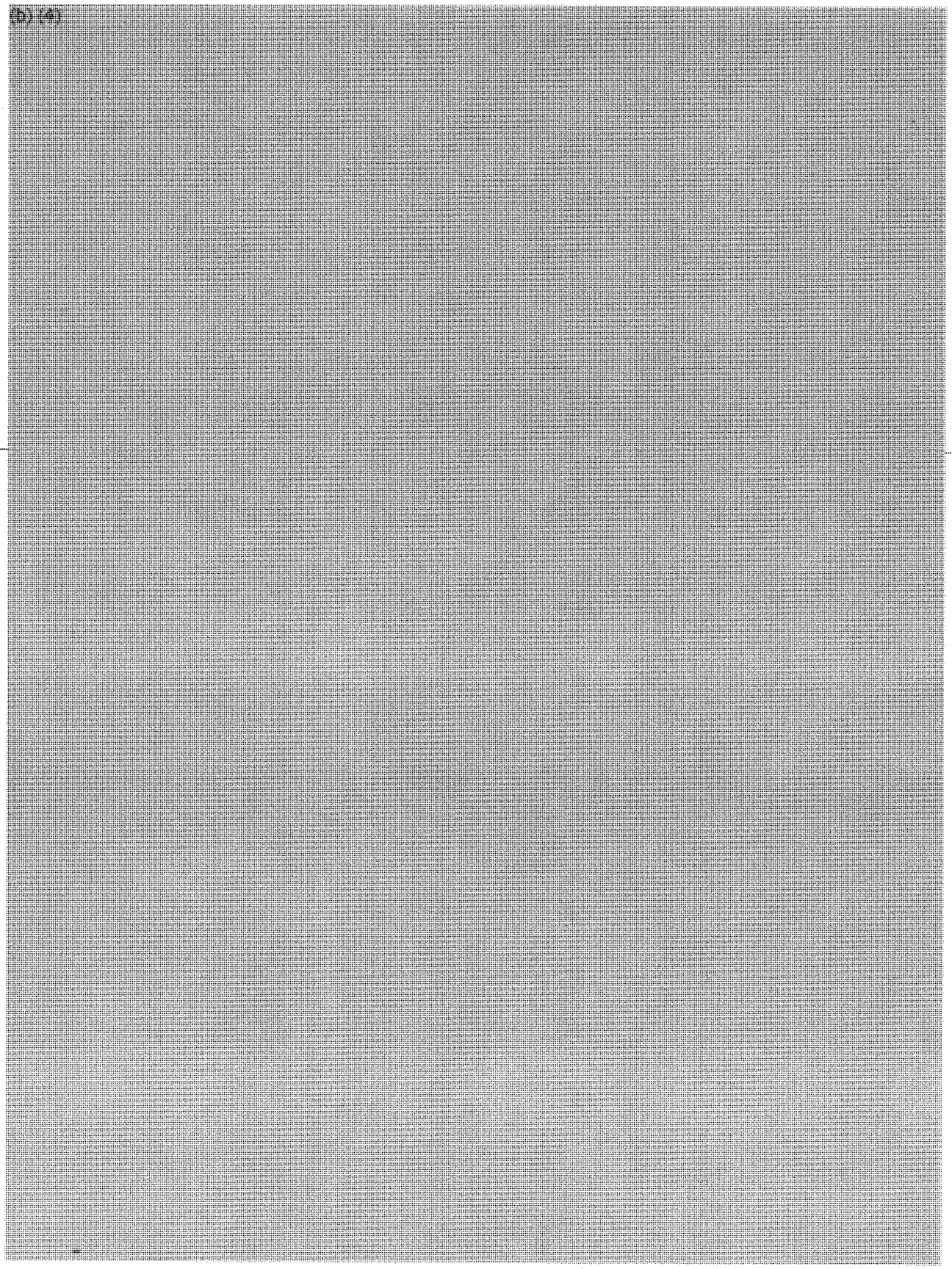
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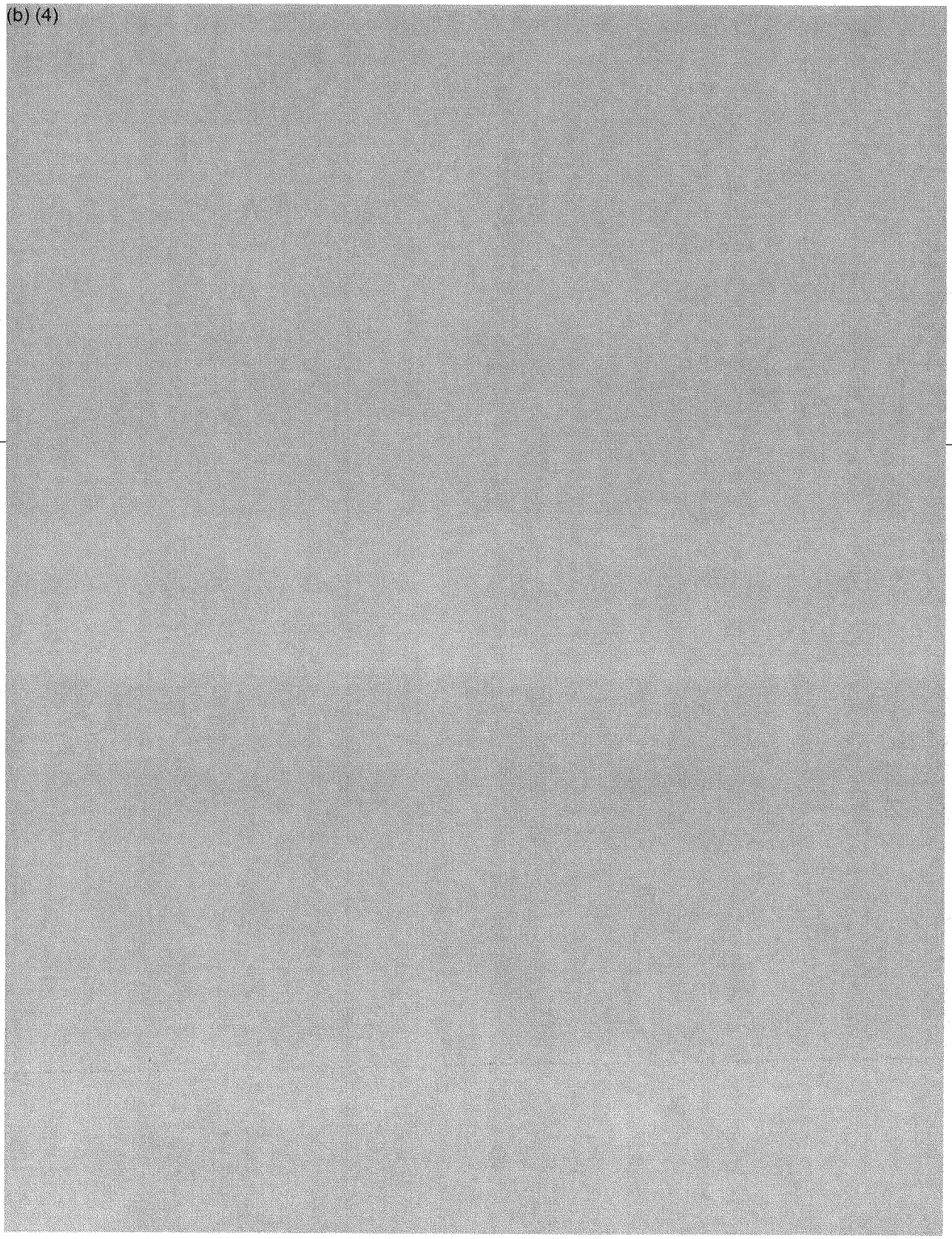
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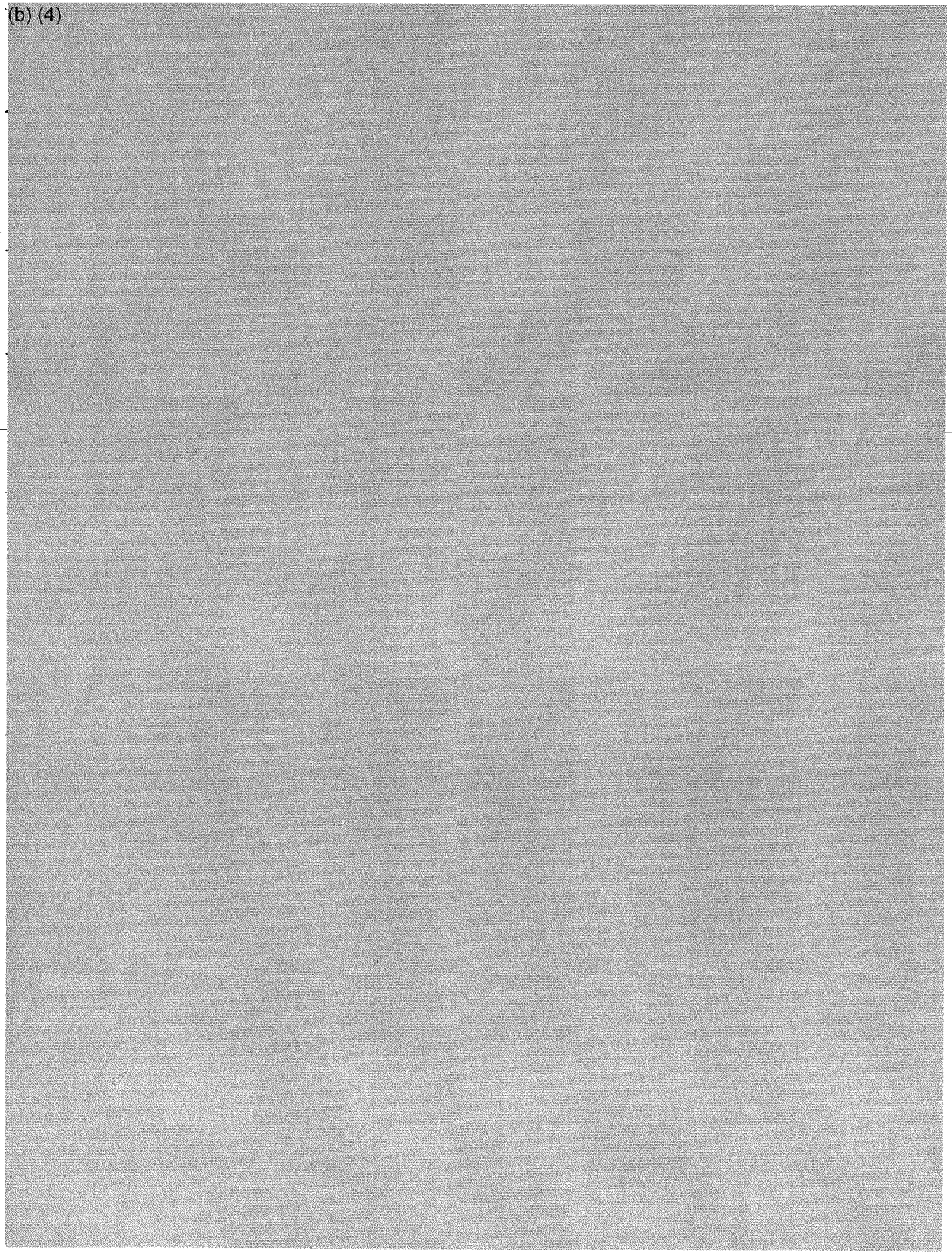
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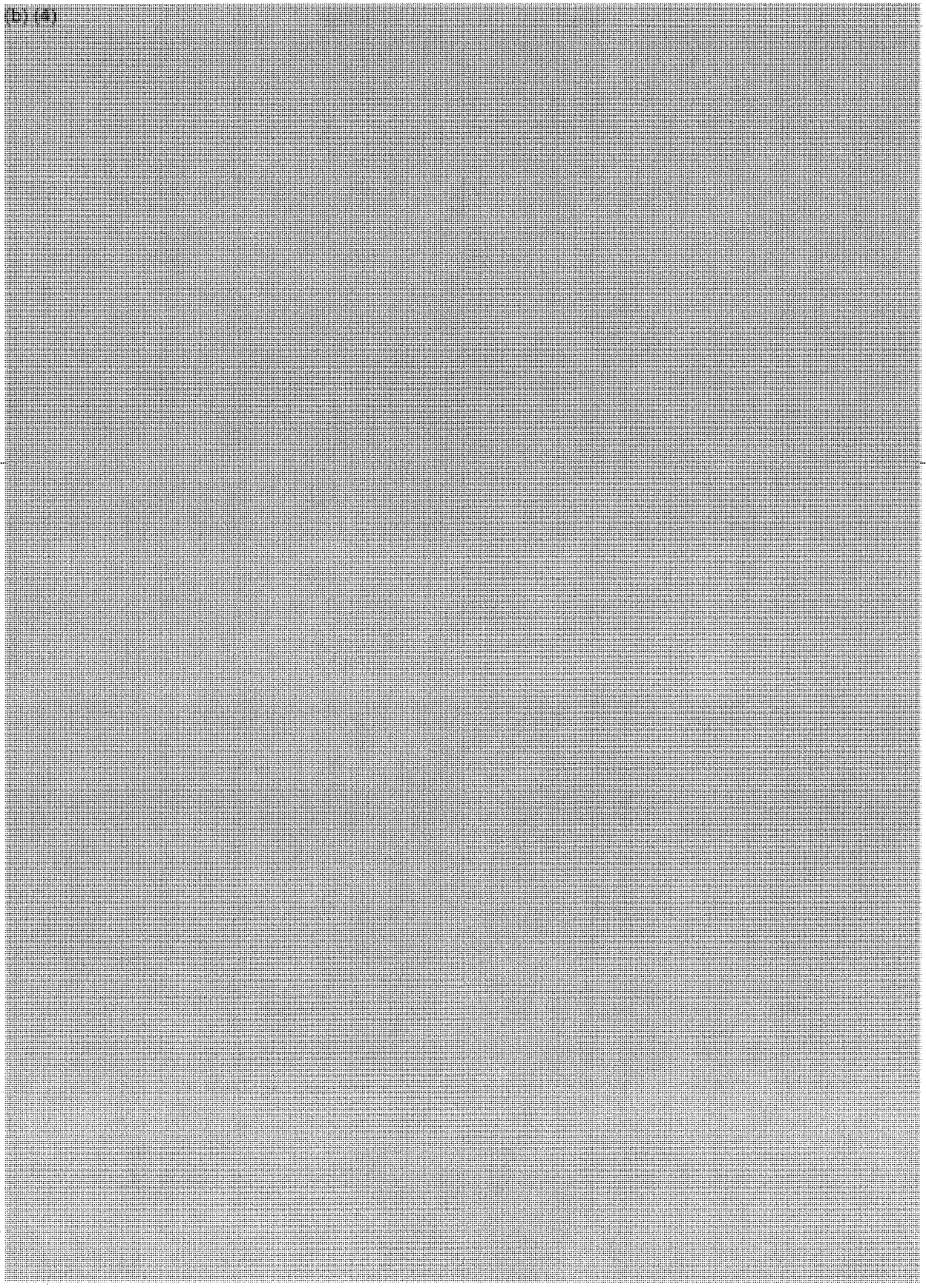


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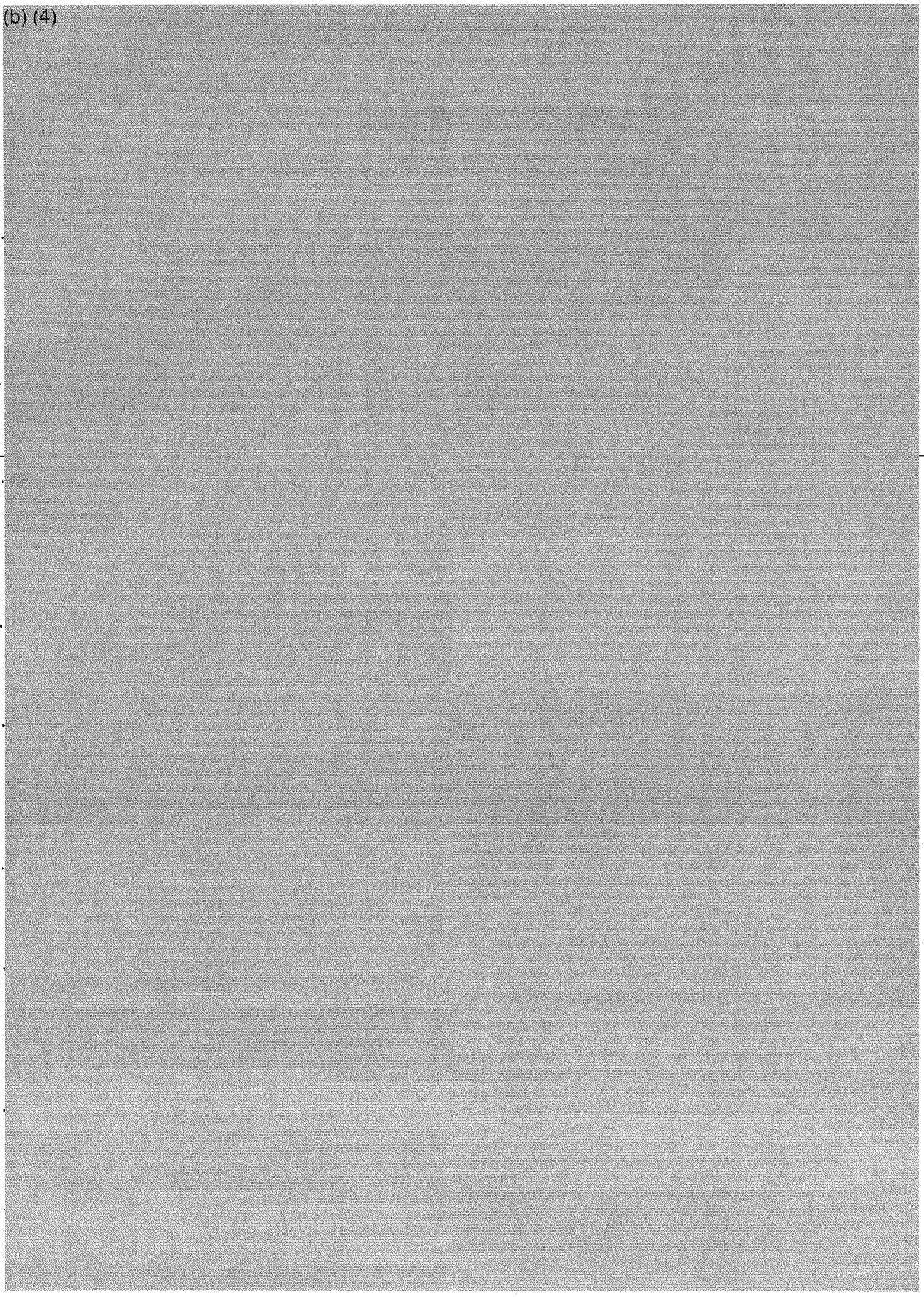


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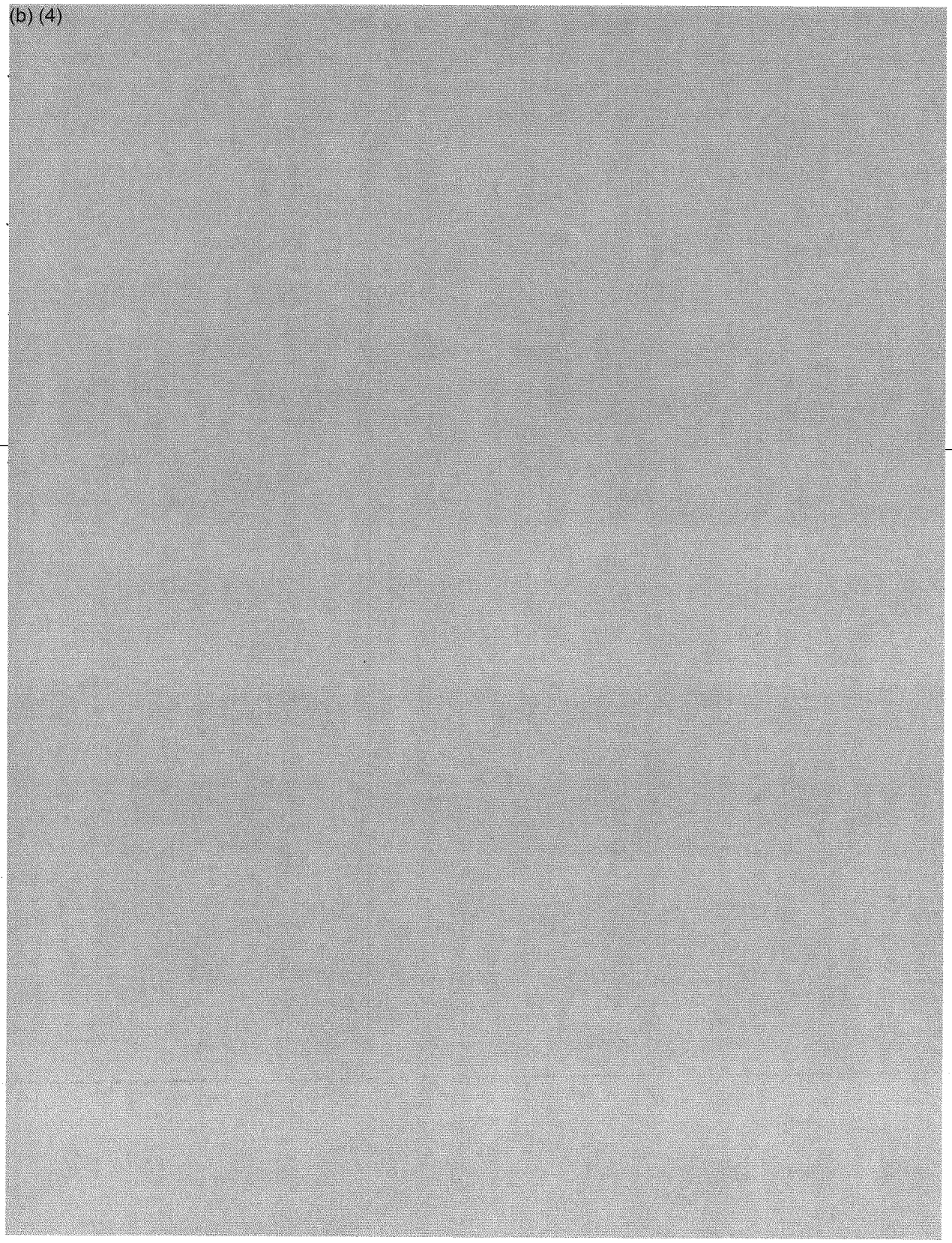



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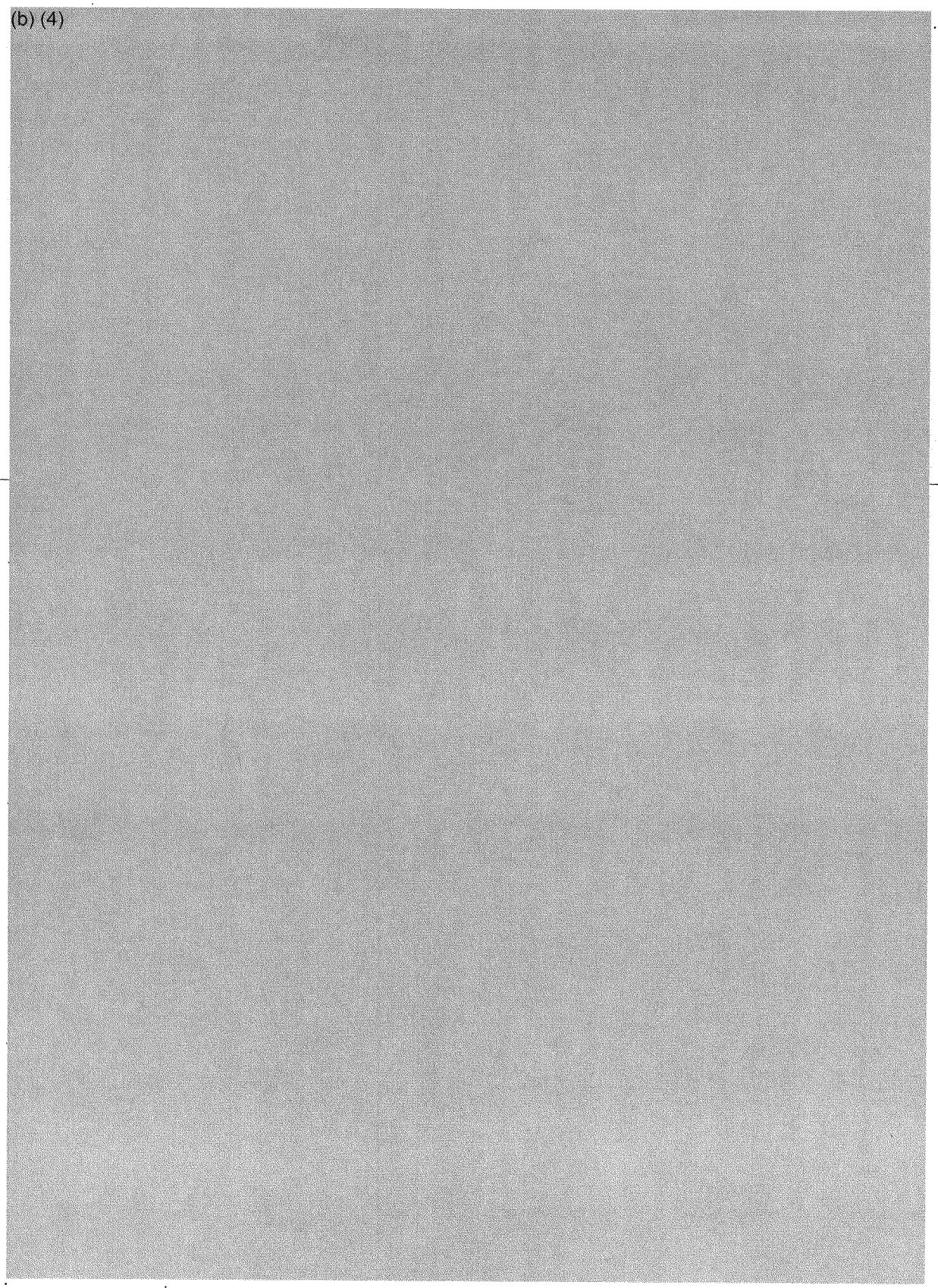
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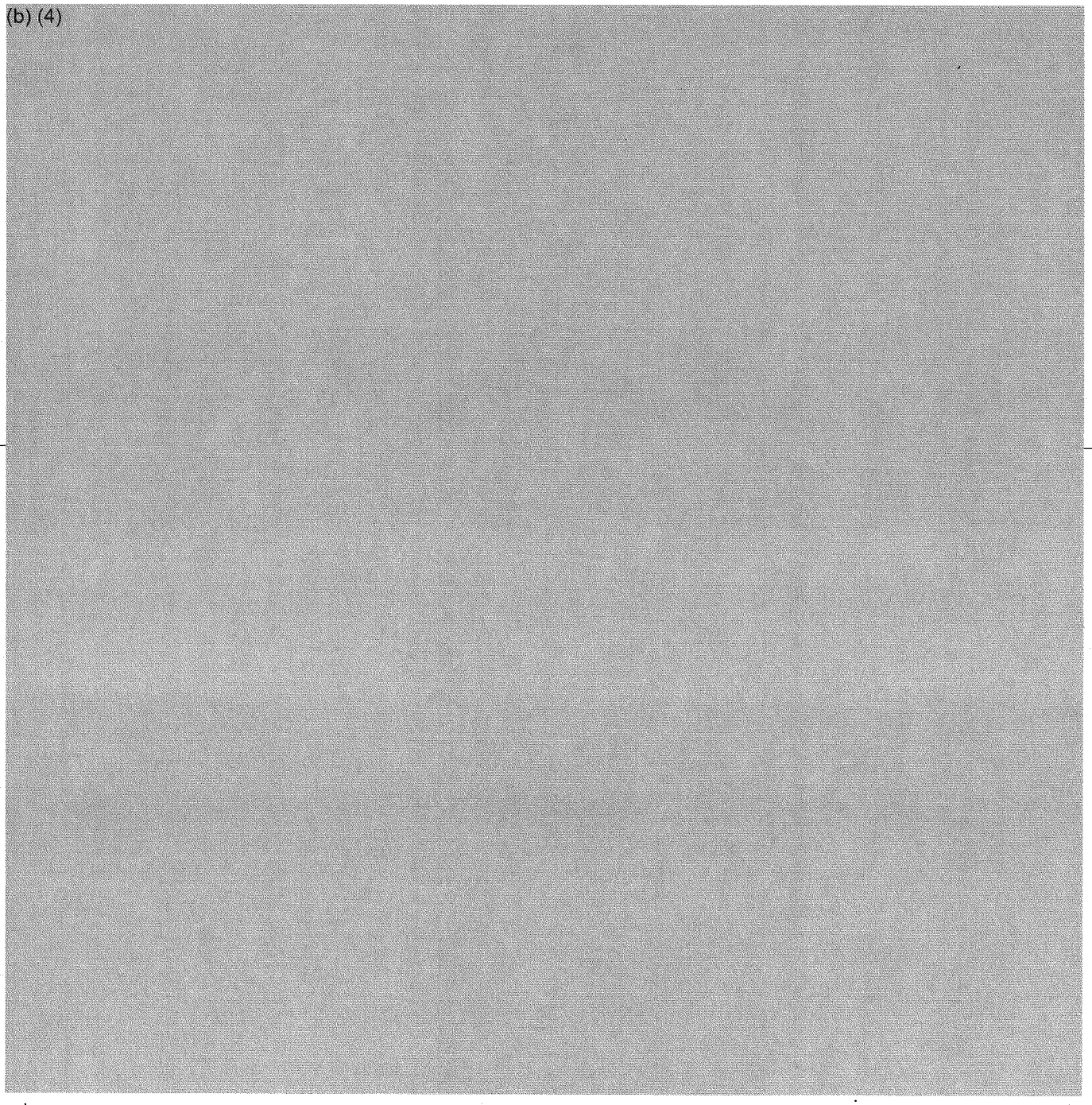
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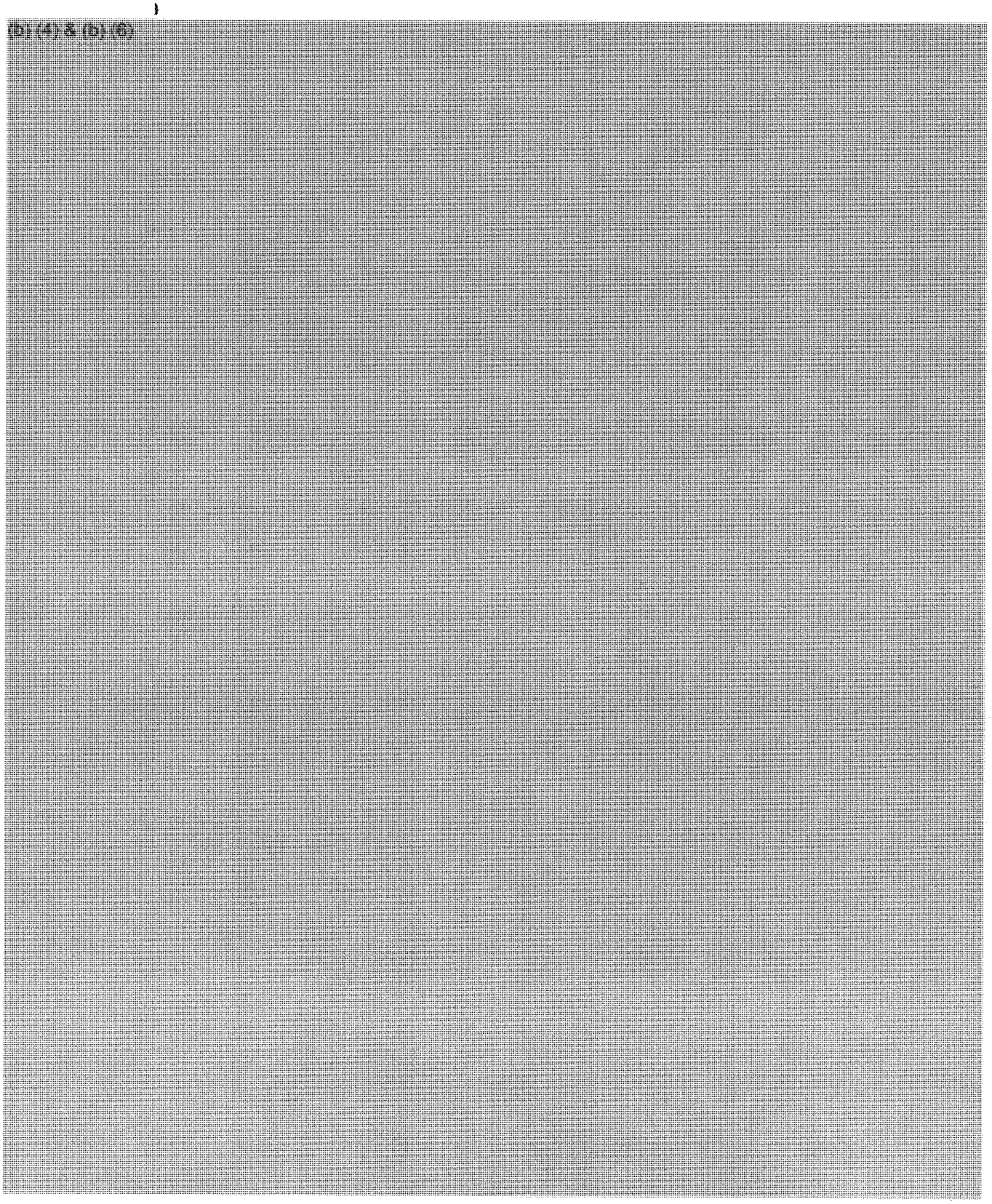


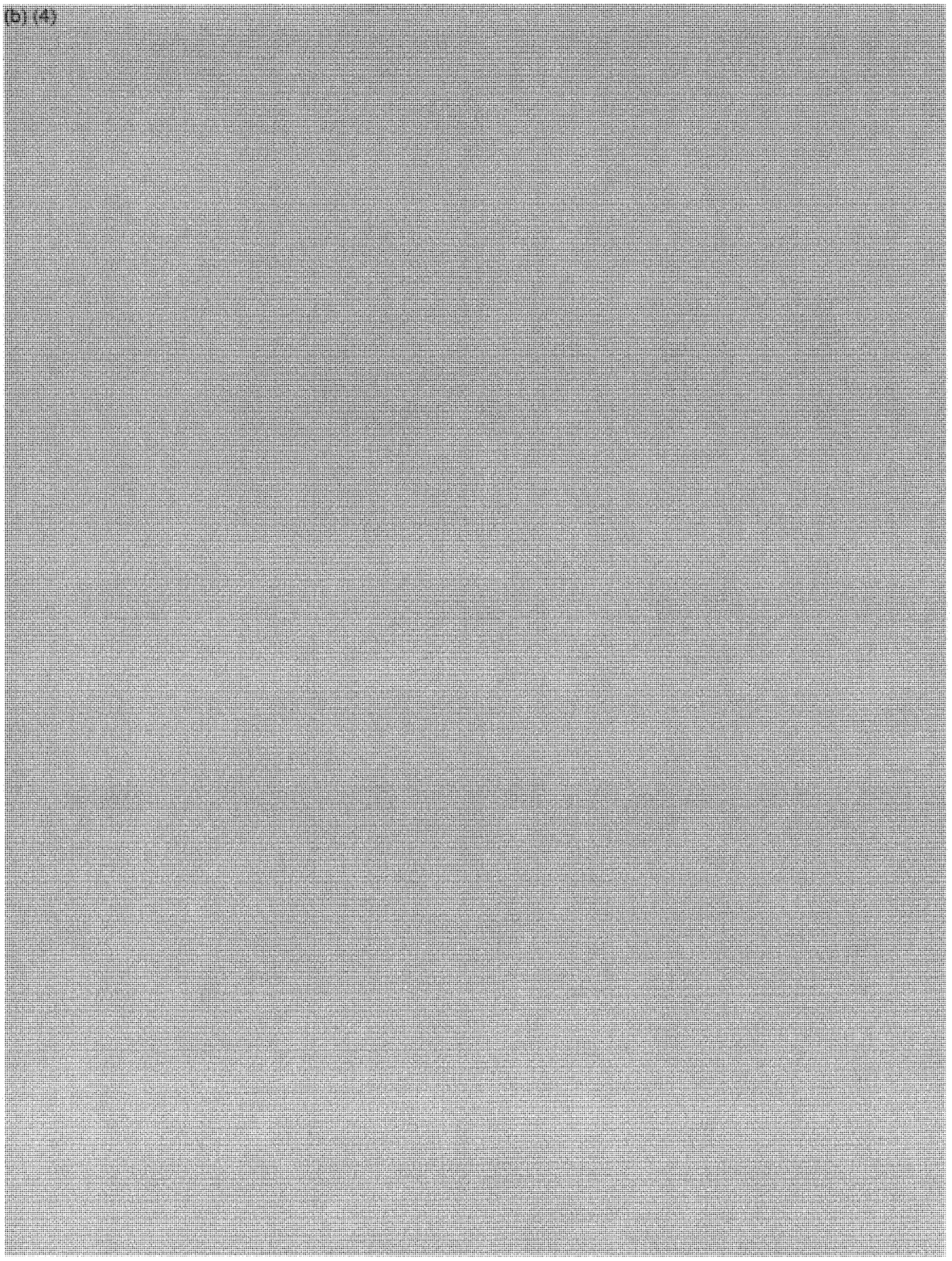
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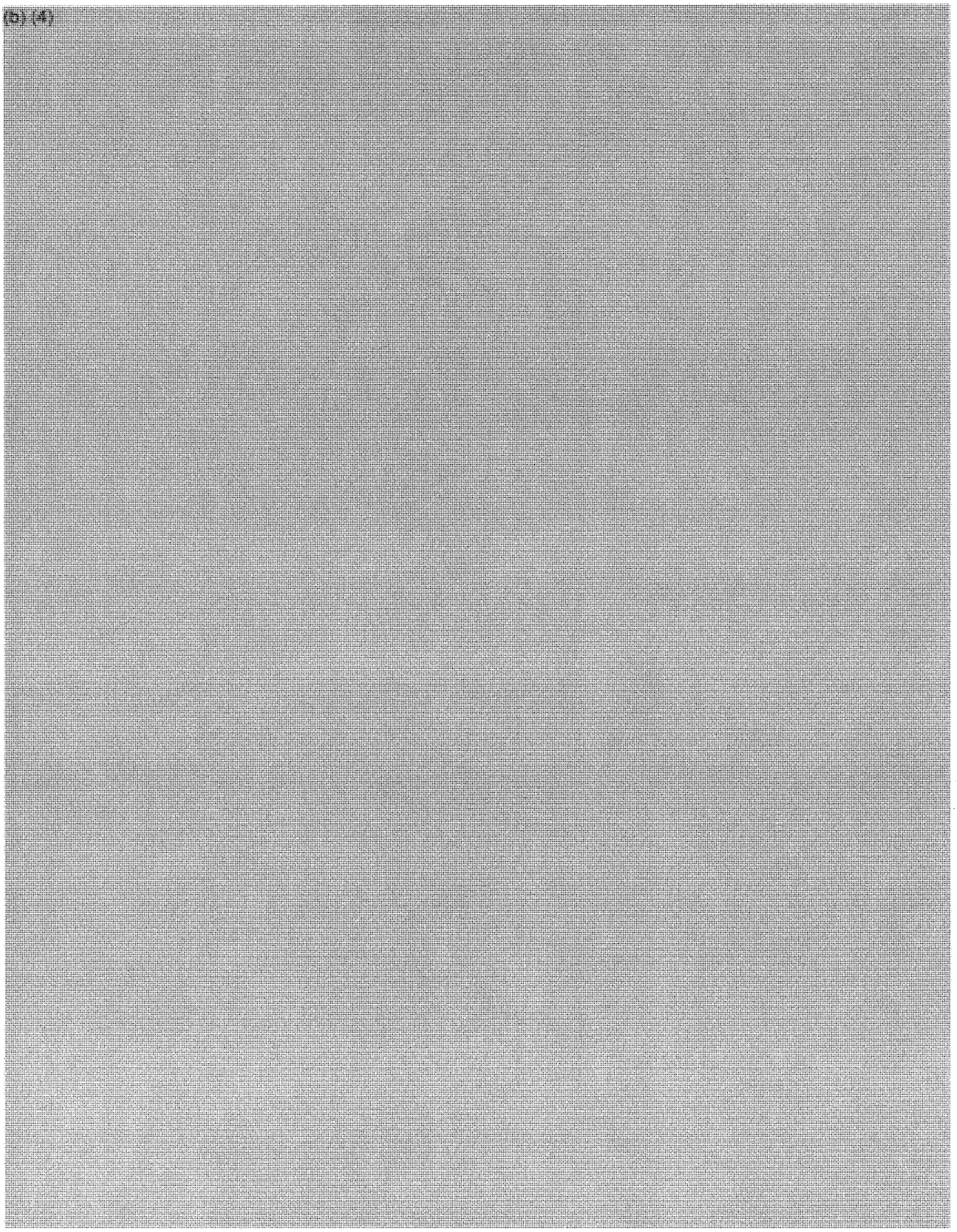


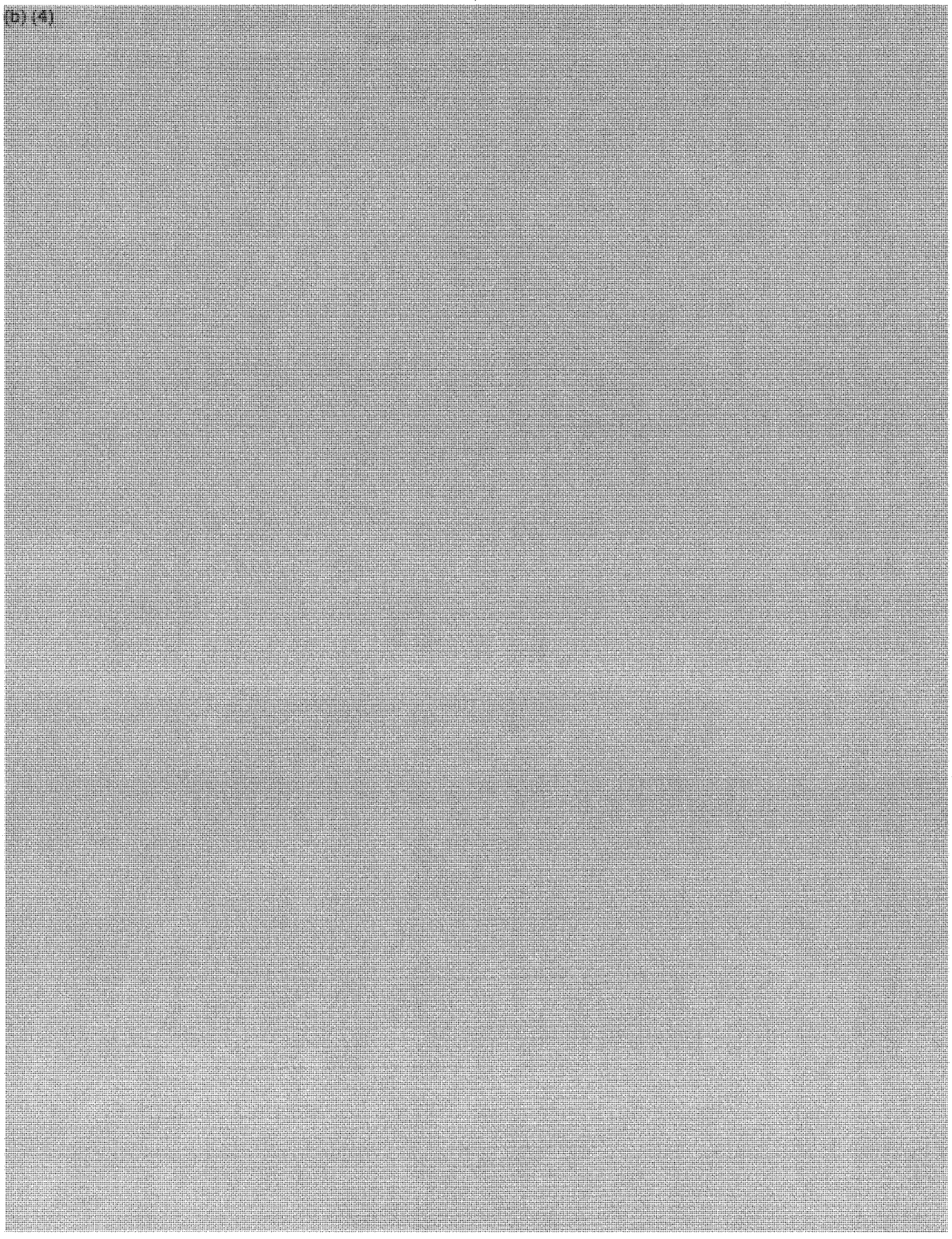
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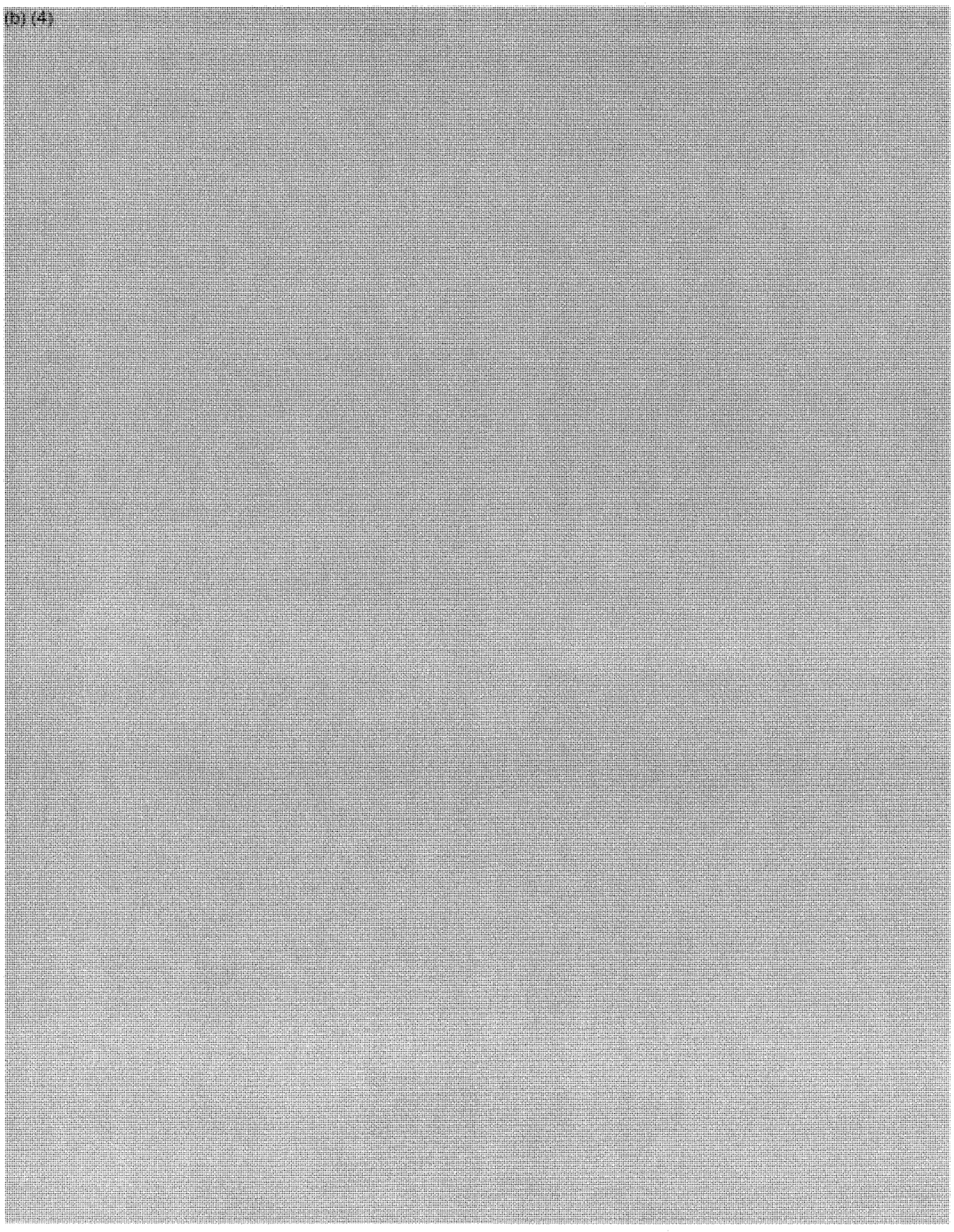

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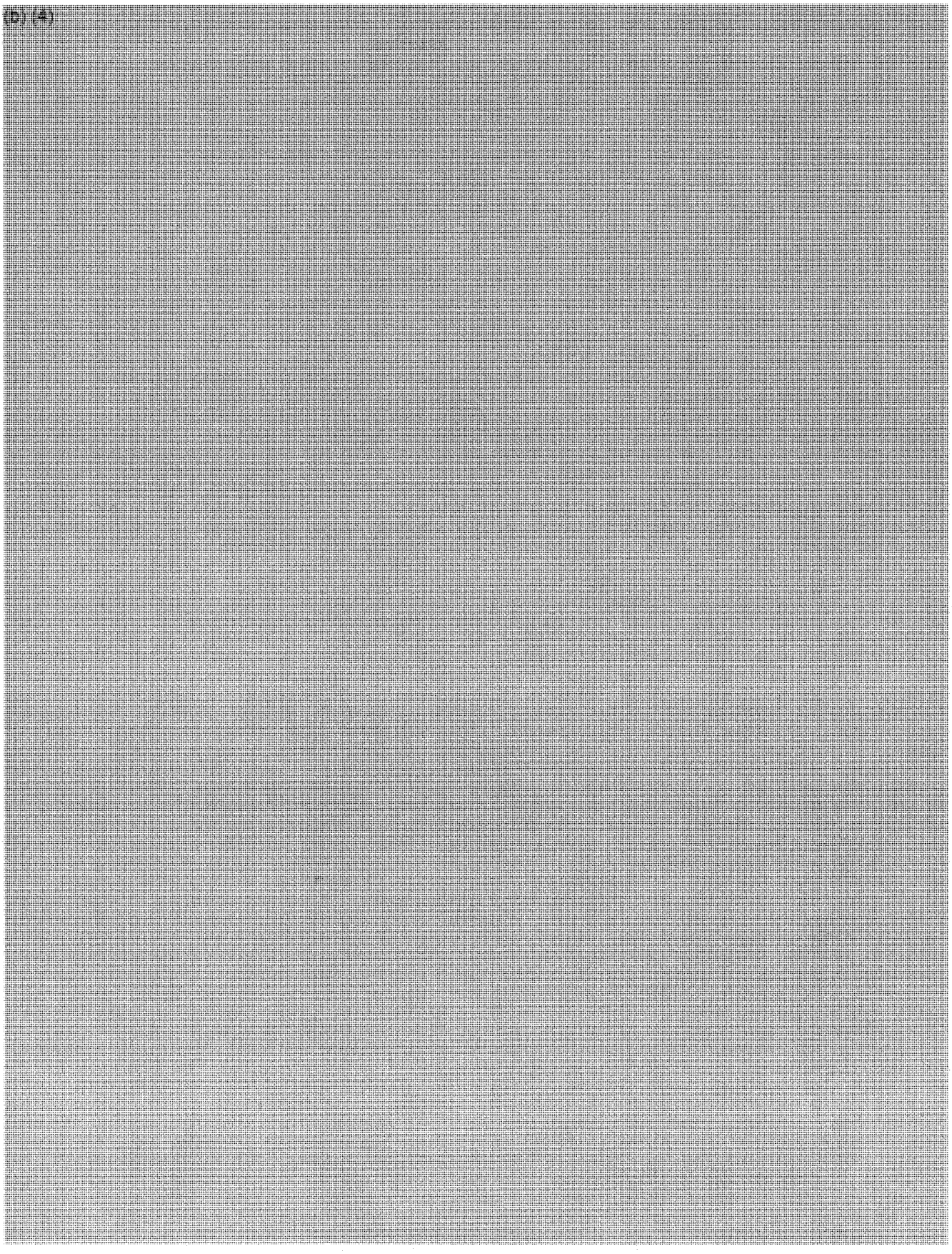

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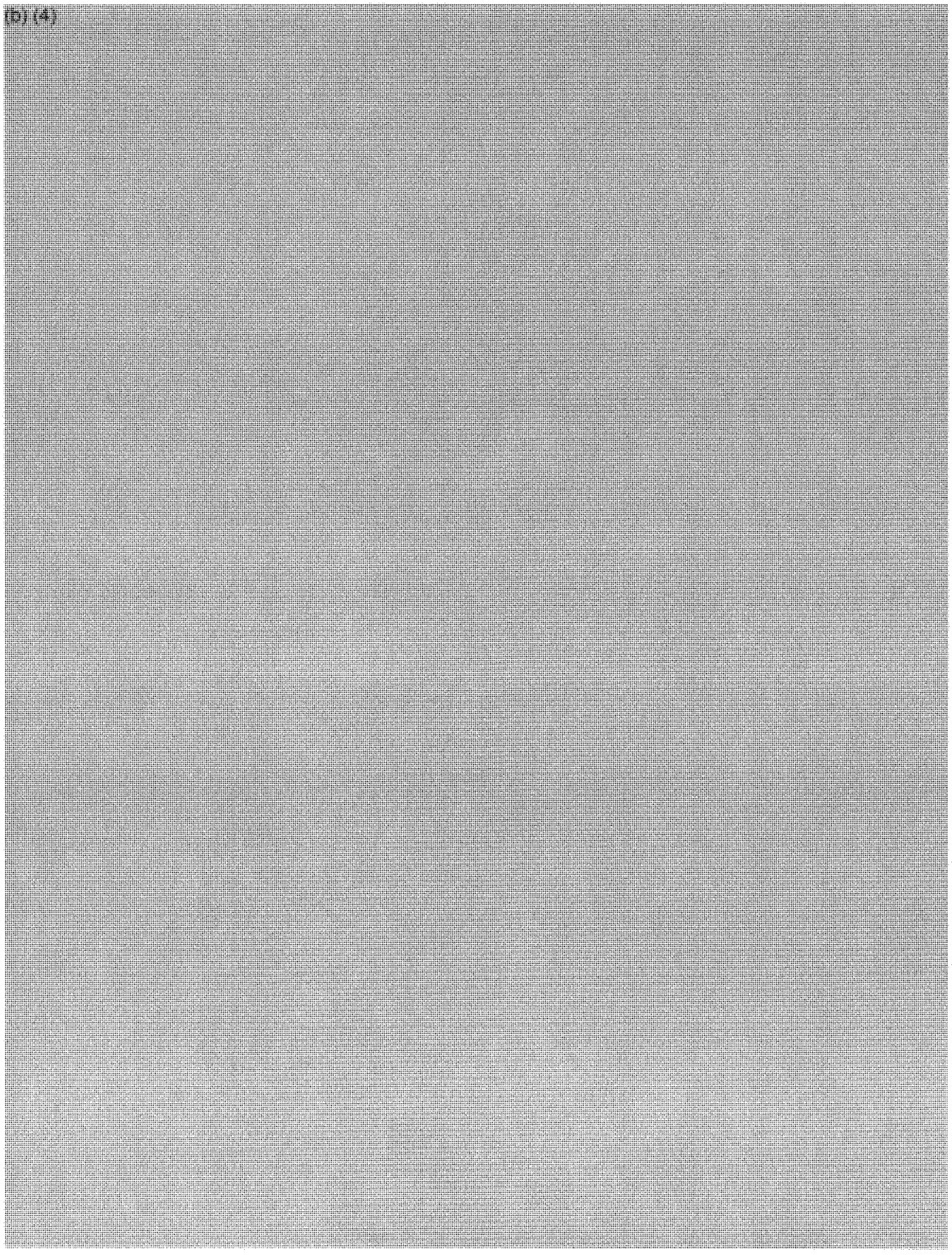
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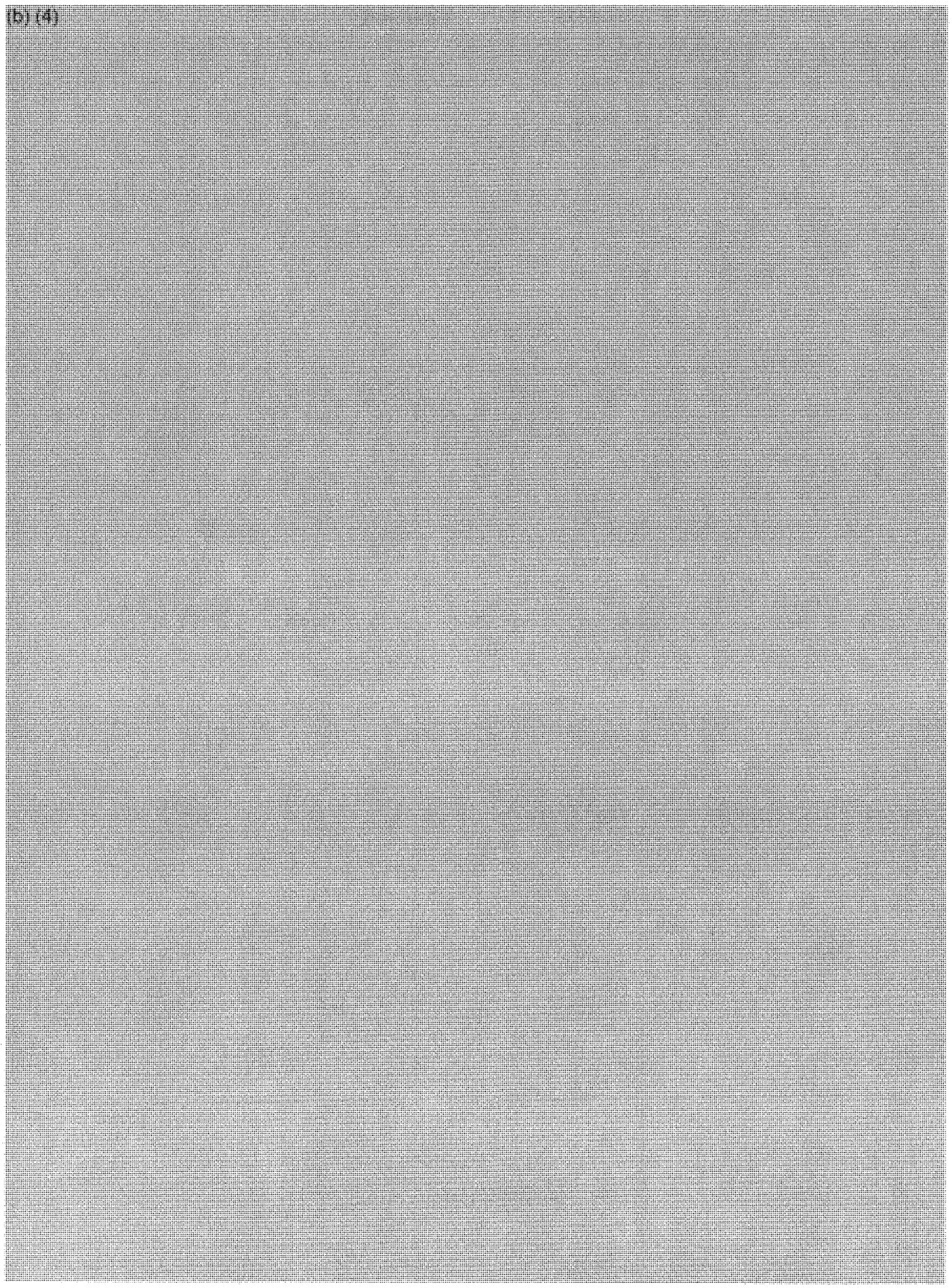


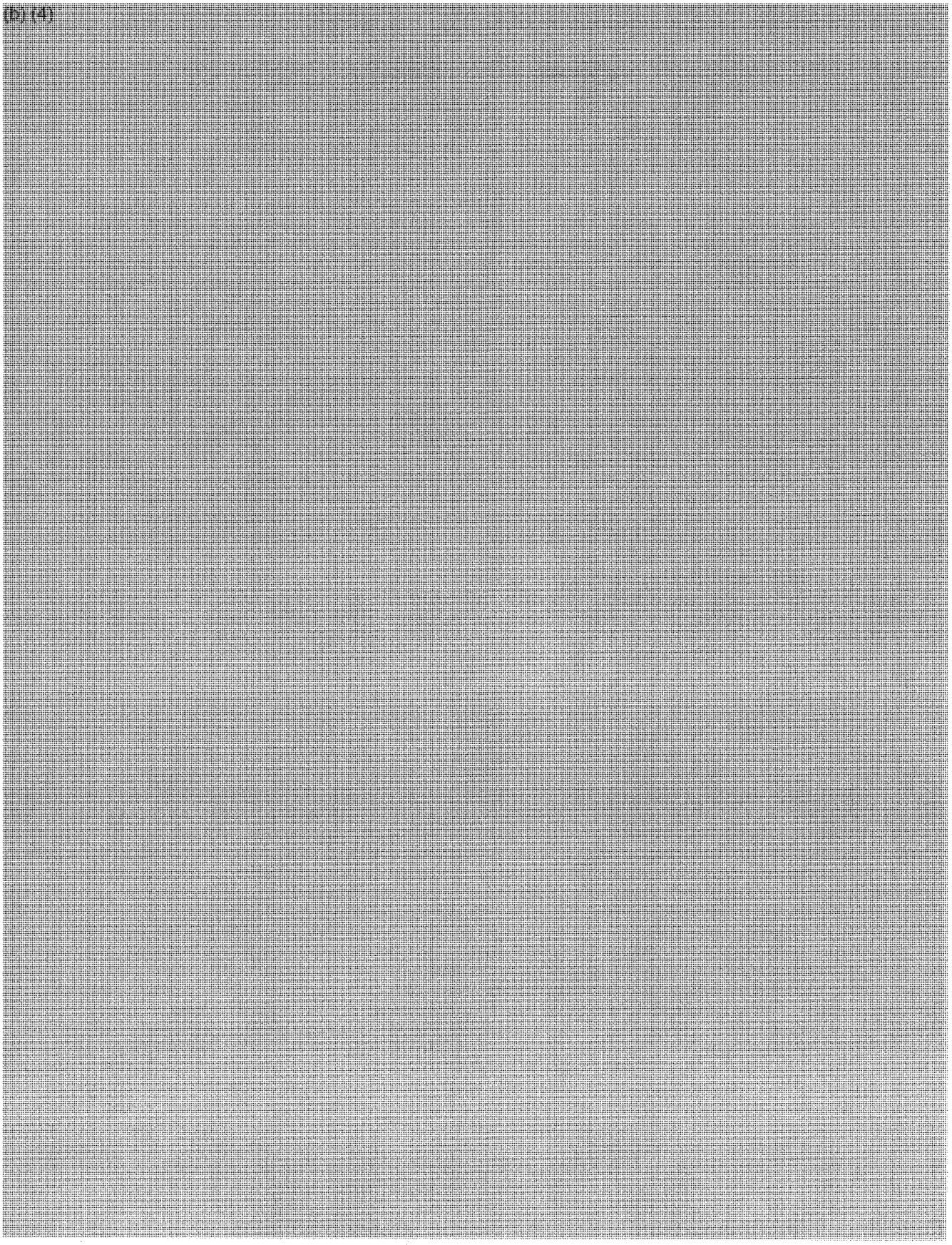
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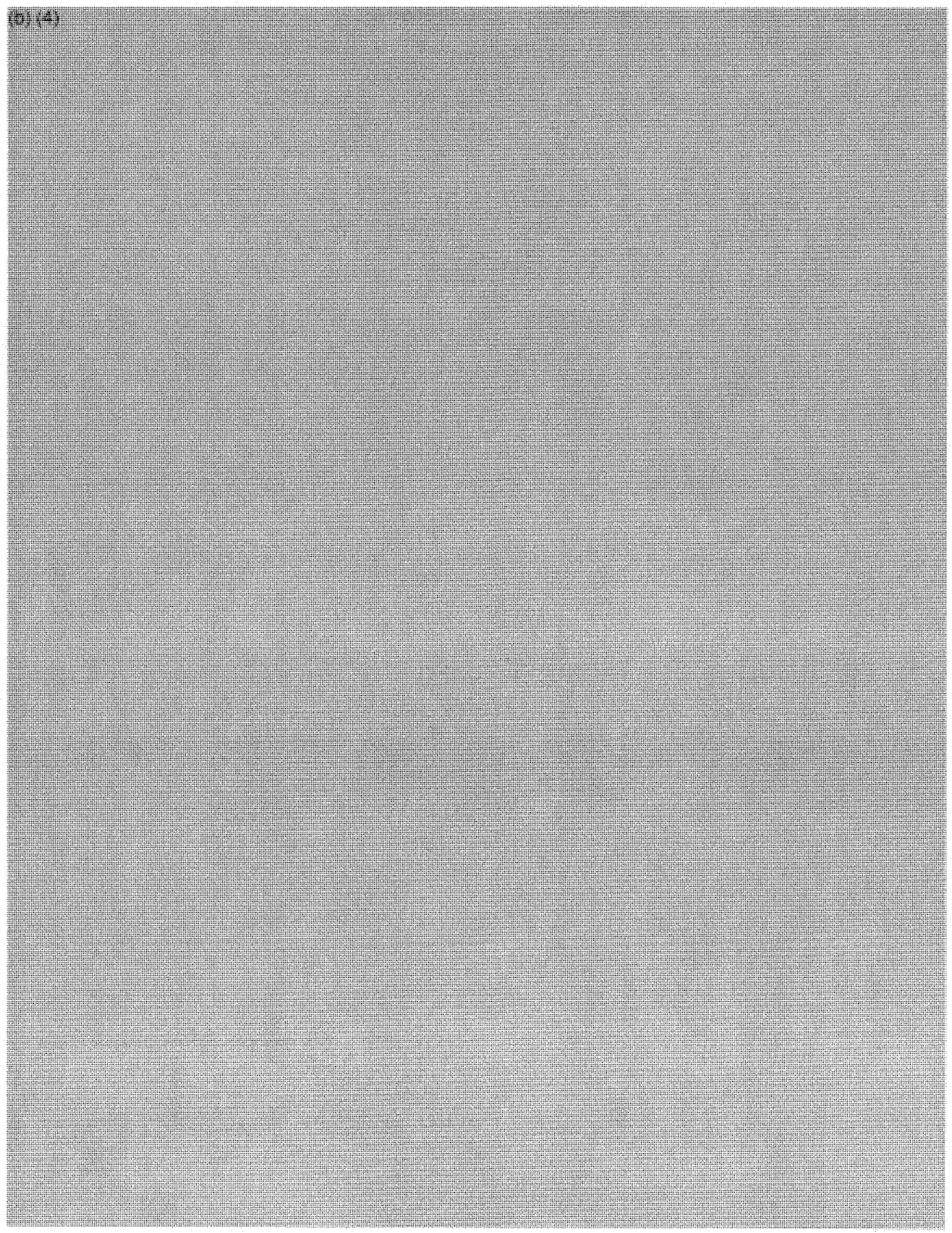
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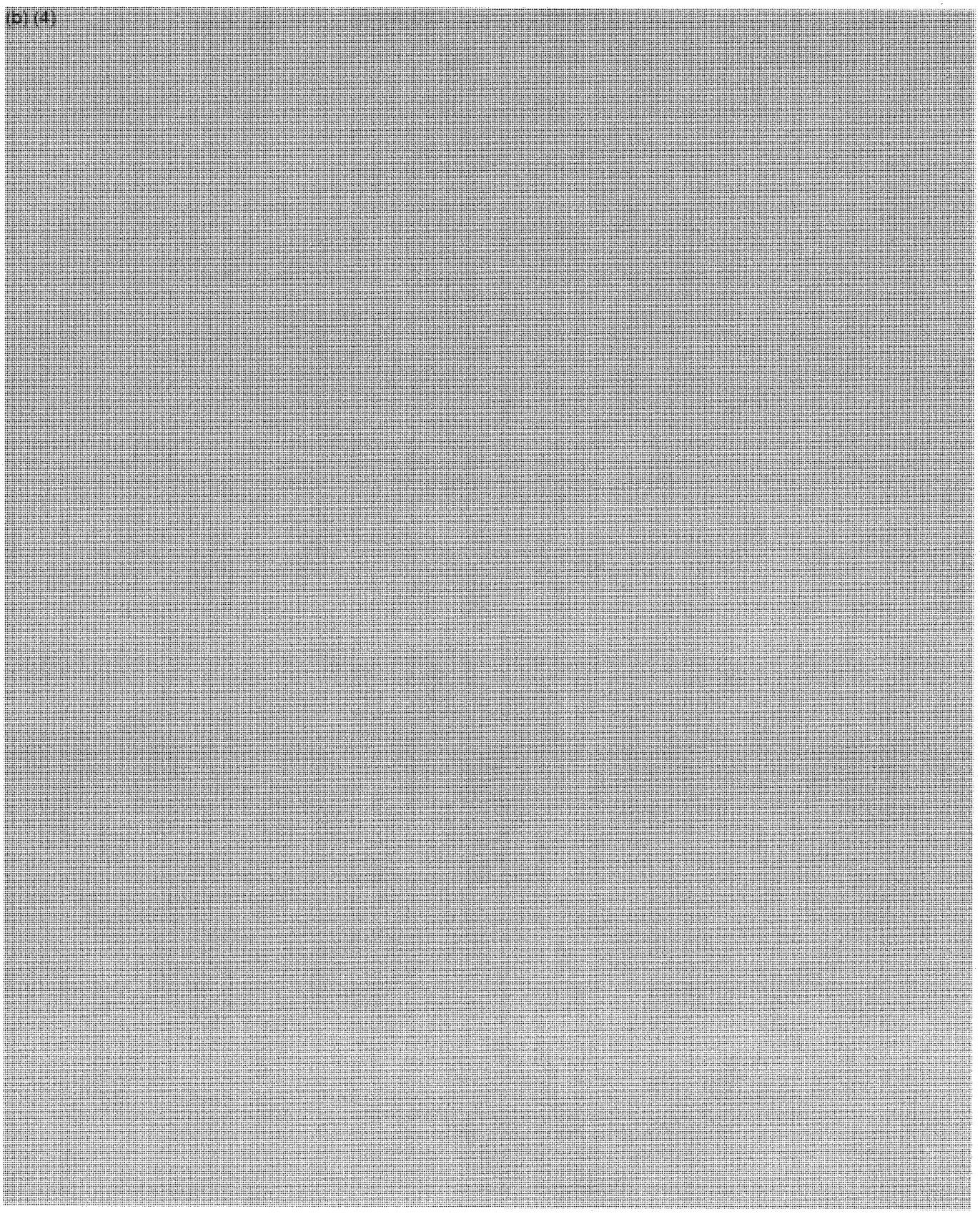



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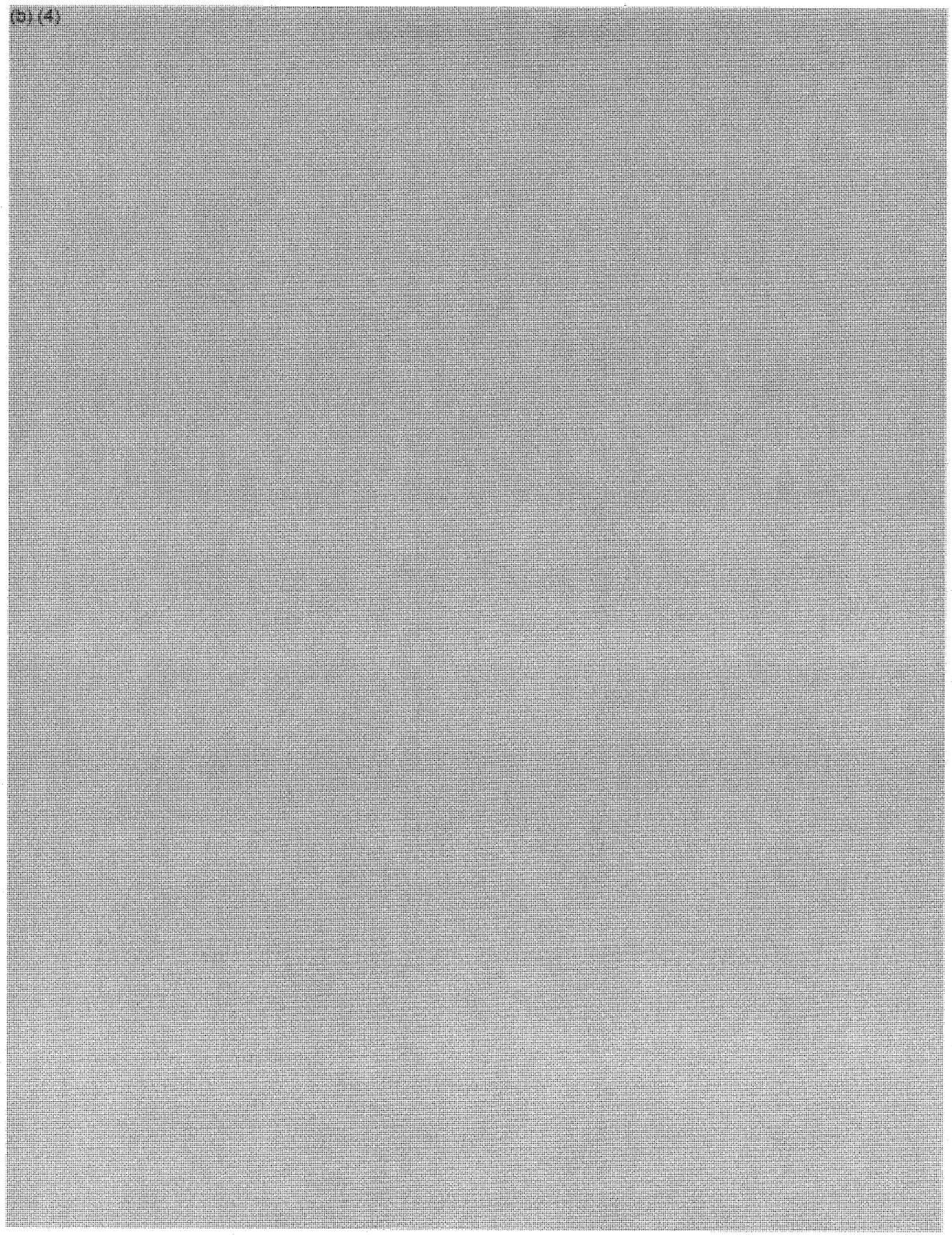

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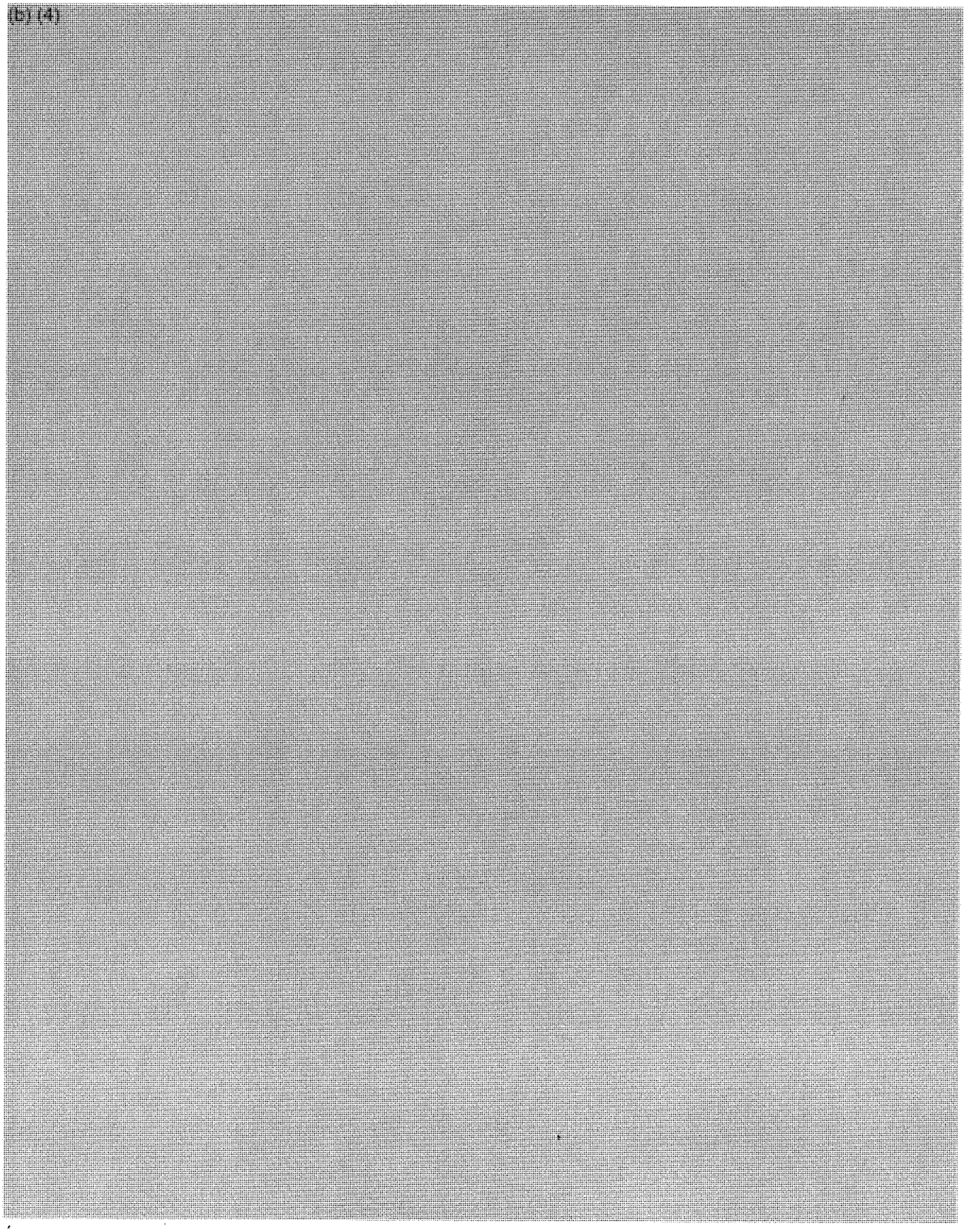
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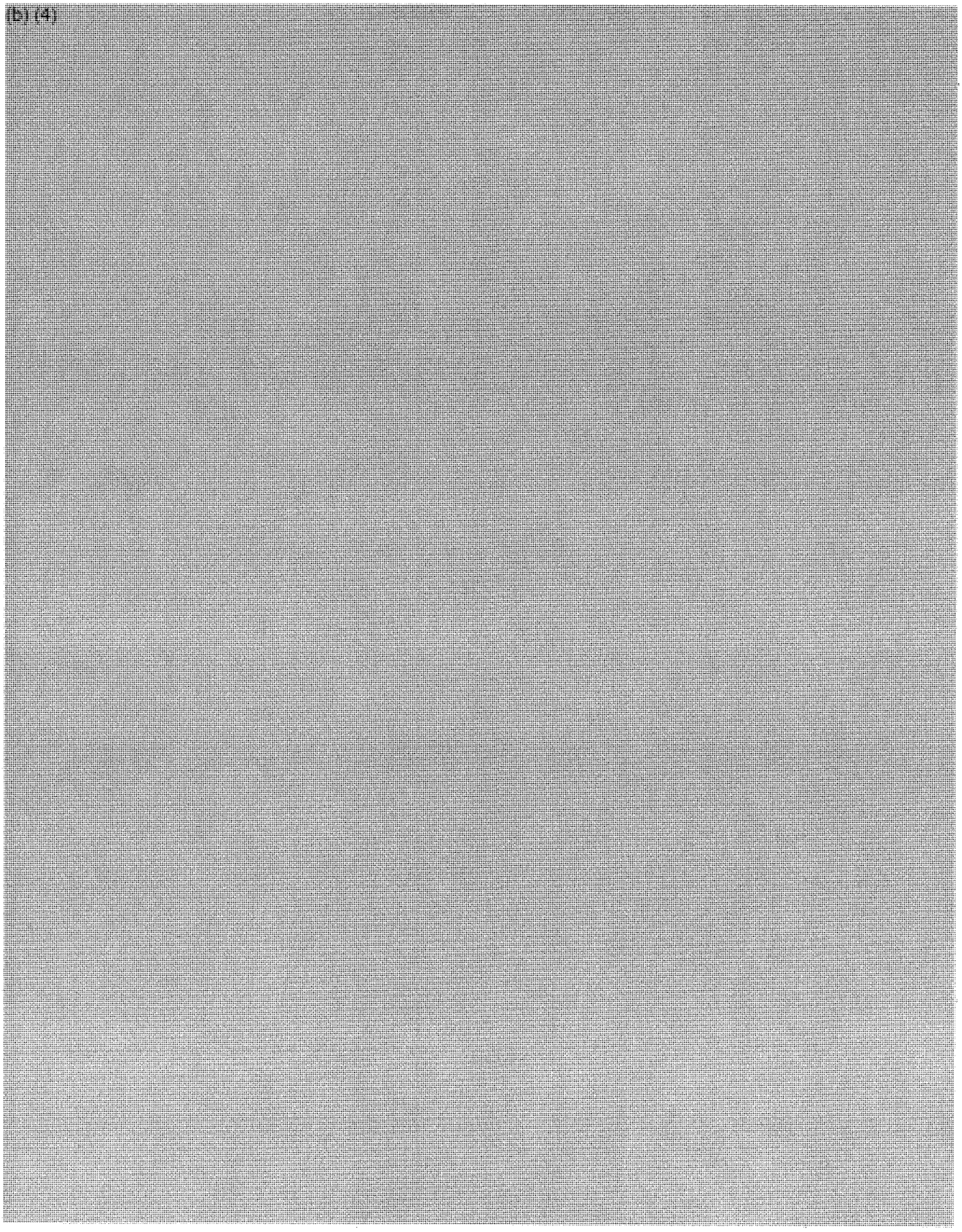


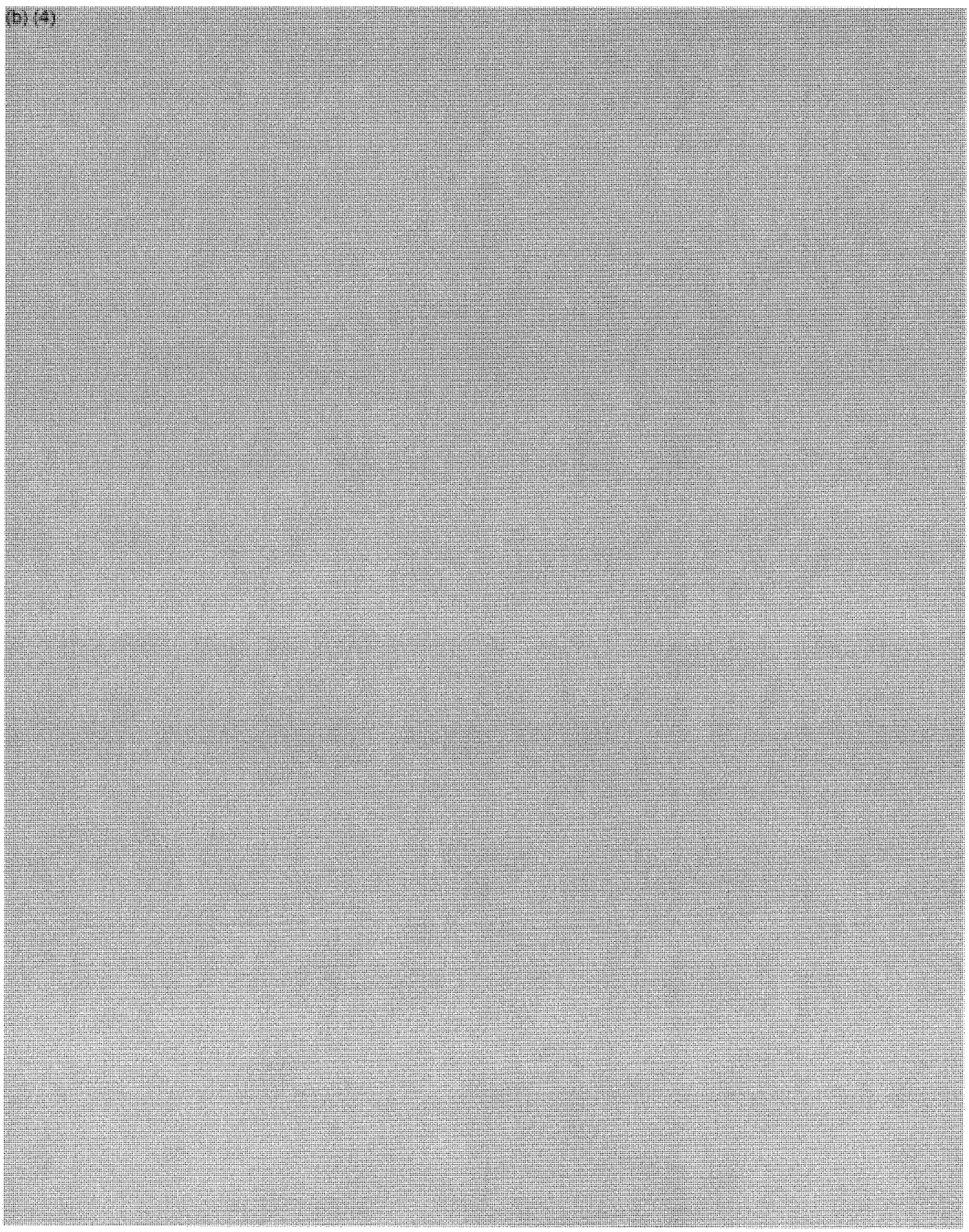

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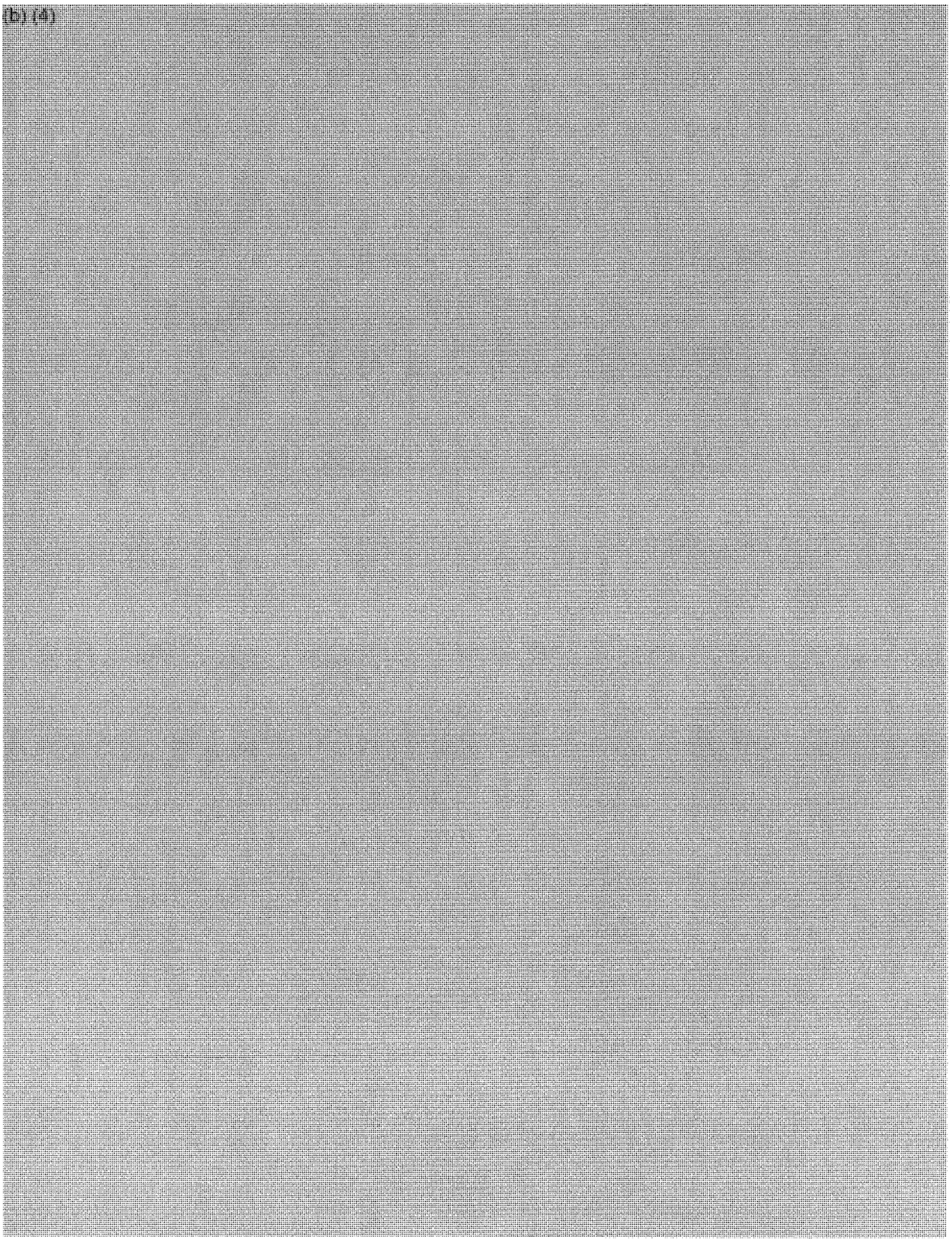
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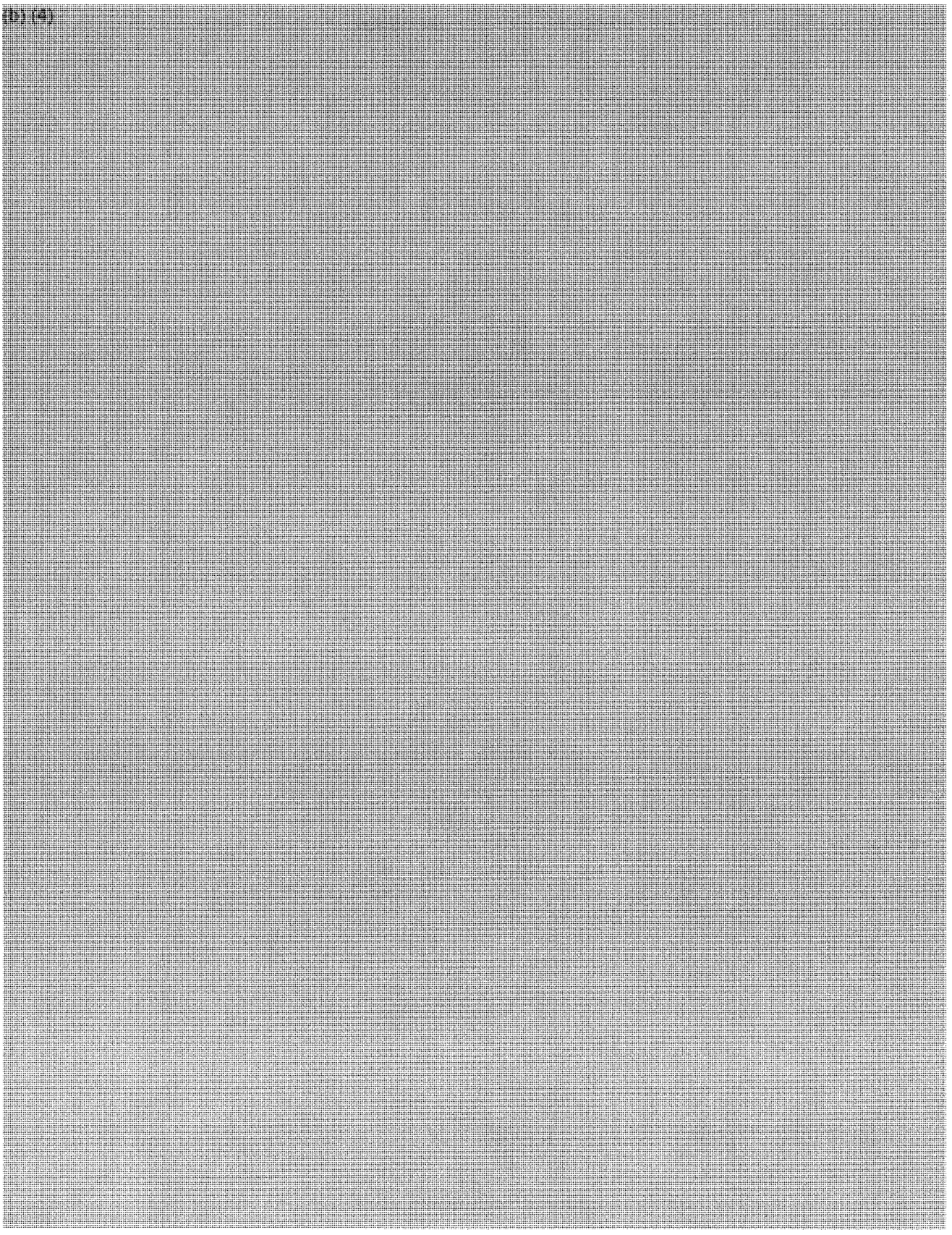


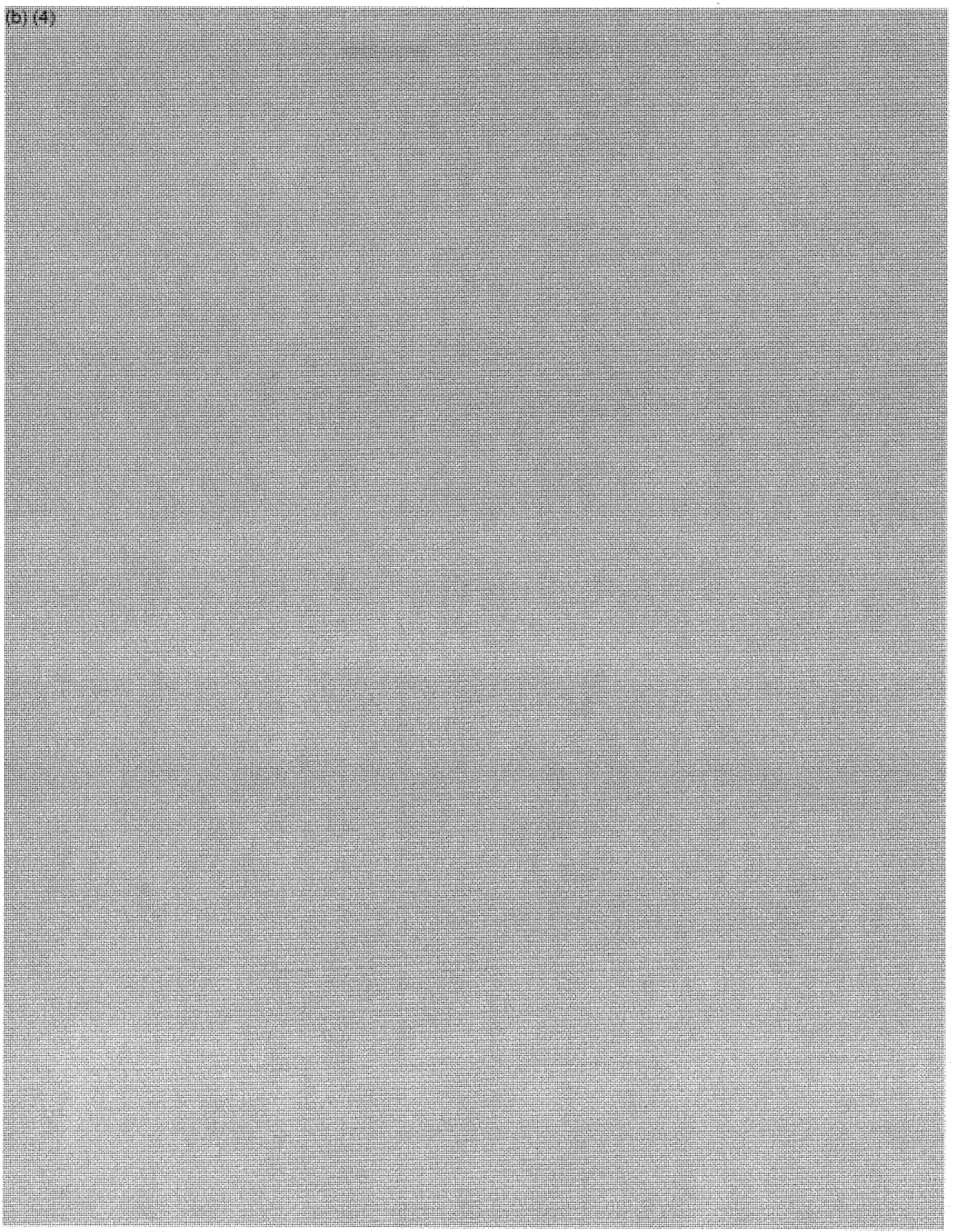

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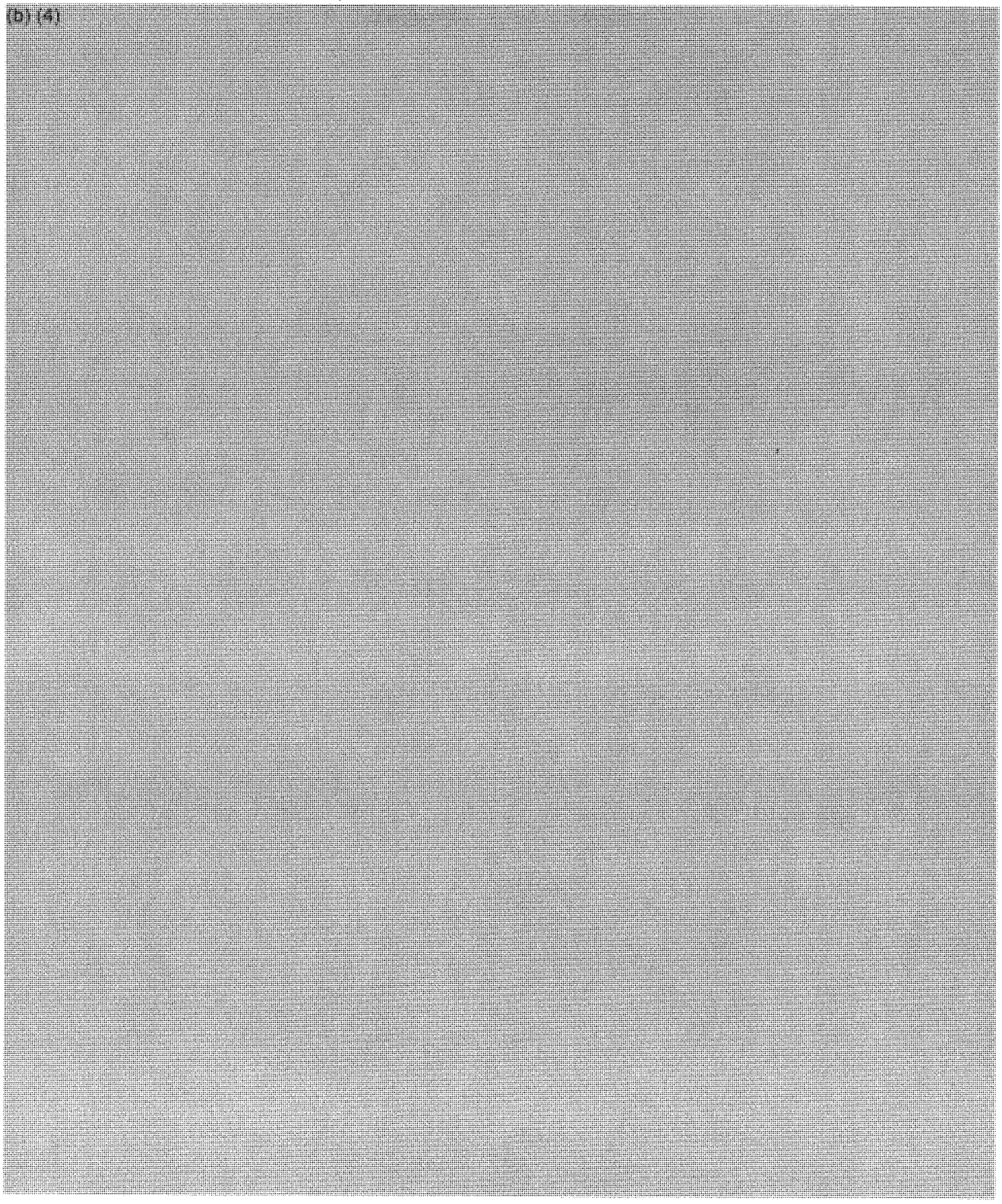

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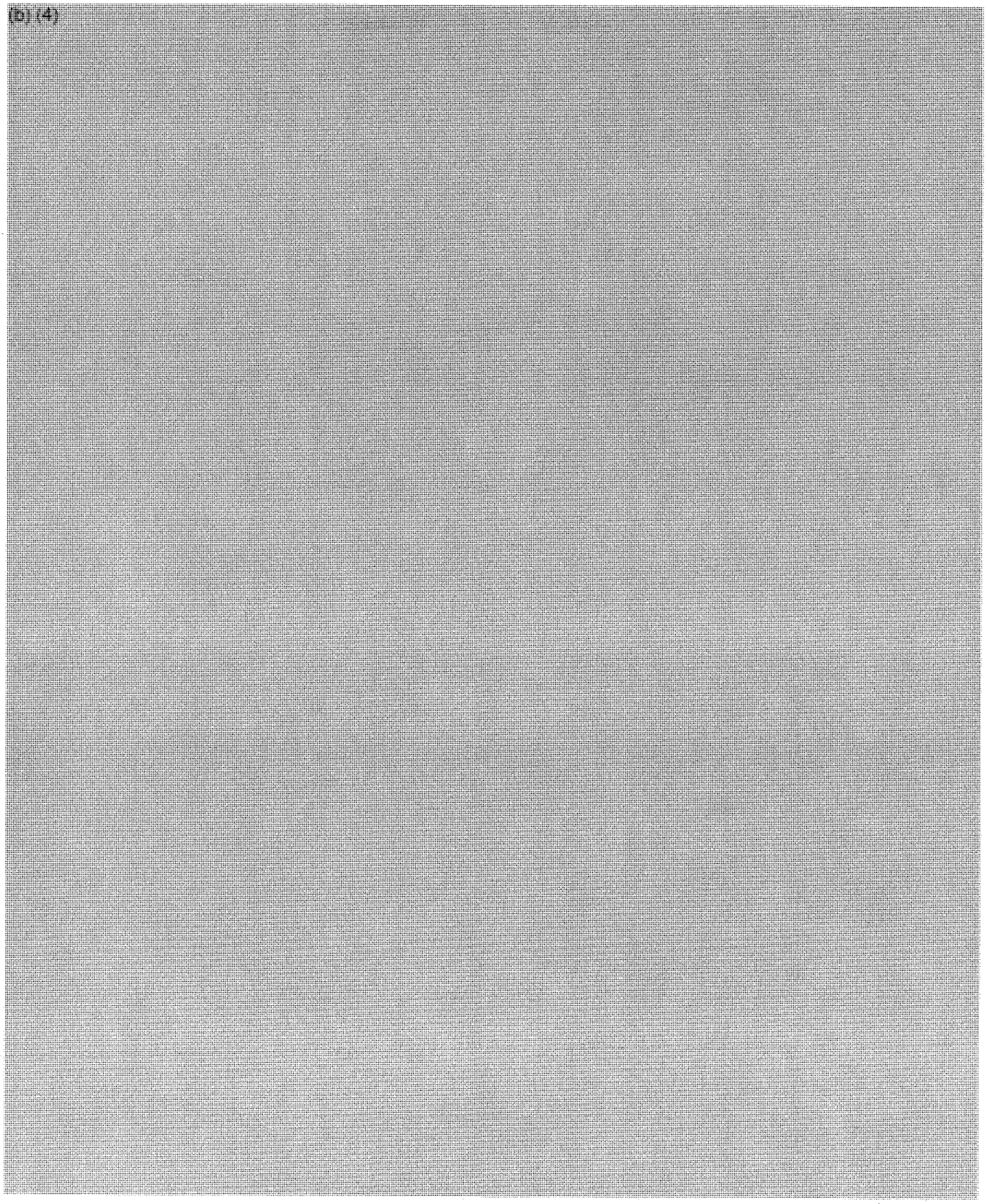

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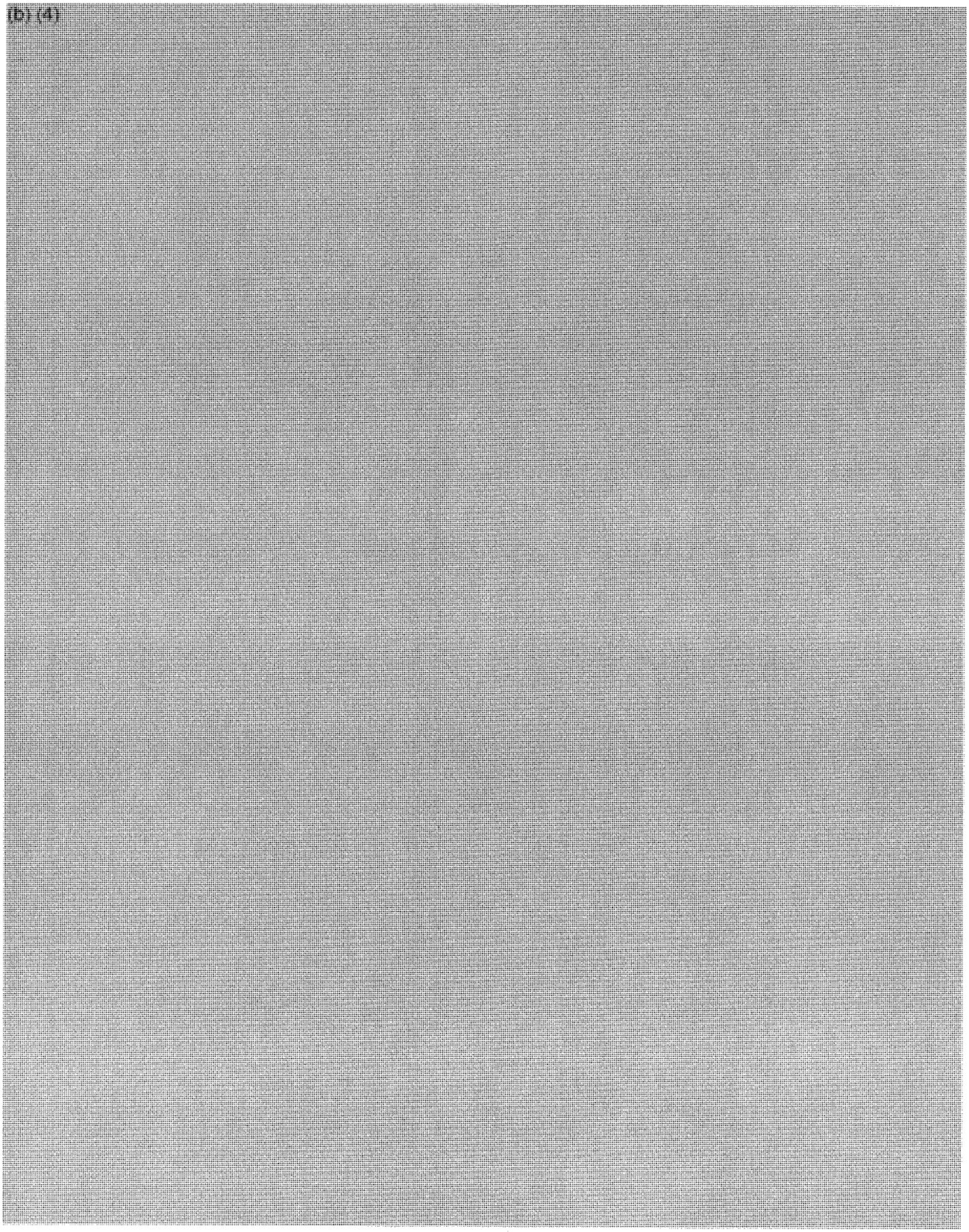

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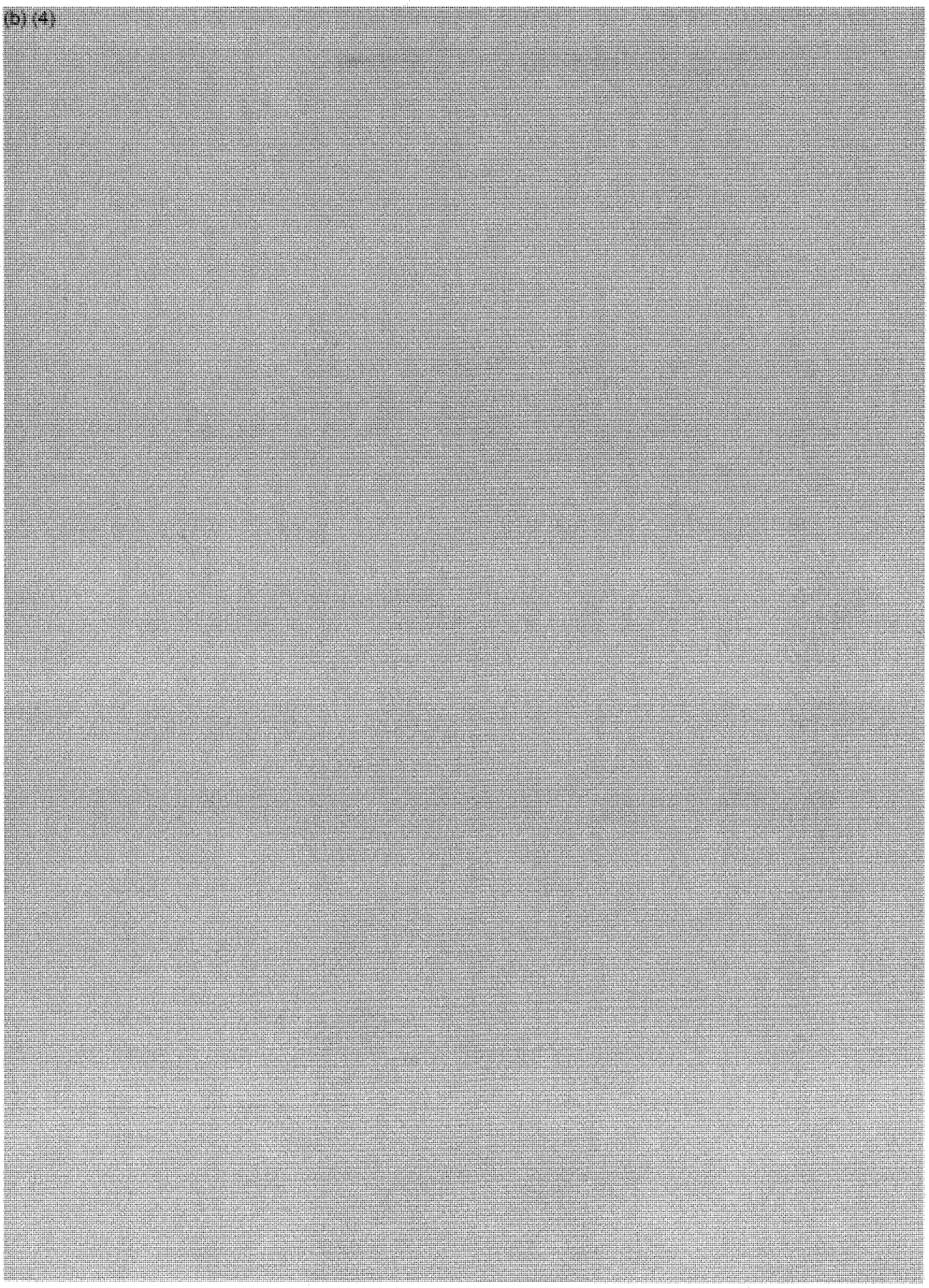


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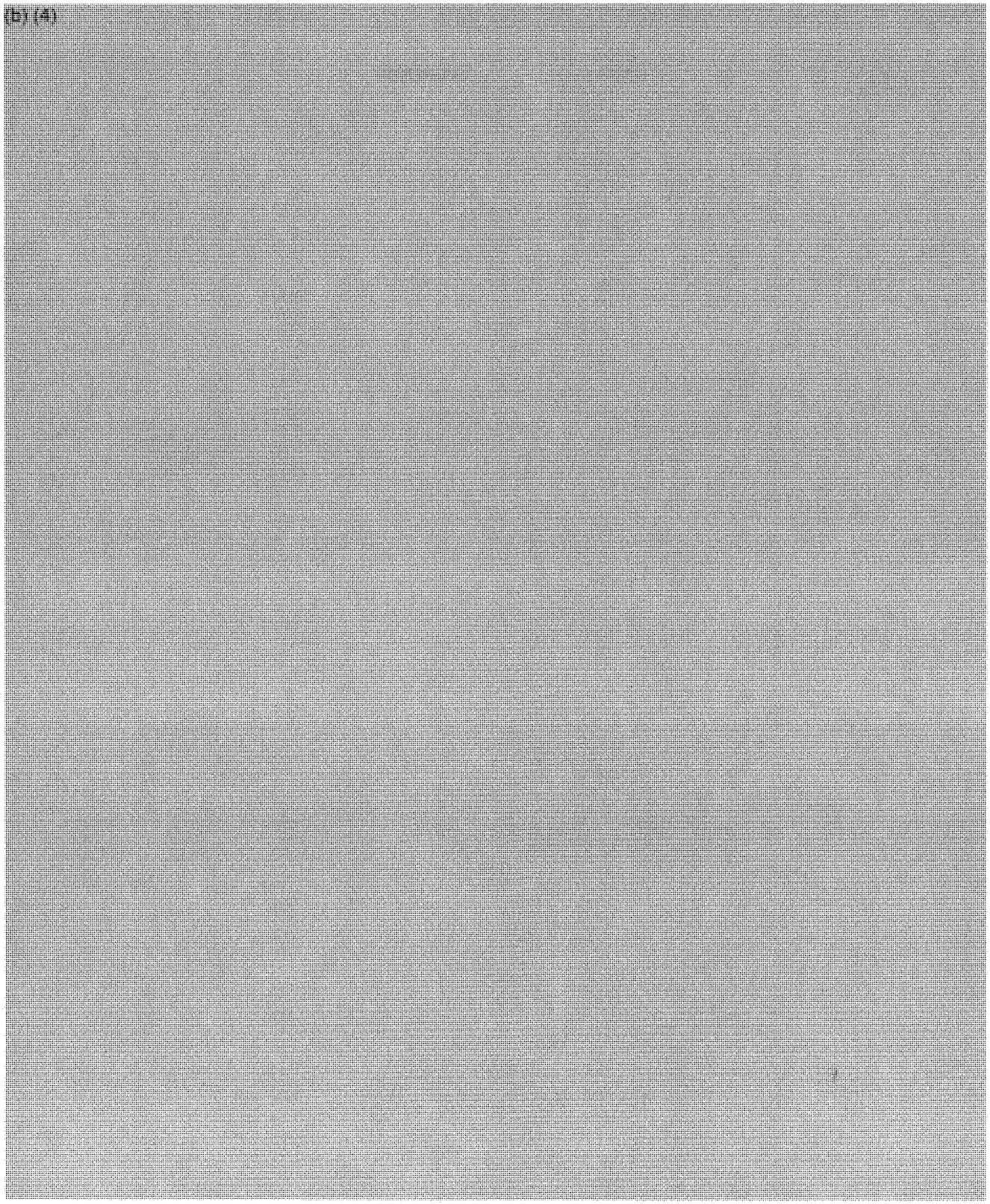

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January 2012

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1986-1987 Chief resident in Pediatrics, Saint Louis Children's Hospital, Saint Louis, Missouri
1987-1988 Resident in Neurology (Adult Neurology), Barnes Hospital, Saint Louis, Missouri (as first year of Pediatric Neurology Fellowship)
1988-1990 Fellow in Child Neurology, Saint Louis Children's Hospital, Saint Louis, Missouri

1990-1993 Research Fellow, NIH Developmental Neurology Training Grant (in the laboratories of Drs. Alan Pearlman and Alan Pestronk)
1990-1993 Fellow in Neuomuscular Disease, Washington Univ. School of Medicine (Dr. Alan Pestronk, director)
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1993-2000 Assistant Professor in Neurology, Washington University
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1986 Missouri #R5F13

Certification:

1989 American Board of Pediatrics
1991 American Board of Psychiatry and Neurology with special qualification in Child Neurology
1993 American Board of Electrodiagnostic Medicine
1996 American Board of Pediatrics-renewed

Honors and Awards:

1976-1980 Indiana Scholar
1980 B.S. Summa Cum Laude
1980 Biology Award for service and academic excellence in biology
1980 Kappa Gamma Pi
1980 Beta Beta Beta Biological Honor Society
1988 Irwin Levy Prize for undergraduate teaching, Washington University
2005 Best Doctors in America
2006 Best Doctors in America
2007 Best Doctors in America
2008 Best Doctors in America
2008-2009 Washington University Neurology Teacher of the Year

Professional Societies and Organizations:

1991-present Child Neurology Society
1993-present American Academy of Neurology

Community Service:

1990-Present: Muscular Dystrophy Association camp doctor

Consulting relationships and Committees

1993-1994 Scientific Selection Committee, Child Neurology Society
1993-present Resident Selection Committee, St. Louis Children's hospital
1997-present Utilization Review subcommittee, St. Louis Children's hospital
1997-present Human IVIG usage committee, St. Louis Children's hospital
1997-present Long range planning committee, Child Neurology Society\
2000-2004 Practice parameters for care of boys with Duchenne Muscular dystrophy.

2006-present International Standard of Care committee for treatment of children with Spinal muscular atrophy
2006-present Committee member for CDC Diagnostic Expert group for DMD
2005-present Committee chair for the Therapeutic Subcommittee of The Clinical International Neuromuscular Research Group (CINRG); Purpose of this committee is to decide which therapies have enough preclinical data to warrant a trial in children.
2007- Member for the SLCH Ethics Committee
2004-present; Consulting for NORD with regard to Neuromuscular Disorders

Invited lectures/workshops:

1. Guillian-Barre syndrome in Childhood, Pediatric Grand rounds, Washington University, St. Louis, June 1994
2. Periodic paralysis in children and adults, Neurology Grand Rounds, Washington University, St. Louis, October, 1995
3. Congenital muscular dystrophy, Neurology Grand rounds, St. Louis University, St. Louis, November, 1996.
4. Workshop on the Development of Guillain-Barre Syndrome following Campylobacter Infection, NIH, Bethesda Maryland, August 1996.
5. Miller fisher syndrome, Pediatric clinical rounds, Washington University, 1996.
6. Duchenne muscular dystrophy, Pediatric clinical rounds, Washington university, 1997.
7. Myasthenia gravis, Pediatric clinical rounds, Washington University, 1997.
8. Guillian Barre syndrome, Pediatric clinical rounds, Washington University, St. Louis, July,1999.
9. Invited Workshop on study of autoimmune mechanisms in Autism and Acquired epileptic aphasia. Chicago, IL March, 2000.
10. Invited Workshop to develop treatment strategies for boys with Duchenne muscular dystrophy. NIH, Bethesda Maryland, May, 2000.
11. Making weak children and mice stronger, Pediatric Grand rounds, Washington University, June 2000.
12. "The floppy infant syndrome" Guest speaker for Italian Neuromuscular Congress, Catania, Italy, Novemeber, 2000.
13. Invited workshop participant: Dancing Eyes Syndrome; Oxford, England, February, 2001.
14. Nemaline rod myopathy; Pediatric clinical rounds, Washington Unversity, St. Louis, June 2001.
15. Presynaptic disorders of neuromuscular transmission, Pediatric clinical rounds, Washington University, St. Louis, MO Nov 2002
16. Duchenne and congenital muscular dystrophy, Washington University, St. Louis, Nov., 2002.
17. Congenital Myasthenic Syndrome, Neurology Grand Rounds, May 2004.
18. Congenital and Duchenne MD: Southern Illinois University Symposium speaker: March, 18, 2005.
19. Spinal Muscular Atrophy; Neurology Grand Rounds, December, 2006.
20. CDC clinical care committee for Duchenne Muscular Dystrophy 2007-2008
21. Clinical care committee for Spinal muscular atrophy 2007-2008
22. Congenital muscular Dystrophy Workshop; July, 2008 Iowa City Iowa.

23. Congenital Muscular Dystrophy Therapeutic Outcomes Workshop; July, 2009 Emery University, Atlanta Georgia
24. Congential Muscular Dystrophy Standard of Care Neuromuscular Section leader, Brussels, 2009.
25. Duchenne Muscular Dystrophy International Symposium, Louisville, KY, 2009

Research Support

1) Principal Investigator, "Humoral immune mechanisms in polyneuropathies" (NIH-K08 NS01648-20) (Date 9/93-9/98)

2) Principal Investigator "Immune factors in acquired epileptic aphasia (Landau Kleffner Syndrome), AEA-variant, and childhood autism" (Cure autism Now foundation) (5/97-5/98)

3) Principal Investigator " Autoanitbodies to human endothelial cells in acquired epileptic aphasia, acquired epileptic aphasia-variant, and childhood autism" 1/1/2000-3/31/2002

4) Principal Investigator "Opsoclonus Myoclonus: characterization of autoantibodies to neural antigens" 1/1/200-12/31/2001

5) Principal Investigator " Complement's role in animal models of muscular dystrophy" (MDA 7/1/2000-6/30/2003)

6) Principal investigator "Role of B-cells and Complemeng in animal models of Muscular Dytrophy (MDA 6/30/03-12/31/06)

7) Co-Principal Investigator; Compositional Analysis of Muscle: Evaluating the Effects of Treatment in Patients with Duchenne Muscular Dystrophy

8) Site Principal Investigator for CINRG (Clinical International Neuromuscular Research Group); Clinical trials in Duchenne Muscular Dystrophy; **Ongoing**

9) Co investigator for AMSMART: Clinical trials in Spinal Muscular Atrophy

10) Collaborator; Quantitative ultrasonic tissue character (Mike Hughes, PI) **Ongoing**; 7/1/05-6/30/07

11) Site PI for MDA-DMD Center at Washington University; -ongoing

12) Site PI for Study of biomarkers in SMA; Ongoing

Clinical title and responsibilities

Professor of Neurology and Pediatrics

1. Neuromuscular clinic weekly at the CAM (Children and adults) and monthly at SLCH
2. Electrodiagnostic laboratory weekly in sedated children at SLCH and twice weekly at the CAM building (Children and adults)
3. Yearly attending on wards (Neurology and Pediatrics)
4. Yearly consulting on wards (Neurology)
5. Consult for children and adults with inpatient Neuromuscular Disorders as needed.
6. Consult by phone to outside child neurologists; average 75-100 such consultations/year

Teaching title and responsibilities

Professor of Neurology and Pediatrics

1) Teacher in the Practice of Medicine course for Third year Students; Washington University School of Medicine; 2004-Present.
2) EMG formal lecture series; Yearly lectures in Pediatric EMG, Brachial Plexus EMG, Late Response, and Facial Nerve Studies

3) Clinical teaching in EMG, neuromuscular clinics involving both adults and children
4) EMG teaching with special expertise in study of brachial plexus injuries and Defects of neuromuscular transmission
5) Muscle Biopsy Histology; Teach residents and fellows at multi-headed microscope
6) Neuromuscular disease of the newborn: Core curriculum neonatology fellows
7) Teaching Neuromuscular disorders for pediatric residents: Core curriculum lectures

Editorial and review responsibilities

1999. Reviewer for the cancer research campaign, London, UK
2001.Invited reviewer for Epilepsia, the journal of the international league against epilepsy on the subject of Landau-Kleffner Syndrome
2001-current: editorial board for Journal of Child Neurology
2001-Invited reviewer for Pediatrics; Opsoclonus myoclonus
2001-2002Invited reviewer for J. Neuroimmunology
2001-present: Invited reviewer for Amer. J. Pathology
2002-Invited reviewer for Pediatric Research: Congeneital Muscular dystrophy
2002-present Invited reviewer for Neuromuscular disorders; Duchenne MD and Congenital muscular dystrophy.
2002-Invited reviewer for Lancet Neurology; Duchenne muscular dystrophy
2003- Invited reviewer for Neurology; neuroimmunology; Cerebellitis.
2003- Invited reviewer for European Journal of Child Neurology; Duchenne Muscular dystrophy
2003-present-Invited reviewer for J. of Cell Biology
2003- present-Invited reviewer for Developmental Med. Child Neurology; Guillian Barre syndrome
2003-present Invited reviewer for Biomed Central; Autoantibodies in Acute Cerebellar Ataxia
2004-present: American Journal of Pathology (mouse model of DMD)
2005-American Academy of Neurology; National meeting abstract reviewer

Bibliography (Invited reviews/ Chapters)

1. Connolly AM and Volpe JJ: Clinical features of bilirubin encephalopathy. Clinics in Perinatology 1990; 17:371-379.
2. Connolly AM. : Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) in Childhood. 2000, Pediatric Neurol 2001:24:17-183.
3. Connolly, AM: The Floppy infant syndrome, In Press
4. Sheirbecker, J. and Connolly, AM. Neuromuscular Disorders: Implications for Women, 2002.
5. Connolly, AM: Nemaline Myopathy, NORD Guide to Rare Disorders, Lippincott Williams &Wilkins Philadelphia, PA 2002.
6. Connolly, AM; Centronuclear and myotubular myopathy, NORD Guide to Rare Disorders, Lippincott Williams &Wilkins Philadelphia, PA 2002.
7. Connolly, AM: Desmin Storage myopathy, NORD Guide to Rare Disorders, Lippincott Williams &Wilkins Philadelphia, PA 2002.

8. Connolly, AM; Fiber type disproportion, NORD Guide to Rare Disorders, Lippincott Williams &Wilkins Philadelphia, PA 2002.
9. Connolly, AM and Iannaccone, S. Anterior Horn Cell and Cranial Motor Neuron Disease; Chapter; Pediatric Neurology: Principles and Practice 4th edition; 2005.
10. Connolly, AM, Canter, C E and Scheirbecker, J: UPDATE: Duchenne and Becker Muscular Dystrophy Volume 29, Issue 4

Peer reviewed publications:

1. Connolly AM, Pestronk, A, Trotter J, Feldman EL, Cornblath DR, and Olney RK. High titer selective serum anti-β-tubulin antibody in Chronic Inflammatory Demyelinating Polyneuropathy. Neurology 1993; 43:557-562.

2. Connolly AM, Rust, RS, Dodson WE, Prensky, AL: Course and outcome of acute cerebellar ataxia. Ann Neurology 1994; 35:673-679.

3. Connolly AM, Pestronk, A. Planer, GJ, Yue, J., Mehta, S., Choksi, R.: Congenital muscular dystrophy syndromes distinguished by alkaline and acid phosphatase, merosin, and dystrophin. Neurology 1996; 46:810-814.

4. Nevo, Y., Pestronk, A., Kornberg, AJ, Connolly, AM, Yee, WC, Iqbal, I. Shield, LK. Childhood chronic inflammatory demyelinating neuropathies: Clinical course and long-term follow-up. Neurology 1996; 47:98-102.

5. Zhang, J, George, AL, Griggs, RC, Fouad, GT, Roberts, J, Kwiecinski, H., Connolly, AM, Ptacek, LJ. Mutations in the human skeletal muscle chloride channel gene (CLCN1) associated with dominant and recessive myotonia congenita. Neurology 1996; 47:993-998.

6. Connolly, AM, Pestronk, A., Mehta, S. Yee, WC, Green, B.J., Fellin, C. Olney, R.K., Miller, R.G., Devor, W.N. Serum IgM monoclonal autoantibody binding to the 301-314 amino acid epitope of b-tubulin: Clinical association with slowly progressive demyelinating polyneuropathy. Neurology 1997,49:243-248.

7. Connolly, AM, Pestronk, A. Mehta, S, Pranzatelli, M.R., and Noetzel, MJ. Serum autoantibodies in childhood opsoclonus-myoclonus syndrome: an analysis of antigenic targets in Neural tissues. J. Pediatr. 1997, 130:878-84.

8. Connolly, AM and Pestronk, A. Anti-tubulin autoantibodies in acquired demyelinating polyneuropathies. J. Infectious Dis. 1997, 176(suppl 2):157-160).

9. Connolly, AM, Pestronk, A. Mehta, S. and Al-Lozi, M. Case of the month: Primary α-sarcoglycan (adhalin) deficiency responsive to immunosuppression over three years. 1998, Muscle Nerve 21: 1549-1553.

10. Pegoraro, E., Marks, H. Garcia, C.A., Crawford, T., Mancias, P., Connolly, A.M., Fanin, M., Martinello, F.et al. Congenital muscular dystrophy (CMD) due to primary merosin (laminin a2) gene mutations; Genotype/penotype studies of 22 patients. Neurology 1998, 51:101-109.

11. Connolly, AM, Chez, MG, Pestronk, A., Arnold, S., Mehta, S., Deuel, RK. Serum autoantibodies to brain in Landau-Kleffner variant, autism, and other neurologic disorders. 1999. J. Peds;134:607-13.

12. Wong, M. Connolly, AM, Noetzel, MJ. A Poliomyelitis-like syndrome associated with Epstein-Barr virus infection. 1999, Pediatr Neurol; 20:235-237.

13. Nevo, Y., Al-Lozi, M. Parsadanian, A.S., Elliott, JL, Connolly, AM, Pestronk, A. Mutation analysis in Emery-Dreifuss muscular dystrophy. 1999, Pediatric Neurol; 21:456-459.

14. Patton, B.L. Connolly, AM, Miner, JH, Martin, PT, Cunningham, JM, Mehta, S. Pestronk, A. Sanes, JR. Distribution of ten laminin chains in dystrophic and regenerating muscles. 1999, Neuromuscular disorders, 9: 423-433.

15. Geller, T.J. Connolly, A.M., Kotagal, S. , Prensky, A.L. Progressive infantile axonal polyneuropathy. 2000, J. Child Neurology; 15:513-517.

16. Nishino, E. Spanazzola, A. Papadimitriou, A. Hammans, S. Steiner, I. Hahn, C D., Connolly, A.M. et al. Clinical Features of MNGIE syndrome. 2000, Neurology, 47: 792-800.

17. Connolly, A. M. : Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) in Childhood. 2001. Pediatr Neurol 24177-82.

18. Falsaperla, R. Romeo, G., DiGiorgio, A. Paano, E. Pavone, P., Connolly, A. M. Long term survival in a child with arthrogryposis multiplex congenital and spinal muscular atrophy. 2001, J. Child Neurol. 16:934-6.

19. Connolly, A. M., Keeling, R.M., Mehta, S. Pestronk, A. Sanes, J.R. Three mouse models of muscular dystrophy; the natural history of strength and fatigue in the *mdx, mdx:utrn-/-* and *dy/dy* mice. 2001, Neuromuscular Disorders; 11:703-712.

20. Connolly, A.M, Keeling R.M., Streif, B. Pestronk, A. Mehta, S. Complement 3 deficiency and oral prednisolone improve strength and prolong survival of laminin α2-deficient mice. 2002, J. Neuroimmunology 127:80-7.

21. Connolly, A.M., Sheirbecker, J., Renna, R.; Florence J. High dose weekly oral prednisone improves strength in boys with Duchenne Muscular Dystrophy. 2002, Neuromuscular Disorders; 12:917-925.

22. Falsaperla R., Romeo G, Sorge A, Bianchini R, DiGiorgio A, Trigilia T, Mattina T, Connolly AM. Mental retardation and early onset of weakness in a girl with a dystrophinopathy and a large Xp21-23 deletion. 2003, J. Child Neurol;18:79-81.

23. Gurnett, CA, Bodnar, Neil, J, Milone, M. Connolly, AM. Congenital Myasthenic Syndrome: Presentation, Electrodiagnosis, and Muscle Biopsy, 2004, J. Child Neurology; 175-82.

24. Marden, FA, Connolly, AM, Siegel, MJ, Rubin, DA: Compositional Analysis of Muscle in Boys with Duchenne Muscular Dystrophy using MRI,. Skeletal Radiology, 2005; 140-8.

25. Moxley, R.T., Ashwal, S., Pandya, S., Connolly, A., Florrence, J. Matthews, K., Baumbach, L. McConald, C. Sussman, M. Wade, C. Practice Paremeter: Corticosteroid treatment of Duchenne MD Practice Parameter 2005; Neurology 64:13-20.

26. Ashford MW, Liu W, Lin SJ, Abraszewski P, Caruthers S.D., Connolly, AM, Yu X, Wickline SA Occult Cardiac Myofiber Dysfunction in Dystrophin-Deficient Children revealed by Cardiac Magnetic Resonance Strain Imaging, 2005, Circulation, 112; 2462-7.

27. Connolly, AM, Chez, M. Streif, E.M., Keeling, RM, Golumbek, PT, Kwon, JM. Riviello, JJ, Robinson, RG, Newman. RJ, Deuel, RM. Brain-Derived Neurotrophic Factor and Autoantibodies to Neural Antigens in Sera of Children with Autistic Spectrum Disorders, Landau-Kleffner Syndrome, and Epilepsy; 2005; Biological Psychiatry.

28. Escolar, D. M. Buyse, G. Henricson, E. Leshner, R. Florence, J. Mayhew, J. Tesi-Rocha, C. Gorni, K. Pasquali, L. Patel, K. M. McCarter, R. Huang, T. Bertorini, T. Carlo, J. Connolly, A. M. Clemens, P. R. Goemans, N. Iannaccone, S. T. Igarashi, M. Nevo, Y. Pestronk, A. Subramony, S. H. Vedanarayanan, V. V. Wessel, H. CINRG randomized controlled trial of creatine and glutamine in Duchenne muscular dystrophy. 2005; Annals of Neurology 58:151-5.

29. Weihl, CC, Connolly AM, Pestronk A. Valproate may improve strength and function in patients with type III/IV spinal muscle atrophy.
Neurology. 2006 Aug 8;67(3):500-

30. Keeling R., Golumbek, P. Streif, Connolly, AM, Effect of weekly prednisone on long term survival and strength in the mdx mouse. Muscle and Nerve.2007 35:43-48.

31. Hughes MS, Marsh KD, Wallace TA, Connolly AM, Lanza GM, Wickline SA, Sensitive Ultrasonic Detection of Dystrophic Skeletal Muscle in Patients with Duchenne Muscular Dystrophy using an Entropy-Based Signal Reciever, 2007 Ultrasound Med Biol. 2007; 33:1236-43.

32. Golumbek, P, Keeling, RM, Connolly, AM. Strength and Corticosteroid Responsiveness of Mdx Mice is Unchanged by RAG2 Gene Knockout. Neuromucular Disorders 2007; 17: 276-84.

33. Wallace, K. Marsh, J, Baldwin, S, Connolly, AM, Keeling, R. Lanz, G. Wickline, S. Hughes, M. Sensitive Ultrasonic Delineation of Steroid Treatment in Living Dystrophic Mice with Energy-based and Entropy-based RadioFrequency Signal Processing. IEEE Transactions on Ultrasonics, Ferroelectrics, and Frequency Control;2007; 54:2291-2299.

34. Golumbek, P, Keeling, RM, Connolly, AM. RAG-2 Gene Knockout in Mice Causes Fatigue. Muscle and Nerve. 2007; 36;471-6.

35. Gurnett, C.A., Boehm, S, Connolly, AM, Reimschisel, T. Dobbs, MB. Impact of congenital talipes equinovarus etiology on treatment outcomes. Dev Med Child Neurol; 2008; 50:7; 498-502.

36. Margeta, M., Connolly, AM, Thomas L. Winder, PhD, Alan Pestronk, Steven A. Moore Cardiac pathology exceeds skeletal muscle pathology in two cases of limb-girdle muscular dystrophy type 2I, Muscle and Nerve 2009; 40(5) 883-889.

37. Zhang, F, Khajavi M, Connolly, AM, Towne, CF, Batish S.D, & Lupski, JR, The DNA replication FoSTeS/MMBIR mechanism can generate genomic, genic and exonic complex rearrangements in humans, Nat Genet 2009; 41(7):849-53.

38. Flanigan, K. M. Dunn, D. M. von Niederhausern, A. Soltanzadeh, P. Gappmaier, E.Howard, M. T.Sampson, J. B.Mendell, J. R.Wall, C.King, W. M.Pestronk, A. Florence, J. M. Connolly, AM, et al, Mutational spectrum of DMD mutations in dystrophinopathy patients: application of modern diagnostic techniques to a large cohort. Human Mutat 30; 1657-66 2009..

39. Flanigan, K. M. Dunn, D. M. von Niederhausern, A. Howard, M. T. Mendell, J. Connolly, AM. et al, DMD Trp3X nonsense mutation associated with a founder effect in North American families with mild Becker muscular dystrophy. Neuromuscul Disord. 19: 743-8 2009.

40. Gurnett, C. A., Desruisseau, DM, McCall, K., Choi, R., Meyer, ZI, Talerico, M, Miller, SE, Ju, JS, Pestronk, A, Connolly, AM, Druley, TE, Weihl, CC, Dobbs, MB. Myosin binding protein C1: a novel gene for autosomal dominant distal arthrogryposis type 1, Hum Mol Genet 19: 1165-73.

41. Soltanzadeh, P, Friez, MJ, Dunn, D., vonNiederhausern, A., Gurvich, OL, Swoboda, KJ, Sampson, JB, Pestronk, A, Connolly, AM, Florence, JM, Finkel, RS, Bonneman, CG, Medne, L, Mendell, JR, Mathews, KD, Wong, BL, Sussman, MD, Zonana, J, Kovak, K, Gospe, SM, Gappmaier E, Taylor, LE, Howard, MT, Weiss, RB, Flanigan, KM. Clinical and genetic characterization of manifesting carriers of DMD mutations, Neuromuscul Disord 2010; 20:499-504.

42. Wang, CH, Bonnemann,CG, Rutkowski, A, Sejersen, T, Bellini, J, Battista, V, Florence, JM, Schara, U, Schuler, PM, Wahbi, K, Aloysius, A, Bash, RO, Beroud, C, Bertini, E, Bushby, K, Cohn,RD, Connolly, AM, Deconnick, N, Desquerre,E, Eagle, M, Estournet-

Mathiaud, B., Ferreiro, A, Fujak,A, Goemans, N,et al, Consensus statement on standard of care for congenital muscular dystrophies. J Child Neurol 2010 25: 1559-81.

43. Merrill, L. J., Gurnett, C., Connolly, AM, Pestronk, A., Dobbs, M. Skeletal Muscle Abnormalities and Genetic factors Related to Vertical Talus 2010 In press, Clinical Orthopaedics and Related Research.

44. Flanigan, K. M., Dunn, D. M.,von Niederhausern, A., Soltanzadeh, P., Howard, M. T., Sampson, J. B., Swoboda, K. J, Bromberg, M. B., Mendell, J. R.,Taylor, L., Anderson, C. B., Pestronk, A.,Florence, J., Connolly, A. M., Mathews, K. D., Wong, B., Finkel, R. S., Bonnemann, C. G., Day, J. W., McDonald, C., Weiss, R. B. Nonsense mutation-associated Becker muscular dystrophy: interplay between exon definition and splicing regulatory elements within the DMD gene. 2010, In press Human Mutat.

45. Zaidman, CM, Connolly, AM,Malkus, EC, Florence, JM, Pestronk, A Quantitataive ultrasound using backscatter analysis in Duchenne and Becker muscular dystrophy. Neuromuscular Disord 2010 20:805-9.

46. Soltanzadeh, P., Friez, M. J., Dunn, D. ,von Niederhausern, A., Gurvich, O. L., Swoboda, K. J. , Sampson, J. B., Pestronk, A., Connolly, A. M., Florence, J. M., Finkel, R. S., Bonnemann, C. G., Medne, L., Mendell, J. R., Mathews, K. D., Wong, B. L., Sussman, M. D., Zonana, J., Kovak, K. , Gospe, S. M., Jr., Gappmaier, E., Taylor, L. E., Howard, M. T., Weiss, R. B., Flanigan, K. M. Clinical and genetic characterization of manifesting carriers of DMD mutations Neuromuscul Disord 2010 20:8; 499-504.

47. Wang, CH, Bonnemann, CG, Rutkowski, A, Sejersen, T, Bellini, J, Battista, V, Florence, JM, Schara, U, Schuler, PM, Wahbi, K, Aloysius, A, Bash, RO, Beroud, C, Bertini, E, Bushby, K, Cohn, RD, Connolly, AM, Deconinck, N, Desguerre, I, Eagle, M, Estournet-Mathiaud, B, Ferreiro, A, Fujak, A, Goemans, N, Iannaccone, ST, Jouinot, P, Main, M, Melacini, P, Mueller-Felber, W, Muntoni, F, Nelson, LL, Rahbek, J, Quijano-Roy, S., Sewry, C., Storhaug, K, Simonds, A, Tseng, B, Vajsar, J, Vianello, A, Zeller, R. Consensus statement on standard of care for congenital muscular dystrophies; J Child Neurol 25: 1559-82.

48. Escolar, DM, Escolar, Rocha TC, Henricson, E, Florence J, Mayhew Gorni K, Pasquali L, Connolly AM, Pestronk A, Martin G, Spurney C, Nie L, and CINRG investigators CINRG Pilot trial of Coenzyme Q10 in steroid treated Duchenne Muscular Dystrophy 2011 Muscle and Nerve 44: 174-178.

49. Escolar DM, Hache LP, Clemens PR, Cnaan A, McDonald CM, Viswanathan V, Andrew Kornberg A, E. Bertorini TE, Nevo Y, Lotze T, Pestronk A, Ryan M, Monasterio E, Day JW, Zimmerman A, Arrieta A, Henricson E, Mayhew J, Florence J, Hu F, and Connolly AM, Randomized, blinded trial of weekend versus daily prednisone in Duchenne muscular dystrophy 2011, Neurology 77:444-452.

50. Zimmerman, A., Clemens, P. R., Tesi-Rocha, C., Connolly, AM., Iannaccone, S. T., Kuntz, N., Arrieta, A., Hache, L., Henricson, E., Hu, F., Mayhew, J., Escolar, D. M. Liquid formulation of pentoxifylline is a poorly tolerated treatment for duchenne dystrophy 2011 Muscle Nerve 44: 170-173.

ONGOING

Research Support

1. PTC pharmaceutical company

PTC-124 phase 2b trial in boys with Duchenne Muscular dystrophy:

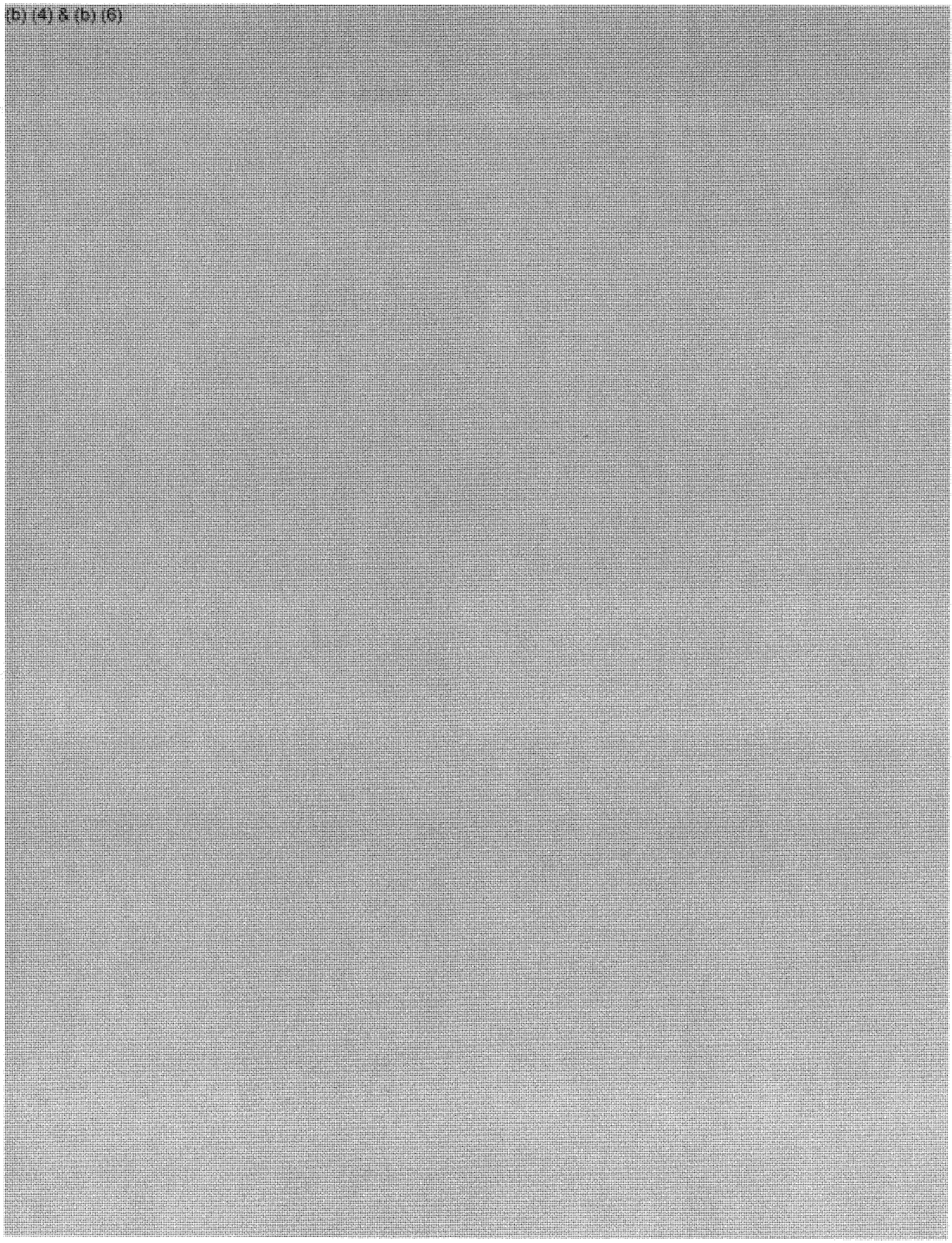
(Site PI)
2008-ongoing
2. Clinical trials in Duchenne Muscular Dystrophy; CINRG (Clinical International Neuromuscular Research Group); (CoPI) 2003-current
3. Muscular Dystrophy Association Grant "MDA-DMD Center at Washington University
(Site PI) Purpose is to advance clinical care and clinical research for boys and men with DMD and develop a clinical trial research group.
Dates: 8/10/08 -7/31/11
4. Muscular Dystrophy Association Grant :Clinical outcome validation in young and non ambulatory boys and Men with Duchenne muscular dystrophy;
(PI). This multicenter trial is designed to develop and validate outcomes in young infants and children with DMD and boys/men with DMD who are no longer able to walk. **Dates: 1/1/10-12/31/12**
5. NIH: 1R01AR05622301A2: Nanoparticals for modulation of inflammation in neuromuscular disease:
(Collaborator): Grant is designed to test modulation of inflammation in mdx mice (model of Duchenne muscular disease). Dr. Samual Wickline is PI
6. NIH 1R01HL08784701A1: Monitoring Disease and Therapy in Dystrophic deficient mice using ultrasound.
(Collaborator): Grant is designed to test non invasive, high resolution ultrasound to monitor dystrophic muscle changes in the mdx model of Duchenne muscular dystrophy.
7. PTC pharmaceutical company
PTC-124 safety trial in non ambulatory boys with Duchenne Muscular dystrophy
(Site PI); 2010-ongoing

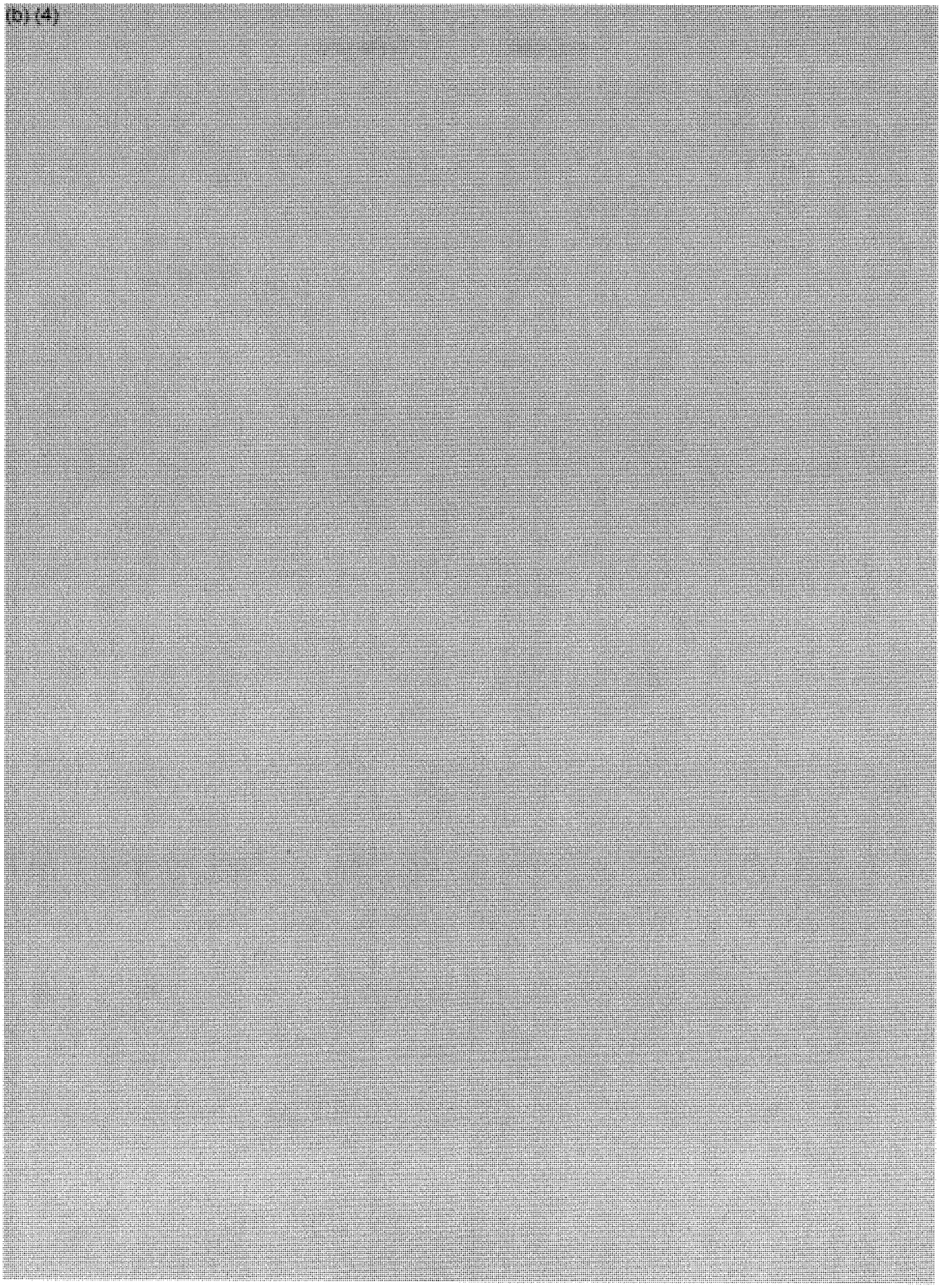
COMPLETED Research Support (last 3 years)
1. Muscular Dystrophy Association Grant #: A. Connolly (PI)
(1/1/06-12/31/08)
"Synergistic effects of steroids, ace inhibitors and exercise in mdx mice"
Synopsis of Research: This work is designed to determine if ace inhibitors have a benefit in the mdx mouse model of Duchenne Muscular inhibitor with or without exercise.
2. NIH treatment of Children with SMA type 2 with sodium phenyl buterate; phase I, IIa multic trial; A. Connolly (Site PI) for Neptune project 2007-2009
3. Quantitative ultrasonic tissue character Collaborator: (Mike Hughes, PI)
7/1/05-6/30/07 The goal of this work was to quantitatively characterized cardiovascular structure an function noninvasively with nondestructive imaging modalities. Role: Collaborator
NIH/UT Southwestern Medical A. Connolly (PI for WU)
12/01/03-6/30/07
4. AMSMART grant #3259-65250
The goal is to treat children with spinal muscular atrophy in a multicenter trial.
Role: Site PI for Washington University.

Muscular Dystrophy A. Connolly (PI) 7/1/2003-12/31/2006
Association Grant # 3259-40234

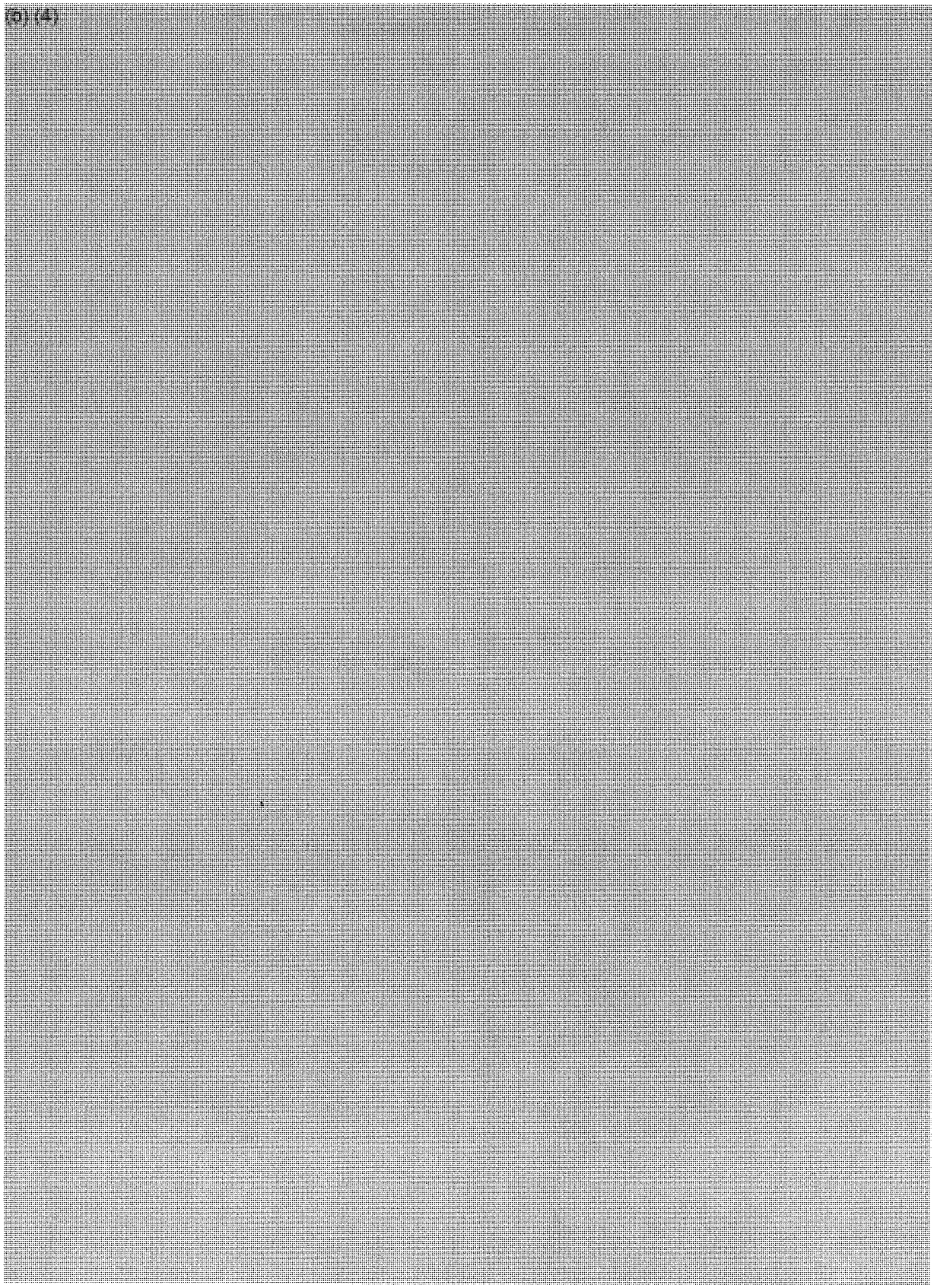
5."Role of complement and B-cell in muscular dystrophy"

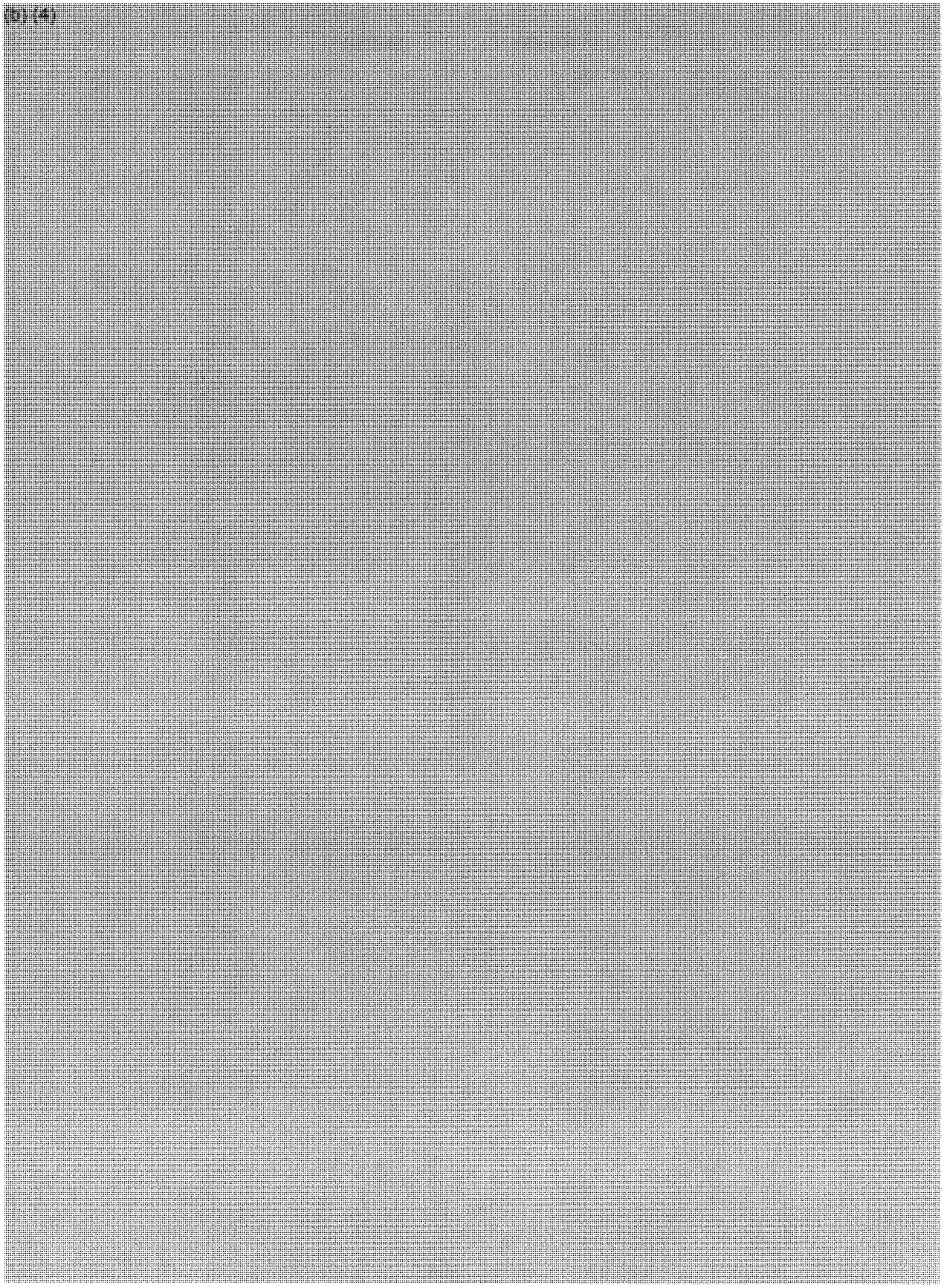
Synopsis of Research: This work is designed to determine the role of complement and B-cells in the pathogenesis of three mouse models of muscular dystrophy; the dydy, the mdx, and the mdx:utrn-/- mouse models of congenital and Duchenne muscular dystrophy..
Role: Principle Investigator

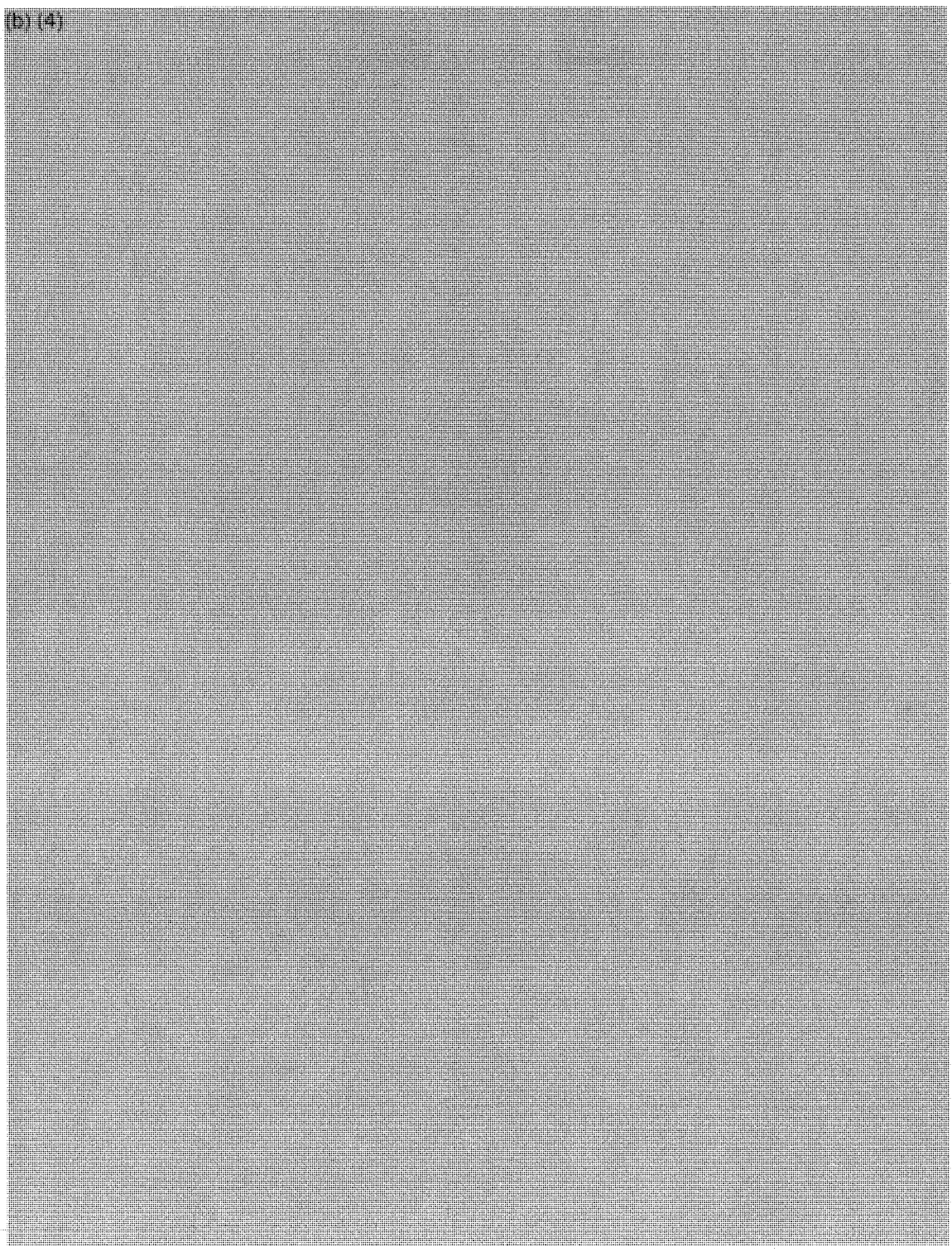

(b) (4) & (b) (6)

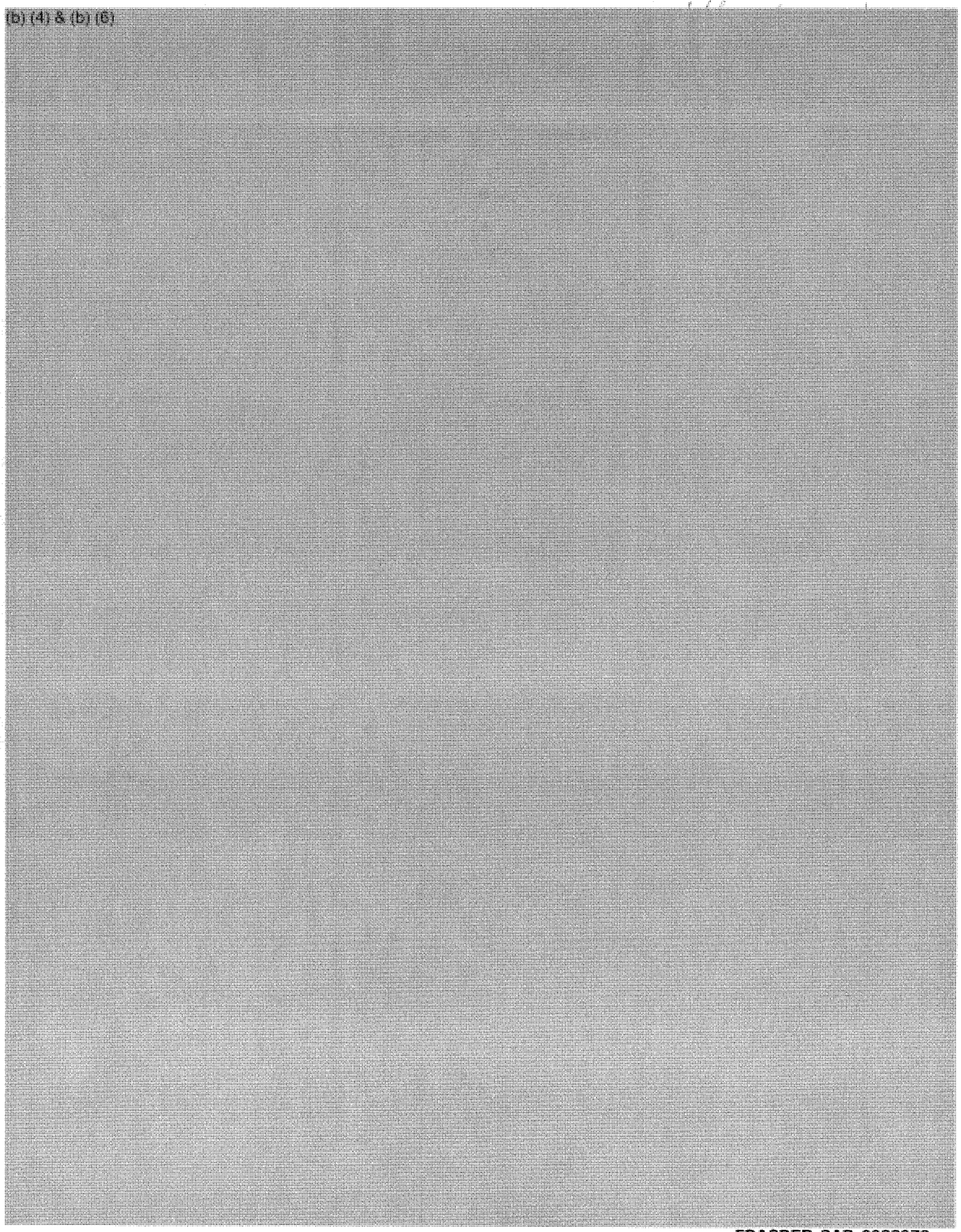

(b) (4)

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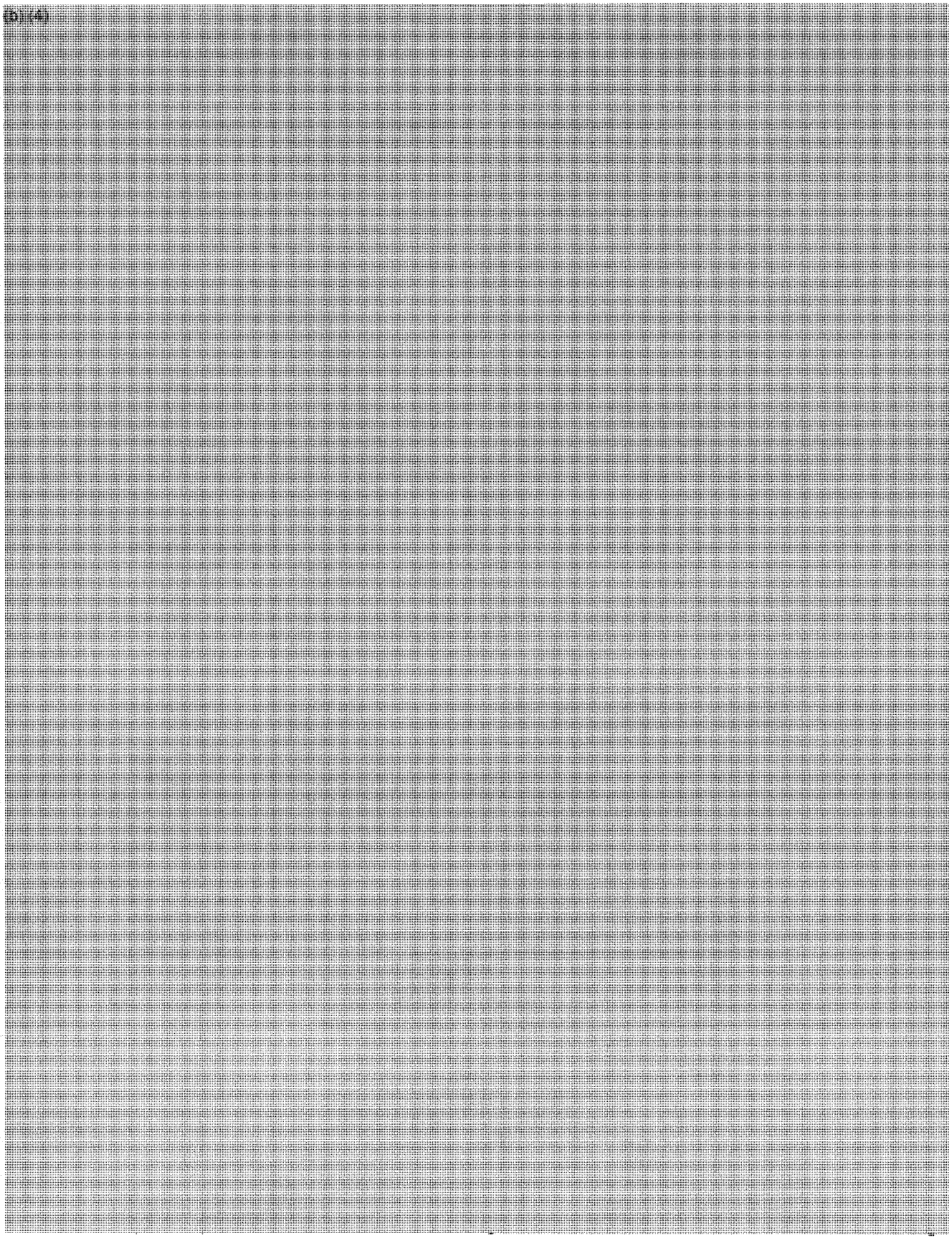



(b) (4)

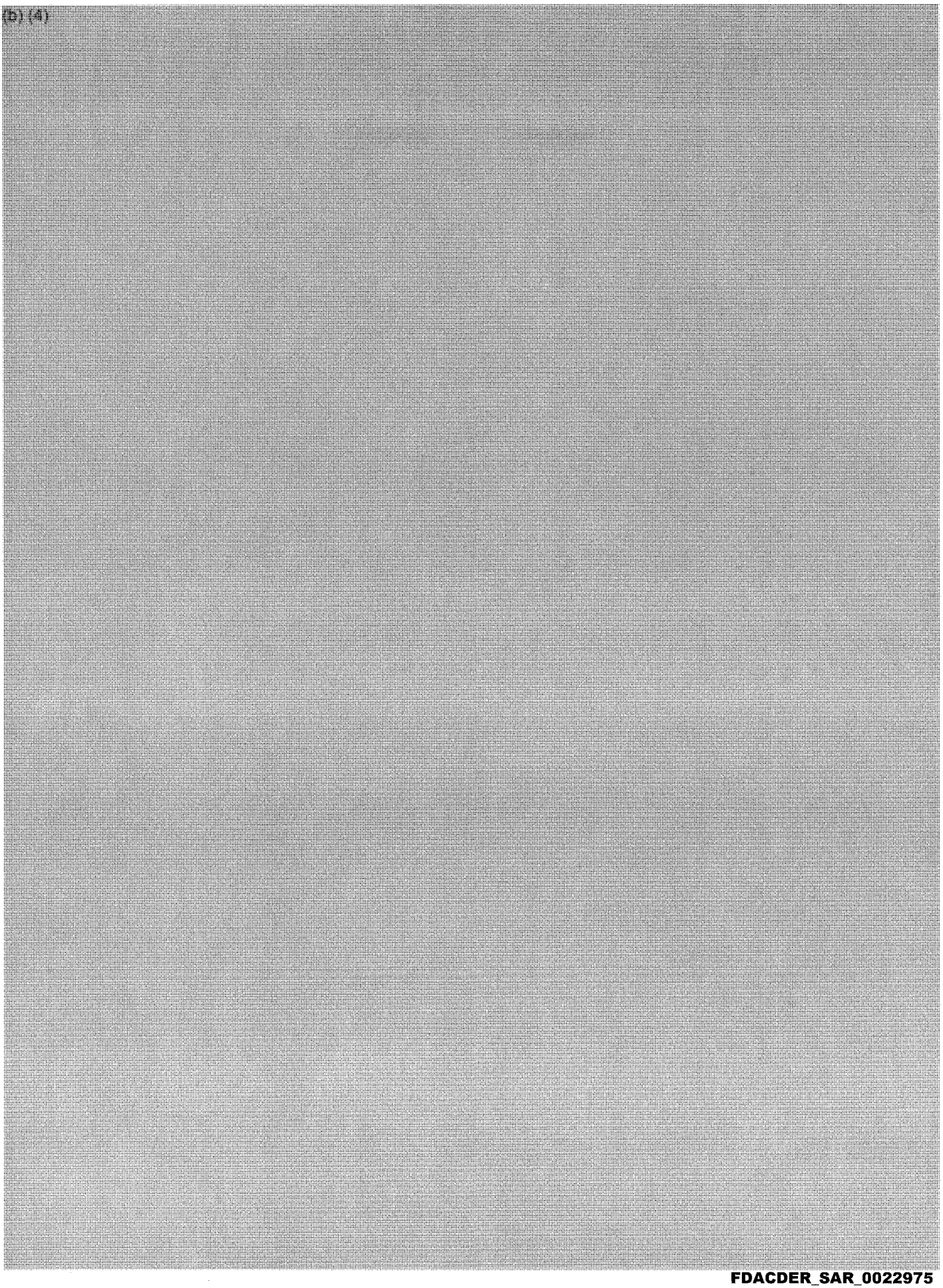

(b) (4)


(b) (4) & (b) (6)

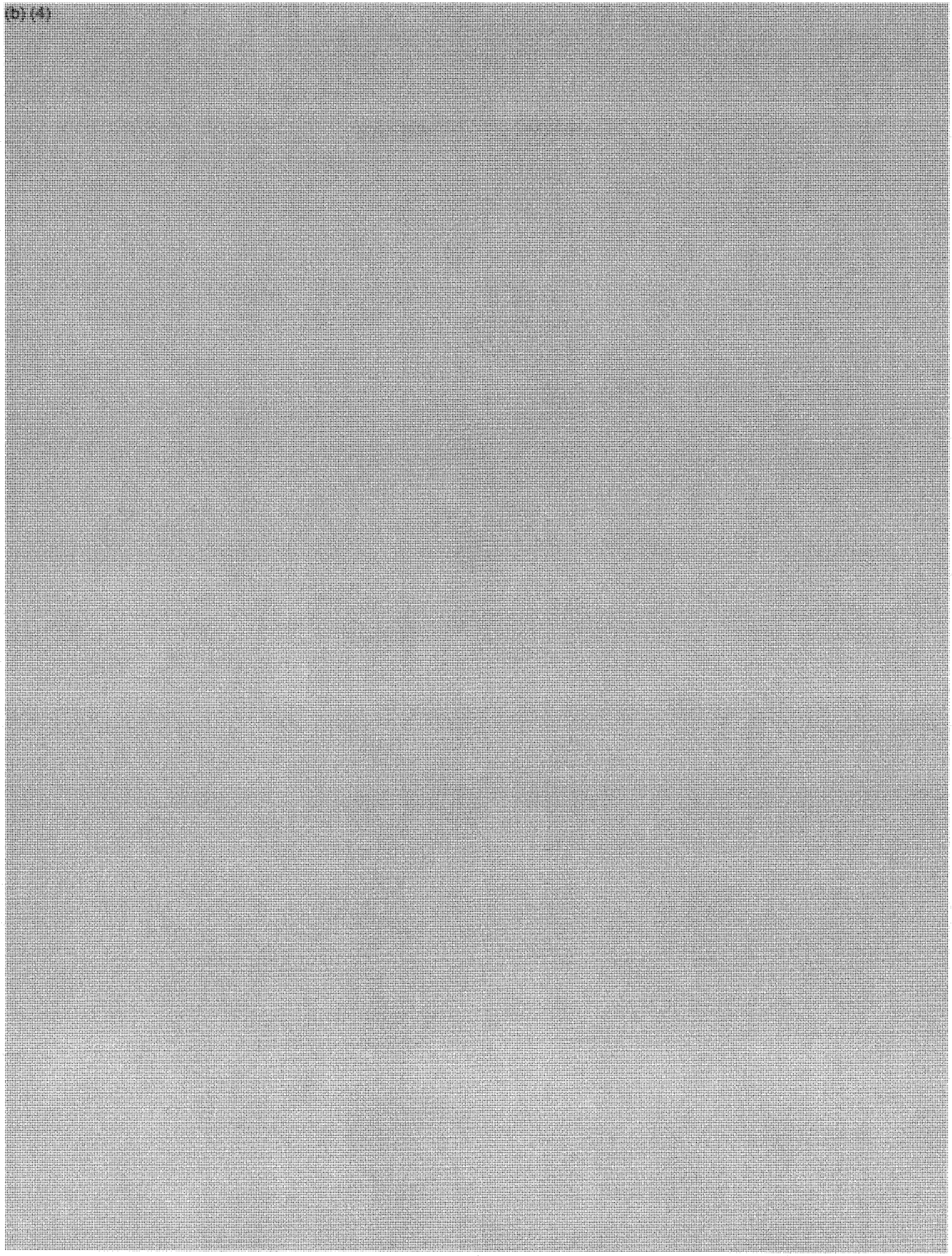
(b) (4)



(b) (4)



(b) (4)



16.1.5 Signatures of Principal Investigator(s) or Sponsor's Responsible Medical Officer

STUDY TITLE: Open-Label, Multiple-Dose, Efficacy, Safety, and Tolerability Study of Eteplirsen in Patients with Duchenne Muscular Dystrophy who Participated in Study 4658-us-201

SIGNATURE OF PRINCIPAL INVESTIGATOR(S): Jerry R. Mendell, MD

I am the Principal Investigator for this study.

(b) (6)

Jerry R. Mendell, MD
Curran-Peters Chair in Pediatric Research
Professor of Pediatrics and Neurology
Director Gene Therapy Center and
Director of Paul D. Wellstone Center
Nationwide Children's Hospital and The Ohio State University

Date

SPONSOR'S RESPONSIBLE MEDICAL OFFICER: Edward M. Kaye, MD

I have read this report and confirm that to the best of my knowledge it accurately describes the conduct and results of the study.

(b) (6)

Edward M. Kaye, MD
Senior Vice President and Chief Medical Officer
Sarepta Therapeutics Inc.
215 First Street
Cambridge, MA 02142, USA

Date

16.1.6 Listing of Subjects Receiving Study Drug from Specific Batches

Site Number or Identifier	Lot Number(s) Shipped to Site	Test Product
Site 01 Jerry Mendell, MD Nationwide Children's Hospital	(b) (4)	Eteplirsen (active test product)
Site 02 (b) (4)	(b) (4)	Eteplirsen (active test product)
Site 03 (b) (4)		Eteplirsen (active test product)
Site 04 Barry Byrne, MD, PhD University of Florida		Eteplirsen (active test product)
Site 05 (b) (4)		Eteplirsen (active test product)

FDACDER_SAR_0022978

Site Number or Identifier	Lot Number(s) Shipped to Site	Test Product
Site 07 (b) (4)	(b) (4)	Eteplirsen (active test product)
Site 08 Peter Heydemann, MD RUSH University		Eteplirsen (active test product)
Site 09 (b) (4)		Eteplirsen (active test product)
Site 10 (b) (4)		Eteplirsen (active test product)
Site 11 Anne Connolly, MD Washington University		Eteplirsen (active test product)

FDACDER_SAR_0022979

Site Number or Identifier	Lot Number(s) Shipped to Site	Test Product
	(b) (4)	
Site 12 (b) (4)		Eteplirsen (active test product)
Site 13 (b) (4)		Eteplirsen (active test product)

[a] 100 mg/mL concentration
[b] 50 mg/mL concentration

FDACDER_SAR_0022980

16.1.7 Randomization Scheme

Please refer to Listing 16.2.1.1, Randomization Assignment, All Patients Enrolled

16.1.8 Audit Certificates

SAREPTA THERAPEUTICS	**Certificate of Audit**	FORM-QA004.2-02 Effective Date: **08-Apr-2014**

This document certifies that an audit of the below-referenced company was conducted by Sarepta Therapeutics[1] for purposes of continuing compliance with FDA Regulations and ICH Guidelines.

Audit Identification/Facility:	(b) (4)	
Audit Scope/Purpose:	Review of Audit Regulatory Binder for Study AVI-4658-US-202 Investigator Site Audit	
Date audit Conducted:	Feb 27-28 2014	
Audit Team:	(b) (4) N/A	GxP Consultant N/A

Certificate Created By:

Certificate of this audit is provided as evidence of completion of the audit activity. Any and all findings have been reviewed with the vendor and responses and corrective actions have been reviewed and found to be acceptable.

(b) (6)

(b) (4) Associate Director of GCP Compliance
Quality Assurance

11 Dec 2014
Date

[1] Audits may be conducted by Sarepta-Contracted Auditing Services or Qualified Sarepta Personnel.

FDACDER_SAR_0022983

SAREPTA	**Certificate of Audit**	

This document certifies that an audit of the clinical study site referenced below was conducted by Sarepta Therapeutics for purposes of confirming compliance with FDA Regulations and ICH Guidelines for the conduct of clinical research investigations.

Audit Identification/Study Site:	Study 4658-us-202 Clinical Site Audit (b) (4)
Audit Scope/Purpose:	Review clinical study records
Date audit Conducted:	October 14 – 15, 2014
Auditor:	(b) (4) GCP Consultant Sarepta Therapeutics, Inc.

Certificate Created By:

Certificate of this audit is provided as evidence of completion of the audit activity. Any and all findings have been reviewed with Clinical Operations and responses and corrective actions have been reviewed and found to be acceptable.

(b) (4) & (b) (6)

Quality Assurance

January 15, 2015

Date

FDACDER_SAR_0022984

SAREPTA	**Certificate of Audit**	FORM-QA004.2-01 Effective Date: 01 Mar 2013

This document certifies that an audit of the below-referenced company was conducted by Sarepta Therapeutics[1] for purposes of continuing compliance with FDA Regulations and ICH Guidelines.

Audit Identification/Facility:	Jerry Mendell, MD Nationwide Children's Hospital 700 Children's Drive Columbus, OH
Audit Scope/Purpose:	GCP Clinical Investigator Site Audit for 4658-US-202 study
Date audit Conducted:	14-16 Nov 2012
Audit Team:	(b) (4) Regulatory Risk Management, LLC

Certificate Created By:

Certificate of this audit is provided as evidence of completion of the audit activity. Any and all findings have been reviewed with the vendor and responses and corrective actions have been reviewed and found to be acceptable.

(b) (4) & (b) (6)

Associate Director, GCP Compliance

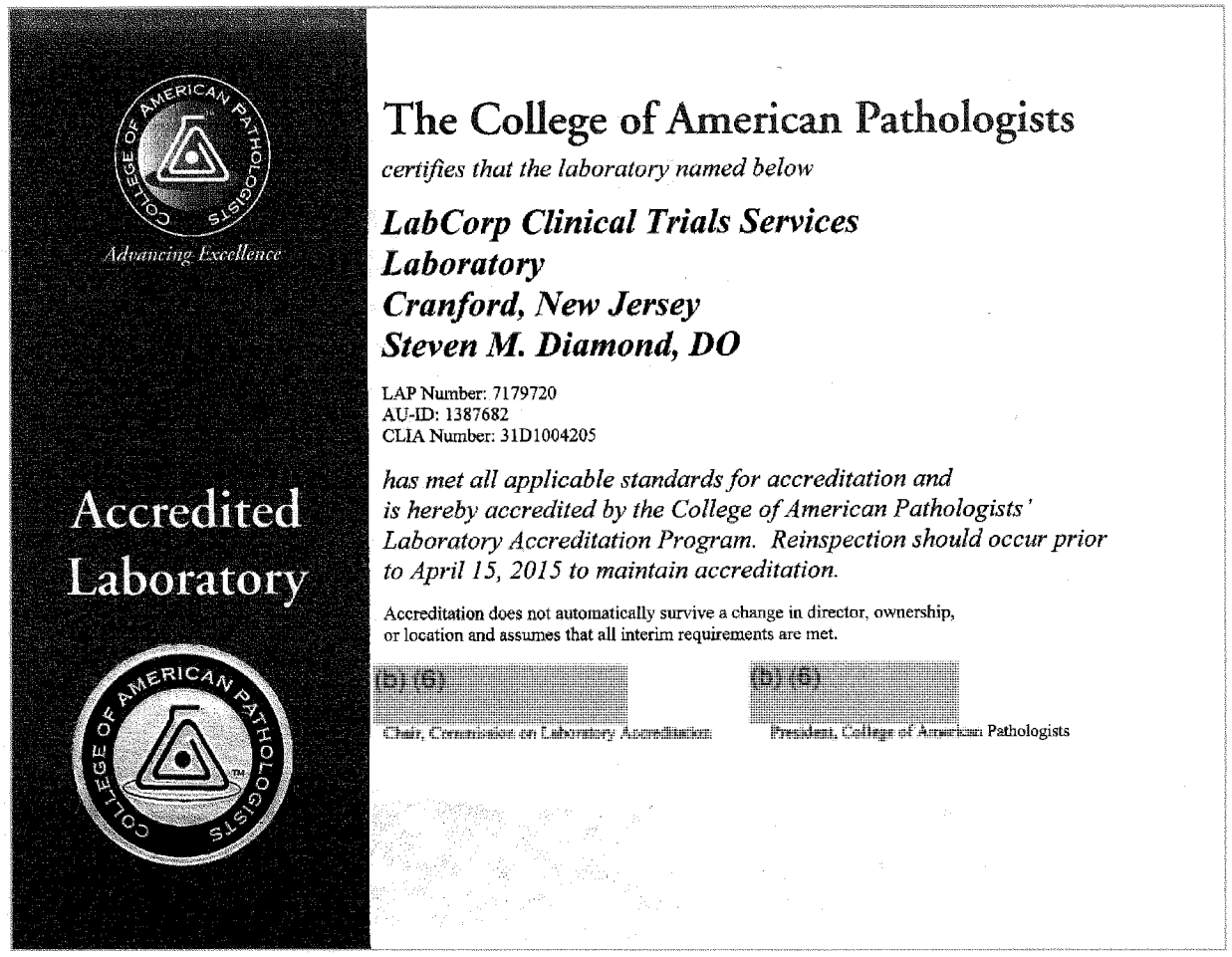
26 Nov 2013
Date

[1] Audits may be conducted by Sarepta-Contracted Auditing Services or Qualified Sarepta Personnel.

FDACDER_SAR_0022985

16.1.10 Documentation of Inter Laboratory Standardization Methods and Quality Assurance Procedures

LABORATORY ACCREDITATION



Advancing Excellence

Accredited Laboratory

The College of American Pathologists

certifies that the laboratory named below

LabCorp Clinical Trials Services
Laboratory
Cranford, New Jersey
Steven M. Diamond, DO

LAP Number: 7179720
AU-ID: 1387682
CLIA Number: 31D1004205

has met all applicable standards for accreditation and is hereby accredited by the College of American Pathologists' Laboratory Accreditation Program. Reinspection should occur prior to April 15, 2015 to maintain accreditation.

Accreditation does not automatically survive a change in director, ownership, or location and assumes that all interim requirements are met.

(b) (6)
Chair, Commission on Laboratory Accreditation

(b) (6)
President, College of American Pathologists

LABORATORY ACCREDITATION

CENTERS FOR MEDICARE & MEDICAID SERVICES
CLINICAL LABORATORY IMPROVEMENT AMENDMENTS

CERTIFICATE OF ACCREDITATION

LABORATORY NAME AND ADDRESS

LABCORP CLINICAL TRIALS
750 WALNUT AVENUE
CRANFORD, NJ 07016

CLIA ID NUMBER
31D1004205

EFFECTIVE DATE
07/01/2013

LABORATORY DIRECTOR
STEVEN M DIAMOND DO

EXPIRATION DATE
06/30/2015

Pursuant to Section 353 of the Public Health Services Act (42 U.S.C. 263a) as revised by the Clinical Laboratory Improvement Amendments (CLIA), the above named laboratory located at the address shown hereon (and other approved locations) may accept human specimens for the purposes of performing laboratory examinations or procedures.
This certificate shall be valid until the expiration date above, but is subject to revocation, suspension, limitation, or other sanctions for violation of the Act or the regulations promulgated thereunder.

(b) (6)

Division of Laboratory Services
Survey and Certification Group
Center for Medicaid and State Operations

CMS
CENTERS for MEDICARE & MEDICAID SERVICES

21 Certs2_060513

If you currently hold a Certificate of Compliance or Certificate of Accreditation, below is a list of the laboratory specialties/subspecialties you are certified to perform and their effective date:

LAB CERTIFICATION (CODE)	EFFECTIVE DATE	LAB CERTIFICATION (CODE)	EFFECTIVE DATE
VIROLOGY (140)	04/03/2007		
GENERAL IMMUNOLOGY (220)	07/01/2003		
ROUTINE CHEMISTRY (310)	07/01/2003		
URINALYSIS (320)	07/01/2003		
ENDOCRINOLOGY (330)	07/01/2003		
TOXICOLOGY (340)	08/23/2004		
HEMATOLOGY (400)	07/01/2003		

FOR MORE INFORMATION ABOUT CLIA, VISIT OUR WEBSITE AT WWW.CMS.HHS.GOV/CLIA
OR CONTACT YOUR LOCAL STATE AGENCY. PLEASE SEE THE REVERSE FOR
YOUR STATE AGENCY'S ADDRESS AND PHONE NUMBER.
PLEASE CONTACT YOUR STATE AGENCY FOR ANY CHANGES TO YOUR CURRENT CERTIFICATE.

APPENDIX 3

LABORATORY ACCREDITATION

Rec'd 5-7-13

Advancing Excellence

Accredited Laboratory

The College of American Pathologists

certifies that the laboratory named below

Laboratory Corporation of America
Regional Laboratory & Center for Esoteric Testing
Burlington, North Carolina
William F. Hancock, MD

LAP Number: 1396901
AU-ID: 1179680
CLIA Number: 34D0655059

has met all applicable standards for accreditation and is hereby accredited by the College of American Pathologists' Laboratory Accreditation Program. Reinspection should occur prior to February 14, 2015 to maintain accreditation.

Accreditation does not automatically survive a change in director, ownership, or location and assumes that all interim requirements are met.

(b) (6)

Chair, Commission on Laboratory Accreditation

(b) (6)

President, College of American Pathologists

APPENDIX 3

LABORATORY ACCREDITATION

Rec'd 10-2-14

CENTERS FOR MEDICARE & MEDICAID SERVICES

CLINICAL LABORATORY IMPROVEMENT AMENDMENTS

CERTIFICATE OF ACCREDITATION

LABORATORY NAME AND ADDRESS	CLIA ID NUMBER
LABORATORY CORPORATION OF AMERICA HOLD 1447 YORK COURT BURLINGTON, NC 27215	34D0655059
	EFFECTIVE DATE 10/20/2014
LABORATORY DIRECTOR	EXPIRATION DATE
WILLIAM F HANCOCK JR M.D.	10/19/2016

Pursuant to Section 353 of the Public Health Services Act (42 U.S.C. 263a) as revised by the Clinical Laboratory Improvement Amendments (CLIA), the above named laboratory located at the address shown hereon (and other approved locations) may accept human specimens for the purposes of performing laboratory examinations or procedures.

This certificate shall be valid until the expiration date above, but is subject to revocation, suspension, limitation, or other sanctions for violation of the Act or the regulations promulgated thereunder.

(b) (6)

Division of Laboratory Services
Survey and Certification Group
Center for Clinical Standards and Quality

92 Certs2_092314

If you currently hold a Certificate of Compliance or Certificate of Accreditation, below is a list of the laboratory specialties/subspecialties you are certified to perform and their effective date:

LAB CERTIFICATION (CODE)	EFFECTIVE DATE
BACTERIOLOGY (110)	07/27/1995
MYCOBACTERIOLOGY (115)	07/27/1995
MYCOLOGY (120)	07/27/1995
PARASITOLOGY (130)	07/27/1995
VIROLOGY (140)	07/27/1995
SYPHILIS SEROLOGY (210)	07/27/1995
GENERAL IMMUNOLOGY (220)	07/27/1995
ROUTINE CHEMISTRY (310)	07/27/1995
URINALYSIS (320)	07/27/1995
ENDOCRINOLOGY (330)	07/27/1995
TOXICOLOGY (340)	02/04/2003
HEMATOLOGY (400)	07/27/1995
ABO & RH GROUP (510)	07/27/1995

LAB CERTIFICATION (CODE)	EFFECTIVE DATE
ANTIBODY NON-TRANSFUSION (530)	07/27/1995
ANTIBODY IDENTIFICATION (540)	07/27/1995
HISTOPATHOLOGY (610)	07/27/1995
ORAL PATHOLOGY (620)	07/27/1995
CYTOLOGY (630)	10/26/2006
RADIOBIOASSAY (800)	10/25/2006

FOR MORE INFORMATION ABOUT CLIA, VISIT OUR WEBSITE AT WWW.CMS.GOV/CLIA
OR CONTACT YOUR LOCAL STATE AGENCY. PLEASE SEE THE REVERSE FOR
YOUR STATE AGENCY'S ADDRESS AND PHONE NUMBER.
PLEASE CONTACT YOUR STATE AGENCY FOR ANY CHANGES TO YOUR CURRENT CERTIFICATE.

REFERENCE RANGES

Protocol Reference Range Definitions

LSN: 101922 Sarepta Therapeutics, 4658-US-202
Unit Type: Conventional, Sex: Male, Age: >= 7 years, < 15 years

Parent Test Name	Test Name	Test Code	Result Type	Sex	Age	Panic Low	Alert Low	Normal Range	Alert High	Panic High	Unit
Auto Diff	Basophils, Absolute	BASOAA	String	Both	11m - 17y			0 - .3			10^3/uL
	Basophils, Percent	BASOPA	Numeric	Both	0y - 17y			0 - 2			%
	Eosinophils, Absolute	EOSNAA	String	Both	24m - 11y			0 - .7			10^3/uL
					11y - 17y			0 - .6			
	Eosinophils, Percent	EOSNPA	Numeric	Both	0y - 17y			0 - 5			%
	Lymphocytes, Absolute	LYMPAA	String	Both	4y - 11y			1.1 - 6.5			10^3/uL
					11y - 17y			1.1 - 5.9			
	Lymphocytes, Percent	LYMPPA	Numeric	Both	4y - 11y			28 - 48			%
					11y - 17y			27 - 47			
	Monocytes, Absolute	MONOAA	String	Both	4y - 11y			.2 - 1.8			10^3/uL
					11y - 17y			.2 - 1.6			
	Monocytes, Percent	MONOPA	Numeric	Both	2y - 12y			4 - 13			%
					12y - 150y			4 - 13			
	Neutrophils, Absolute	NEUTAA	String	Both	4y - 17y	0.5	1	1.5 - 7.8	14		10^3/uL
	Neutrophils, Percent	NEUTPA	Numeric	Both	4y - 11y			38 - 58			%
					11y - 17y			38 - 63			
Chemistry Panel	ALT (SGPT)	TALT	Numeric	Male	All			0 - 55	500		IU/L
	AST (SGOT)	TAST	Numeric	Both	All			0 - 40	500		IU/L
	Albumin	TALB	Numeric	Both	2y - 59y		2	3.5 - 5.5	6		g/dL
	Alkaline Phosphatase	TALP	Numeric	Male	1y - 9y			100 - 400	1,000		IU/L
					9y - 14y			150 - 530	1,000		
					14y - 20y			60 - 400	1,000		
	Amylase	TAMY	Numeric	Both	All		5	28 - 100	400		U/L
	Blood Urea Nitrogen	TBUN	Numeric	Both	1y - 18y		2	5 - 18	75		mg/dL
	Calcium	TCAL	Numeric	Both	All	7		8.5 - 10.6		13	mg/dL
	Chloride	TCL	Numeric	Both	All		75	96 - 109	115		mEq/L
	Creatine Kinase	TCK	Numeric	Male	All			24 - 204			IU/L
	Creatinine	TCRE	Numeric	Male	7y - 9y			.37 - .62	7.5		mg/dL
					9y - 11y			.39 - .7	7.5		
					11y - 13y			.42 - .75	7.5		
					13y - 15y			.49 - .9	7.5		
	Gamma Glutamyl Transferase	TGGT	Numeric	Male	All			0 - 65	650		IU/L
	Glucose, Serum	TGLS	Numeric	Both	All	40		65 - 99		500	mg/dL
	LDH	TLDH	Numeric	Both	All			100 - 250			IU/L

Note: All age ranges are inclusive on the low end and exclusive on the high (i.e. an age range of 18y - 60y includes patients from their 18th birthday up to their 60th birthday). All tests in the protocol are displayed, even if no reference range is defined.

REFERENCE RANGES

Protocol Reference Range Definitions

LSN: 101922 Sarepta Therapeutics, 4658-US-202
Unit Type: Conventional, Sex: Male, Age: >= 7 years, < 15 years

Parent Test Name	Test Name	Test Code	Result Type	Sex	Age	Panic Low	Alert Low	Normal Range	Alert High	Panic High	Unit
Chemistry Panel	Potassium	TK	Numeric	Both	All	2.5		3.5 - 5.5		6.5	mEq/L
	Sodium	TNA	Numeric	Both	All	120		134 - 144		160	mEq/L
	Total Bili	TTBL	Numeric	Both	All			.1 - 1.2	12	17	mg/dL
	Uric Acid	TUA	Numeric	Male	12m - 12y			1.9 - 5.8	15		mg/dL
					12y - 18y			3.4 - 7.8	15		
Coagulation	INR	TINRM	Numeric	Both	0y - 150y			.9 - 1.3		5.9	Ratio
	PT	PTV	Numeric	Both	0y - 150y			8.8 - 14.1			seconds
	PTT	PTTV	Numeric	Both	All			24 - 39	59	89	seconds
Diff / Morphology Comments	Differential Comments	DIFCOM	String	Both	All			Normal reference range = Not applicable			
	Platelet Assessment	PLTASS	String	Both	All			Reference Range = Normal			
	RBC Morphology	RBCMOR	String	Both	All			Reference Range = Normal			
	WBC Morphology	WBCMOR	String	Both	All			Reference Range = Normal			
Hematology Battery	Hematocrit	HCT	String	Both	4y - 11y	18.1		33 - 45		64.4	%
					11y - 17y	18.1		34 - 46		64.4	
	Hemoglobin	HGB	String	Both	4y - 11y	6.1	7.1	11.5 - 14.5	19.9	21.4	g/dL
					11y - 17y	6.1	7.1	11.8 - 14.8	19.9	21.4	
	Platelet Count	PLT	String	Both	0y - 17y	31	50	140 - 440	799	999	10^3/uL
	Red Blood Cells	RBC	String	Both	4y - 11y		2.76	3.9 - 5.1	6.99		10^6/uL
					11y - 17y		2.76	3.8 - 5.2	6.99		
	White Blood Cells	WBC	String	Both	4y - 11y	1.1	2	4 - 13.5	19.9	49.9	10^3/uL
					11y - 17y	1.1	2	4 - 12.5	19.9	49.9	
Manual Diff	Bands, Absolute	BANDAM	Numeric	Both	All			Not established			10^3/uL
	Bands, Percent	BANDPM	String	Both	11m - 17y			5 - 11			%
	Basophils Manual Percent	BASOPM	String	Both	0y - 17y			0 - 2			%
	Basophils, Manual Absolute	BASOAM	String	Both	11m - 17y			0 - .3			10^3/uL
	Blasts, Absolute	BLSTAM	String	Both	All			- 0			10^3/uL
	Blasts, Percent	BLSTPM	String	Both	All			0			%
	Eosinophils Manual Percent	EOSNPM	String	Both	0y - 17y			0 - 5			%
	Eosinophils, Manual Absolute	EOSNAM	String	Both	2y - 11y			0 - .7			10^3/uL

Note: All age ranges are inclusive on the low end and exclusive on the high (i.e. an age range of 18y - 60y includes patients from their 18th birthday up to their 60th birthday). All tests in the protocol are displayed, even if no reference range is defined.

REFERENCE RANGES

Protocol Reference Range Definitions

LSN: 101922 Sarepta Therapeutics, 4658-US-202
Unit Type: Conventional, Sex: Male, Age: >= 7 years, < 15 years

Parent Test Name	Test Name	Test Code	Result Type	Sex	Age	Panic Low	Alert Low	Normal Range	Alert High	Panic High	Unit
Manual Diff	Eosinophils, Manual Absolute	EOSNAM	String	Both	11y - 17y			0 - .6			10^3/uL
	Lymphocytes Atypical, Absolute	LYMAAM	String	Both	All			- 0			10^3/uL
	Lymphocytes Atypical, Percent	LYMAPM	String	Both	All			- 0			%
	Lymphocytes Manual Percent	LYMPPM	String	Both	4y - 11y			28 - 48			%
					11y - 17y			27 - 47			
	Lymphocytes, Manual Absolute	LYMPAM	String	Both	4y - 11y			1.1 - 6.5			10^3/uL
					11y - 17y			1.1 - 5.9			
	Metamyelocytes, Absolute	METAAM	String	Both	All			- 0			10^3/uL
	Metamyelocytes, Percent	METAPM	String	Both	All			- 0			%
	Monocytes Manual Percent	MONOPM	String	Both	2y - 12y			4 - 13			%
					12y - 150y			4 - 13			
	Monocytes, Manual Absolute	MONOAM	String	Both	4y - 11y			.2 - 1.8			10^3/uL
					11y - 17y			.2 - 1.6			
	Myelocytes, Absolute	MYELAM	String	Both	All			- 0			10^3/uL
	Myelocytes, Percent	MYELPM	String	Both	All			- 0			%
	Neutrophils Manual Percent	NEUTPM	String	Both	4y - 11y			38 - 58			%
					11y - 17y			38 - 63			
	Neutrophils, Manual Absolute	NEUTAM	String	Both	4y - 17y	0.5	1	1.5 - 7.8	14		10^3/uL
	Nucleated RBC Manual Absolute	NRBCAM	String	Both	All			- 0			10^3/uL
	Nucleated RBC Manual Percent	NRBCPM	String	Both	All			- 0			%
	Plasma Cells, Absolute	PLSMAM	String	Both	All			- 0			10^3/uL
	Plasma Cells, Percent	PLSMPM	String	Both	All			- 0			%
	Promyelocytes, Absolute	PRMYAM	String	Both	All			- 0			10^3/uL
	Promyelocytes, Percent	PRMYPM	String	Both	All			- 0			%
Urinalysis Macroscopic	Specific gravity	TSG	Numeric	Both	All			1.005 - 1.03			SGU
	UA Blood	TBLD	String	Both	All			Normal Reference Interval = Negative			

Note: All age ranges are inclusive on the low end and exclusive on the high (i.e. an age range of 18y - 60y includes patients from their 18th birthday up to their 60th birthday). All tests in the protocol are displayed, even if no reference range is defined.

REFERENCE RANGES

Protocol Reference Range Definitions

LSN: 101922 Sarepta Therapeutics, 4658-US-202
Unit Type: Conventional, Sex: Male, Age: >= 7 years, < 15 years

Parent Test Name	Test Name	Test Code	Result Type	Sex	Age	Panic Low	Alert Low	Normal Range	Alert High	Panic High	Unit
Urinalysis Macroscopic	UA Glucose	TGLUA	String	Both	All			Normal Reference Interval = Negative			
	UA Ketones	TKET	String	Both	All			Normal Reference Interval = Negative			
	UA Micro Reflex	UMRFX2	String								
	Urine Protein	TPROT	String	Both	All			Normal Reference Interval = Negative to Trace			
	pH	TPH	Numeric	Both	All			5 - 7.5			pH
Urine Microscopic	Ammonium Biurate	AMMB	String	Both	All			Normal Reference Interval = None Seen/Few			
	Amorphous Urates or Phosphates	AMURPH	String	Both	All			Normal Reference Interval = None Seen/Few			
	Bacteria	BACUA	String	Both	All			Normal Reference Interval = None Seen			
	Bili Crystal	BILC	String	Both	All			Normal Reference Interval = None Seen			
	Calcium Oxalate	CALC	String	Both	All			Normal Reference Interval = None Seen/Few			
	Cellular Cast	CELC	String	Both	All			Normal Reference Interval = None Seen			
	Chol Crystal	CHOLC	String	Both	All			Normal Reference Interval = None Seen			
	Cystine	CYSTC	String	Both	All			Normal Reference Interval = None Seen			
	Fat Droplets	FAT	String	Both	All			Normal			

Note: All age ranges are inclusive on the low end and exclusive on the high (i.e. an age range of 18y - 60y includes patients from their 18th birthday up to their 60th birthday). All tests in the protocol are displayed, even if no reference range is defined.

REFERENCE RANGES

Protocol Reference Range Definitions

LSN: 101922 Sarepta Therapeutics, 4658-US-202
Unit Type: Conventional, Sex: Male, Age: >= 7 years, < 15 years

Parent Test Name	Test Name	Test Code	Result Type	Sex	Age	Panic Low	Alert Low	Normal Range	Alert High	Panic High	Unit
								Reference Interval = None Seen			
Urine Microscopic	Fatty Cast	FATC	String	Both	All			Normal Reference Interval = None Seen			
	Granular Cast	GRANC	String	Both	All			Normal Reference Interval = None Seen			
	Hippuric Acid	HIPP	String	Both	All			Normal Reference Interval = None Seen			
	Hyaline Cast	HYLC	String	Both	All			Normal Reference Interval = 0-3 casts/lpf			
	Leucine	LEUCN	String	Both	All			Normal Reference Interval = None Seen			
	Mucus	MUCUS	String	Both	All			Normal Reference Interval = Not Established			
	Pollen	POLLEN	String	Both	All			Normal Reference Interval = None Seen			
	RBC Cast	RBCC	String	Both	All			Normal Reference Interval = None Seen			
	RBC Urine	RBCUA	String	Both	All			Normal Reference Interval = 0-3 cells/hpf			
	Renal Tubular Epithelial Cells	RTE	String	Both	All			Normal Reference Interval = 0-8 cells/hpf			
	Sperm	SPERM	String	Both	All			Normal Reference Interval = None Seen			

Note: All age ranges are inclusive on the low end and exclusive on the high (i.e. an age range of 18y - 60y includes patients from their 18th birthday up to their 60th birthday). All tests in the protocol are displayed, even if no reference range is defined.

REFERENCE RANGES

Protocol Reference Range Definitions

LSN: 101922 Sarepta Therapeutics, 4658-US-202
Unit Type: Conventional, Sex: Male, Age: >= 7 years, < 15 years

Parent Test Name	Test Name	Test Code	Result Type	Sex	Age	Panic Low	Alert Low	Normal Range	Alert High	Panic High	Unit
Urine Microscopic	Squamous Epithelial Cells	SEP	String	Both	All			Normal Reference Interval = 0-8 cells/hpf			
	Starch	STARCH	String	Both	All			Normal Reference Interval = None Seen			
	Sulfonamide	SULFA	String	Both	All			Normal Reference Interval = None Seen			
	Transitional Epithelial Cells	TEP	String	Both	All			Normal Reference Interval = 0-8 cells/hpf			
	Triple Phosphate	AMMTPH	String	Both	All			Normal Reference Interval = None Seen/Few			
	Tyrosine	TYRO	String	Both	All			Normal Reference Interval = None Seen			
	UA Comments	UACOM	String	Both	All			Not Applicable			
	Uric Acid Crystal	UACRY	String	Both	All			Normal Reference Interval = None Seen/Few			
	WBC Cast	WBCC	String	Both	All			Normal Reference Interval = None Seen			
	WBC Urine	WBCUA	String	Both	All			Normal Reference Interval = 0-5 cells/hpf			
	Waxy Cast	WAXC	String	Both	All			Normal Reference Interval = None Seen			
	Yeast	YSTUA	String	Both	All			Normal Reference Interval = None Seen			

Note: All age ranges are inclusive on the low end and exclusive on the high (i.e. an age range of 18y - 60y includes patients from their 18th birthday up to their 60th birthday). All tests in the protocol are displayed, even if no reference range is defined.

REFERENCE RANGES

Protocol Reference Range Definitions

LSN: 101922 Sarepta Therapeutics, 4658-US-202
Unit Type: Conventional, Sex: Male, Age: >= 7 years, < 15 years

Parent Test Name	Test Name	Test Code	Result Type	Sex	Age	Panic Low	Alert Low	Normal Range	Alert High	Panic High	Unit
	Ampicillin	AMPC	String	Both	All			Normal Reference Interval = None Seen			
	C-reactive Protein (CRP)	TTCRP	Numeric	Both	0y - 150y			Normal <5.0			mg/L
	CBC Comments	CBCCOM	String								
	CBC trigger Reflex if C	MDITC2	String								
	CBC trigger Reflex if S	MDITS2	String								
	Clue Cells	CLUE	String	Both	All			Normal Reference Interval = None Seen			
	Eosinophils, Urine	EOSUA	String	Both	All			Normal Reference Interval = None Seen			
	Fiber	FIBER	String	Both	All			Normal Reference Interval = None Seen			
	Macrophage	MACPG	String	Both	All			Normal Reference Interval = None Seen			
	Macrophage Bacteria	MACPGB	String	Both	All			Normal Reference Interval = None Seen			
	Macrophage Fungi	MACPGF	String	Both	All			Normal Reference Interval = None Seen			
	Non-Hemoglobin Pigment	NHCBP	String	Both	All			Normal Reference Interval = None Seen			
	RTE with Fat Globules	RTEFAT	String	Both	All			Normal Reference Interval = None Seen			
	RTE with Hemosiderin	RTEHEM	String	Both	All			Normal Reference Interval = None Seen			
	RTE with Viral Inclusion	RTEVIR	String	Both	All			Normal Reference Interval =			

Note: All age ranges are inclusive on the low end and exclusive on the high (i.e. an age range of 18y - 60y includes patients from their 18th birthday up to their 60th birthday). All tests in the protocol are displayed, even if no reference range is defined.

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REFERENCE RANGES

LabCorp Clinical Trials
www.labcorp.com

Protocol Reference Range Definitions

LSN: 101922 Sarepta Therapeutics, 4868-US-202
Unit Type: Conventional, Sex: Male, Age: >= 7 years, < 15 years

Parent Test Name	Test Name	Test Code	Result Type	Sex	Age	Panic Low	Alert Low	Normal Range	Alert High	Panic High	Unit
								None Seen			
	Radiograph	RADIOG	String	Both	All			Normal Reference Interval = None Seen			
	Serum Cystatin C	TSYSC	Numeric	Both	All			.53 - .95			mg/L
	Trichomonas	TRICH	String	Both	All			Normal Reference Interval = None Seen			
	eGFR	TGFRW	Numeric	Both	All			>/= 60			mL/min/1.73 m^2
	eGFR - If African American	TGFRB	Numeric	Both	All			>/= 60			mL/min/1.73 m^2

Note: All age ranges are inclusive on the low end and exclusive on the high (i.e. an age range of 18y - 60y includes patients from their 18th birthday up to their 60th birthday). All tests in the protocol are displayed, even if no reference range is defined.

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CENTERS FOR MEDICARE & MEDICAID SERVICES

CLINICAL LABORATORY IMPROVEMENT AMENDMENTS

CERTIFICATE OF ACCREDITATION

LABORATORY NAME AND ADDRESS

MYRIAD RBM, INC
3300 DUVAL RD STE 110
AUSTIN, TX 78759

CLIA ID NUMBER

45D1037483

EFFECTIVE DATE

02/09/2014

LABORATORY DIRECTOR

JAMES P MAPES Ph.D.

EXPIRATION DATE

02/08/2016

Pursuant to Section 353 of the Public Health Services Act (42 U.S.C. 263a) as revised by the Clinical Laboratory Improvement Amendments (CLIA), the above named laboratory located at the address shown hereon (and other approved locations) may accept human specimens for the purposes of performing laboratory examinations or procedures.

This certificate shall be valid until the expiration date above, but is subject to revocation, suspension, limitation, or other sanctions for violation of the Act or the regulations promulgated thereunder.

(b) (4) & (b) (6)

Division of Laboratory Services
Survey and Certification Group
Center for Medicaid and State Operations

CMS
CENTERS for MEDICARE & MEDICAID SERVICES

307 Certs2_011414

If you currently hold a Certificate of Compliance or Certificate of Accreditation, below is a list of the laboratory specialties/subspecialties you are certified to perform and their effective date:

LAB CERTIFICATION (CODE)	EFFECTIVE DATE	LAB CERTIFICATION (CODE)	EFFECTIVE DATE
GENERAL IMMUNOLOGY (220)	07/03/2007		
ROUTINE CHEMISTRY (310)	02/09/2006		
ENDOCRINOLOGY (330)	02/09/2006		

FOR MORE INFORMATION ABOUT CLIA, VISIT OUR WEBSITE AT WWW.CMS.HHS.GOV/CLIA
OR CONTACT YOUR LOCAL STATE AGENCY. PLEASE SEE THE REVERSE FOR
YOUR STATE AGENCY'S ADDRESS AND PHONE NUMBER.
PLEASE CONTACT YOUR STATE AGENCY FOR ANY CHANGES TO YOUR CURRENT CERTIFICATE.

This certificate makes known that



Has Certified That

Myriad RBM, Inc

COLA ID #: 17151

Has met all criteria for

Laboratory Accreditation

12/16/2013

This certificate expires two years from this date

(b) (6)

Chairman, Board of Directors

ISODOC-24-60

(b) (6)

Chief Executive Officer

MYRIAD RBM

Myriad RBM ranges for Cystatin-C and KIM-1:

Analytes	Cystatin-C	Kidney Injury Molecule-1 (KIM-1)
Units	ng/mL	ng/mL
Myriad RBM LDD	2.0	0.0085
Myriad RBM Urine Low Range	3.9	0.023
Myriad RBM Urine High Range	79	0.67

Myriad RBM, Inc. | 3300 Duval Rd., Austin, TX 78759
Tel: 512.835.8026 | Fax: 512.835.4687

Advancing Excellence

Accredited Laboratory

The College of American Pathologists

certifies that the laboratory named below

Nationwide Children's Hospital
Main Laboratory
Columbus, Ohio
Sue Hammond, MD

CAP Number: 1637201
AU-ID: 1182118
CLIA Number: 36D0665271

has met all applicable standards for accreditation and is hereby accredited by the College of American Pathologists' Laboratory Accreditation Program. Reinspection should occur prior to November 15, 2016 to maintain accreditation.

Accreditation does not automatically survive a change in director, ownership, or location and assumes that all interim requirements are met.

(b) (6)

Chair, Commission on Laboratory Accreditation

(b) (6)

President, College of American Pathologists

CENTERS FOR MEDICARE & MEDICAID SERVICES

CLINICAL LABORATORY IMPROVEMENT AMENDMENTS

CERTIFICATE OF ACCREDITATION

LABORATORY NAME AND ADDRESS

NATIONWIDE CHILDREN'S HOSPITAL DEPARTM
MEDICINE
700 CHILDREN'S DRIVE
COLUMBUS, OH 43205

CLIA ID NUMBER

36D0665271

EFFECTIVE DATE

02/09/2015

LABORATORY DIRECTOR

SUE HAMMOND MD

EXPIRATION DATE

02/08/2017

Pursuant to Section 353 of the Public Health Services Act (42 U.S.C. 263a) as revised by the Clinical Laboratory Improvement Amendments (CLIA), the above named laboratory located at the address shown hereon (and other approved locations) may accept human specimens for the purposes of performing laboratory examinations or procedures.

This certificate shall be valid until the expiration date above, but is subject to revocation, suspension, limitation, or other sanctions for violation of the Act or the regulations promulgated thereunder.

(b) (4) & (b) (6)

CMS
CENTERS FOR MEDICARE & MEDICAID SERVICES

Division of Laboratory Services
Survey and Certification Group
Center for Clinical Standards and Quality

411 Certs2_011315

If you currently hold a Certificate of Compliance or Certificate of Accreditation, below is a list of the laboratory specialties/subspecialties you are certified to perform and their effective date:

LAB CERTIFICATION (CODE)	EFFECTIVE DATE
HISTOCOMPATIBILTY (010)	07/19/2013
BACTERIOLOGY (110)	07/27/1995
MYCOBACTERIOLOGY (115)	07/27/1995
MYCOLOGY (120)	07/27/1995
PARASITOLOGY (130)	07/27/1995
VIROLOGY (140)	07/27/1995
SYPHILIS SEROLOGY (210)	07/27/1995
GENERAL IMMUNOLOGY (220)	07/27/1995
ROUTINE CHEMISTRY (310)	07/27/1995
URINALYSIS (320)	07/27/1995
ENDOCRINOLOGY (330)	07/27/1995
TOXICOLOGY (340)	07/27/1995
HEMATOLOGY (400)	07/27/1995

LAB CERTIFICATION (CODE)	EFFECTIVE DATE
ABO & RH GROUP (510)	07/27/1995
ANTIBODY TRANSFUSION (520)	07/27/1995
ANTIBODY NON-TRANSFUSION (530)	07/27/1995
ANTIBODY IDENTIFICATION (540)	07/27/1995
COMPATIBILITY TESTING (550)	07/27/1995
HISTOPATHOLOGY (610)	07/27/1995
ORAL PATHOLOGY (620)	07/27/1995
CYTOLOGY (630)	07/27/1995
RADIOBIOASSAY (800)	06/11/2012
CYTOGENETICS (900)	07/27/1995

FOR MORE INFORMATION ABOUT CLIA, VISIT OUR WEBSITE AT WWW.CMS.GOV/CLIA OR CONTACT YOUR LOCAL STATE AGENCY. PLEASE SEE THE REVERSE FOR YOUR STATE AGENCY'S ADDRESS AND PHONE NUMBER.
PLEASE CONTACT YOUR STATE AGENCY FOR ANY CHANGES TO YOUR CURRENT CERTIFICATE.

ChildLab Reference Ranges

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Reference Range | Verify Range

CHEMISTRY

Albumin **Test code: ALB** **Units** g/dL

Age	Male and Female	Male and Female
0 M - 1 M	2.1-4.5	<1.6 and >7
2 M - 4 Y	3.4-5.1	<1.6 and >7
5 Y - 13 Y	3.4-5.3	<1.6 and >7
14 Y - Adult	3.4-5.2	<1.6 and >7

Alk Phosphatase **Test code: ALP** **Units** U/L

Age	Male	Female
0 D - 29 D	60-350	60-350
1 M - 5 M	65-500	65-500
6 M - 11 M	55-380	55-380
12 M - 3 Y	85-360	85-360
4 Y - 6 Y	85-320	85-370
7 Y - 9 Y	95-340	95-350
10 Y - 11 Y	100-455	90-400
12 Y - 13 Y	100-400	50-350
14 Y - 15 Y	55-360	50-230
16 Y - Adult		50-150
16 Y - 16 Y	55-240	
17 Y - Adult	55-240	

ALT **Test code: ALT** **Units** U/L

Age	Male and Female
0 Y - 1 Y	7-110
2 Y - Adult	7-90

AST **Test code: AST** **Units** U/L

Age	Male and Female
0 Y - 1 Y	5-105
2 Y - Adult	5-60

BUN **Test code: BUN** **Units** mg/dL

Age	Male and Female	Male and Female
0 M - 1 M	4-15	>=40
2 M - Adult	5-18	>=40

Calcium **Test code: CA** **Units** mg/dL

Age	Male and Female	Male and Female
0 D - 13 D	6-10	<6 and >12
14 D - Adult	8-10.5	<6 and >12

Calcium **Test code: CALCI** **Units** mg/dL

Age	Male and Female	Male and Female
0 D - 0 D	9.0-11.0	<6 and >12
1 D - 1 D	7.0-11.0	<6 and >12
2 D - Adult	9.0-11.0	<6 and >12

FDACDER_SAR_0023020

ChildLab Reference Ranges

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CHEMISTRY

Chloride **Test code: CL** — **Units** mmol/L

Age	Reference Range: Male and Female	Verify Range: Male and Female
0 M - 1 M	95-110	<80 and >125
2 M - Adult	95-106	<80 and >125

CK **Test code: CK** — **Units** U/L

Age	Reference Range: Male and Female
0 D - 20 D	37-1450
21 D - 89 D	37-580
3 M - 15 Y	37-430
16 Y - Adult	37-289

Creatinine **Test code: CREA** — **Units** mg/dL

Age	Reference Range: Male and Female	Verify Range: Male and Female
0 M - 11 M	0.10-0.30	>=2.1
12 M - 1 Y	0.10-0.50	>=2.1
2 Y - 7 Y	0.10-0.60	>=2.1
8 Y - 10 Y	0.20-0.70	>=2.1
11 Y - 12 Y	0.20-0.80	>=2.1
13 Y - 17 Y	0.40-1.10	>=2.1
18 Y - Adult	0.50-1.20	>=2.1

CRP **Test code: CRP** — **Units** mg/dL

Age	Reference Range: Male and Female
0 Y - Adult	<1.2

Direct Bilirubin, Neonatal **Test code: CBIL** — **Units** mg/dL

Age	Reference Range: Male and Female	Verify Range: Male and Female
0 Y - Adult	<0.6	>=2.0

GGTP **Test code: GGT** — **Units** U/L

Age	Reference Range: Male and Female
0 M - 5 M	8-468
6 M - Adult	8-78

Glucose **Test code: GLUC** — **Units** mg/dL

Age	Reference Range: Male and Female	Verify Range: Male and Female
0 D - 2 D	50-110	<40 and >300
3 D - Adult	60-115	<50 and >350

Indirect Bilirubin **Test code: IBIL** — **Units** mg/dL

Age	Reference Range: Male and Female	Verify Range: Male and Female
0 D - 2 D	1.3-9.9	>=15
3 D - 3 D	0.7-9.9	>=15
4 D - 5 D	0.1-9.9	>=15
6 D - 13 D	0.1-4.0	>=10
14 D - Adult	0.1-1.0	>=5.0

FDACDER_SAR_0023021

ChildLab Reference Ranges

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Reference Range | Verify Range

CHEMISTRY

LDH **Test code: LDH** **Units** U/L

Age	Male and Female
0 D - 29 D	600-3500
1 M - 1 Y	600-1400
2 Y - 16 Y	400-1250
17 Y - Adult	350-1000

Potassium **Test code: K** **Units** mmol/L

Age	Male and Female	Male and Female
0 D - 13 D	4.5-6.8	<3 and >7
14 D - 89 D	4-6.4	<3 and >7
3 M - 11 M	4-5.9	<3 and >6.5
12 M - 15 Y	3.7-5.6	<3 and >6
16 Y - Adult	3.7-5.3	<3 and >6

Protein, Total **Test code: PRT** **Units** g/dL

Age	Male and Female	Male and Female
0 D - 6 D	4.3-7.7	<4.3 and >9.4
7 D - D	5-7.4	<4.5 and >9.4
2 M - 2 Y	5.6-7.4	<4.5 and >9.4
3 Y - 15 Y	5.8-8.7	<4.5 and >9.4
16 Y - Adult	6.4-8.4	<4.5 and >9.4

Sodium **Test code: NA** **Units** mmol/L

Age	Male and Female	Male and Female
0 M - 1 M	132-142	<124 and >154
2 M - Adult	135-145	<124 and >154

Total Bilirubin **Test code: TBIL** **Units** mg/dL

Age	Male and Female	Male and Female
0 D - 2 D	1.3-11.3	>=15
3 D - 3 D	0.7-12	>=15
4 D - 5 D	0.1-12	>=15
6 D - 13 D	0.1-4	>=12
14 D - Adult	0.1-1.0	>=5.0

Total Bilirubin, Neonatal **Test code: NBILR** **Units** mg/dL

Age	Male and Female	Male and Female
0 D - 2 D	1.3-11.3	>=15
3 D - 3 D	0.7-12.0	>=15
4 D - 5 D	0.1-12.0	>=15.0
6 D - 13 D	0.1-4.0	>=12.1
14 D - Adult	0.1-1.0	>=5

Uric Acid **Test code: URIC** **Units** mg/dL

Age	Male	Female	Male and Female
0 Y - 13 Y	2-7	2-7	>=10
14 Y - Adult	3-8	2-7	>=10

FDACDER_SAR_0023022

ChildLab Reference Ranges

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Reference Range | Verify Range

COAGULATION

APTT **Test code: APTT** **Units** sec

Age	Male	Female	Male	Female
0 Y - Adult	24-36		>=125	
0 Y - Adult		24-36		>=125

INR **Test code: INR** **Units**

Age	Male	Female	Male and Female
0 Y - Adult			>=3.01

Prothrombin Time **Test code: PTV** **Units** sec

Age	Male	Female	Male	Female
0 Y - Adult	12.4-14.7		<5.1 and >34.9	
0 Y - Adult		12.4-14.7		<5.1 and >34.9

FDACDER_SAR_0023023

Reference Range | Verify Range

FLUID/URINE/STOOL ANALYSIS

Bilirubin **Test code: UBIL** **Units**

Age	Male and Female
0 Y - Adult	NEG

Glucose **Test code: UGLC** **Units** mg/dL

Age	Male and Female
0 Y - Adult	NEG

Ketones **Test code: UKET** **Units** mg/dL

Age	Male and Female
0 Y - Adult	NEG

Nitrite **Test code: UNTR** **Units**

Age	Male and Female
0 Y - Adult	NEG

Occult Blood **Test code: UOCB** **Units**

Age	Male and Female
0 Y - Adult	NEG

pH **Test code: UPH** **Units**

Age	Male and Female
0 Y - Adult	4.5-8.0

Protein **Test code: UPRO** **Units** mg/dL

Age	Male and Female
0 Y - Adult	NEG

Protein, Urine Output **Test code: PROUT** **Units** mg/24h

Age	Male and Female
0 Y - Adult	<250

RBC **Test code: URBC** **Units** /HPF

Age	Male and Female
0 Y - Adult	0-2

Urobilinogen **Test code: UURO** **Units** mg/dL

Age	Male and Female
0 Y - Adult	<1.1

WBC **Test code: UWBC** **Units** /HPF

Age	Male and Female
0 Y - Adult	<6

Yeast Hyphae, Urine **Test code: UYEAH** **Units**

Age	Male and Female
0 Y - Adult	NEG

ChildLab Reference Ranges

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Reference Range Verify Range

HEMATOLOGY

Band **Test code: BAND** **Units** %

Age	Male and Female
0 D - 0 D	11-19
1 D - 6 D	10-18
7 D - 13 D	8-16
14 D - 29 D	6-14
1 M - 5 M	6-12
6 M - 11 M	5-11
12 M - 1 Y	5-11
2 Y - 3 Y	5-11
4 Y - 5 Y	5-11
6 Y - 9 Y	5-11
10 Y - 20 Y	5-11
21 Y - Adult	5-11

Basophil **Test code: BASO** **Units** %

Age	Male and Female
0 Y - Adult	0-1

Blast **Test code: BLAST** **Units** %

Age	Male and Female
0 Y - Adult	0

Eosinophil **Test code: EOS** **Units** %

Age	Male and Female
0 D - 29 D	1-5
1 M - Adult	1-4

Hematocrit **Test code: HCT** **Units** %

Age	Male	Female	Male and Female
0 D - 2 D	45-67	45-67	<15.1 and >68
3 D - 6 D	42-66	42-66	<15.1 and >68
7 D - 13 D	39-63	39-63	<15.1 and >65.9
14 D - 29 D	31-55	31-55	<15.1 and >65.9
1 M - 1 M	28-42	28-42	<15.1 and >65.9
2 M - 5 M	29-41	29-41	<15.1 and >65.9
6 M - 1 Y	33-39	33-39	<15.1 and >65.9
2 Y - 5 Y	34-40	34-40	<15.1 and >65.9
6 Y - 11 Y	35-45	35-45	<15.1 and >65.9
12 Y - 17 Y	37-49	36-48	<15.1 and >65.9
18 Y - Adult	41-53	36-46	<15.1 and >65.9

FDACDER_SAR_0023025

ChildLab Reference Ranges

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Reference Range Verify Range

HEMATOLOGY

Hemoglobin **Test code: HGB** **Units** g/dL

Age	Male	Female	Male and Female
0 D - 2 D	14.5-22.5	14.5-22.5	<5.1 and >22.6
3 D - 6 D	13.5-21.5	13.5-21.5	<5.1 and >21.9
7 D - 13 D	12.5-20.5	12.5-20.5	<5.1 and >21.9
14 D - 29 D	10-18	10-18	<5.1 and >21.9
1 M - 1 M	9-14	9-14	<5.1 and >21.9
2 M - 5 M	9.5-13.5	9.5-13.5	<5.1 and >21.9
6 M - 1 Y	10.5-13.5	10.5-13.5	<5.1 and >21.9
2 Y - 5 Y	11.5-13.5	11.5-13.5	<5.1 and >21.9
6 Y - 11 Y	11.5-15.5	11.5-15.5	<5.1 and >21.9
12 Y - 17 Y	13-15	12-16	<5.1 and >21.9
18 Y - Adult	13.5-17.5	12-16	<5.1 and >21.9

Lymphocyte **Test code: LYMP** **Units** %

Age	Male and Female
0 D - 0 D	19-36
1 D - 6 D	26-36
7 D - 13 D	36-46
14 D - 27 D	43-53
28 D - D	41-71
6 M - 1 Y	46-76
2 Y - 3 Y	44-74
4 Y - 5 Y	35-65
6 Y - 9 Y	27-57
10 Y - 15 Y	28-48
16 Y - 20 Y	25-45
21 Y - Adult	24-44

MCH **Test code: MCH** **Units** pg

Age	Male and Female
0 D - 2 D	31-37
3 D - 6 D	28-38
7 D - 13 D	28-38
14 D - 29 D	28-38
1 M - 1 M	26-34
2 M - 5 M	25-35
6 M - 1 Y	23-31
2 Y - 5 Y	24-30
6 Y - 11 Y	25-33
12 Y - 17 Y	25-35
18 Y - Adult	26-34

MCHC **Test code: MCHC** **Units** %

Age	Male and Female
0 Y - Adult	31.0-37.0

FDACDER_SAR_0023026

ChildLab Reference Ranges

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Reference Range | Verify Range

HEMATOLOGY

MCV **Test code: MCV** **Units** fL

Age	Male and Female
0 D - 2 D	95-121
3 D - 6 D	88-126
7 D - 12 D	86-124
13 D - 29 D	85-123
1 M - 1 M	77-115
2 M - 5 M	74-108
6 M - 1 Y	70-86
2 Y - 5 Y	75-88
6 Y - 11 Y	77-95
12 Y - 17 Y	78-102
18 Y - Adult	80-100

Monocyte **Test code: MONO** **Units** %

Age	Male and Female
0 D - 6 D	3-9
7 D - 29 D	6-12
1 M - 5 M	3-9
6 M - 20 Y	2-8
21 Y - Adult	1-7

MPV **Test code: MPV** **Units** fL

Age	Male and Female
0 Y - Adult	9.3-13.0

Myelocyte **Test code: MYELO** **Units** %

Age	Male and Female
0 Y - Adult	0

Neutrophil **Test code: NEUT** **Units** %

Age	Male and Female
0 D - 0 D	43-87
1 D - 6 D	42-80
7 D - 13 D	27-65
14 D - 29 D	20-58
1 M - 5 M	21-47
6 M - 11 M	18-44
12 M - 1 Y	20-46
2 Y - 3 Y	28-56
4 Y - 5 Y	37-65
6 Y - 9 Y	36-72
10 Y - 20 Y	39-75
21 Y - Adult	41-77

Platelet Count **Test code: PLTC** **Units** K/cu mm

Age	Male and Female	Male and Female
0 Y - Adult	140-440	<41 and >799

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ChildLab Reference Ranges

Reference Range | Verify Range

HEMATOLOGY

Promyelocyte **Test code: PMYEL** **Units** %

Age	Male and Female
0 Y - Adult	0

RBC **Test code: RBC** **Units** M/cu mm

Age	Male	Female
0 D - 2 D	4.0-6.6	4.0-6.6
3 D - 6 D	3.9-6.3	3.9-6.3
7 D - 13 D	3.6-6.2	3.6-6.2
14 D - 29 D	3.0-5.4	3.0-5.4
1 M - 1 M	2.7-4.9	2.7-4.9
2 M - 5 M	3.1-4.5	3.1-4.5
6 M - 1 Y	3.7-5.3	3.7-5.3
2 Y - 5 Y	3.9-5.3	3.9-5.3
6 Y - 11 Y	4.0-5.2	4.0-5.2
12 Y - 17 Y	4.5-5.3	4.1-5.1
18 Y - Adult	4.5-5.9	4.0-5.2

RDW **Test code: RDW** **Units** %

Age	Male and Female
0 Y - Adult	10-14.1

Seg **Test code: SEG** **Units** %

Age	Male and Female
0 D - 0 D	32-68
1 D - 6 D	32-62
7 D - 13 D	19-49
14 D - 29 D	14-44
1 M - 5 M	15-35
6 M - 1 Y	13-33
2 Y - 3 Y	15-35
4 Y - 5 Y	23-45
6 Y - 9 Y	32-54
10 Y - 15 Y	31-61
16 Y - 20 Y	34-64
21 Y - Adult	36-66

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ChildLab Reference Ranges

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Reference Range

Verify Range

HEMATOLOGY

WBC **Test code: WBC**

Units K/cu mm

Age	Male and Female	Male and Female
0 D - 0 D	9-38	<2.1 and >99.9
1 D - 6 D	9.4-34	<2.1 and >99.9
7 D - 13 D	5-21	<2.1 and >99.9
14 D - 29 D	5-20	<2.1 and >99.9
1 M - 5 M	5-19.5	<2.1 and >99.9
6 M - 11 M	6-17.5	<2.1 and >99.9
12 M - 1 Y	6-17.5	<2.1 and >99.9
2 Y - 3 Y	6-17	<2.1 and >99.9
4 Y - 5 Y	5.5-15.5	<2.1 and >99.9
6 Y - 9 Y	5-14.5	<2.1 and >99.9
10 Y - 20 Y	4.5-13.5	<2.1 and >99.9
21 Y - Adult	4.5-11	<2.1 and >99.9

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Result table and reporting equivalencies

ANALYTE	TEST NAME	UNITS	ABNORMAL THRESHOLD	iCHEM OUTPUT	SQUEST INPUT
BLOOD	UOCB		TR	-	NEG
				+1/5-10	SM
				+2/50	MOD
				+3/300	LG
BILIRUBIN	UBIL		TR	-	NEG
				+1	TR
				+2	SM
				+3	MOD
				+4	LG
UROBILINOGEN	UURO	mg/dL	2.0	NORMAL	0.2
				+1	2.0
				+2	4.0
				+3	8.0
				+4	>12.0
KETONE	UKET	mg/dL	TR	-	NEG
				+1	10.0
				+2	40.0
				+3	80.0
				+4	150.0
GLUCOSE	UGLC	mg/dL	TR	NORMAL	NEG
				+1	70
				+2	150
				+3	300
				+4	1000
PROTEIN	UPRO	mg/dL	TR	-	NEG
				+1	30
				+2	100
				+3	300
				+4	>600
NITRITE	UNTR		POS	-	NEG
				+1	POS
				+2	POS
LEUK. EST.	ULES		TR	NEG	NEG
				25	TR
				75	SM
				250	MOD
				500	LG

16.1.11 Publications Based on Study

Mendell, 2013

Eteplirsen for the Treatment of Duchenne Muscular Dystrophy

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Objective: In prior open-label studies, eteplirsen, a phosphorodiamidate morpholino oligomer, enabled dystrophin production in Duchenne muscular dystrophy (DMD) with genetic mutations amenable to skipping exon 51. The present study used a double-blind placebo-controlled protocol to test eteplirsen's ability to induce dystrophin production and improve distance walked on the 6-minute walk test (6MWT).
Methods: DMD boys aged 7 to 13 years, with confirmed deletions correctable by skipping exon 51 and ability to walk 200 to 400 m on 6 MWT, were randomized to weekly intravenous infusions of 30 or 50 mg/kg/wk eteplirsen or placebo for 24 weeks (n = 4/group). Placebo patients switched to 30 or 50 mg/kg eteplirsen (n = 2/group) at week 25; treatment was open label thereafter. All patients had muscle biopsies at baseline and week 48. Efficacy included dystrophin-positive fibers and distance walked on the 6MWT.
Results: At week 24, the 30 mg/kg eteplirsen patients were biopsied, and percentage of dystrophin-positive fibers was increased to 23% of normal; no increases were detected in placebo-treated patients ($p \leq 0.002$). Even greater increases occurred at week 48 (52% and 43% in the 30 and 50 mg/kg cohorts, respectively), suggesting that dystrophin increases with longer treatment. Restoration of functional dystrophin was confirmed by detection of sarcoglycans and neuronal nitric oxide synthase at the sarcolemma. Ambulation-evaluable eteplirsen-treated patients experienced a 67.3 m benefit compared to placebo/delayed patients ($p \leq 0.001$).
Interpretation: Eteplirsen restored dystrophin in the 30 and 50 mg/kg/wk cohorts, and in subsequently treated, placebo-controlled subjects. Duration, more than dose, accounted for dystrophin production, also resulting in ambulation stability. No severe adverse events were encountered.

ANN NEUROL 2013;00:000–000

Duchenne muscular dystrophy (DMD) is a progressive, disabling genetic neuromuscular disorder caused by an absence of dystrophin, with an incidence of 1 in 5,000 newborn boys.[1] Affected boys develop muscle weakness in the first years of life, lose the ability to walk during childhood, and succumb to respiratory and

View this article online at wileyonlinelibrary.com. DOI: 10.1002/ana.23982

Received May 31, 2013, and in revised form Jul 5, 2013. Accepted for publication Jul 17, 2013.

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Members of the Eteplirsen Study Group are listed in the Appendix on page 10.

Additional Supporting Information may be found in the online version of this article.

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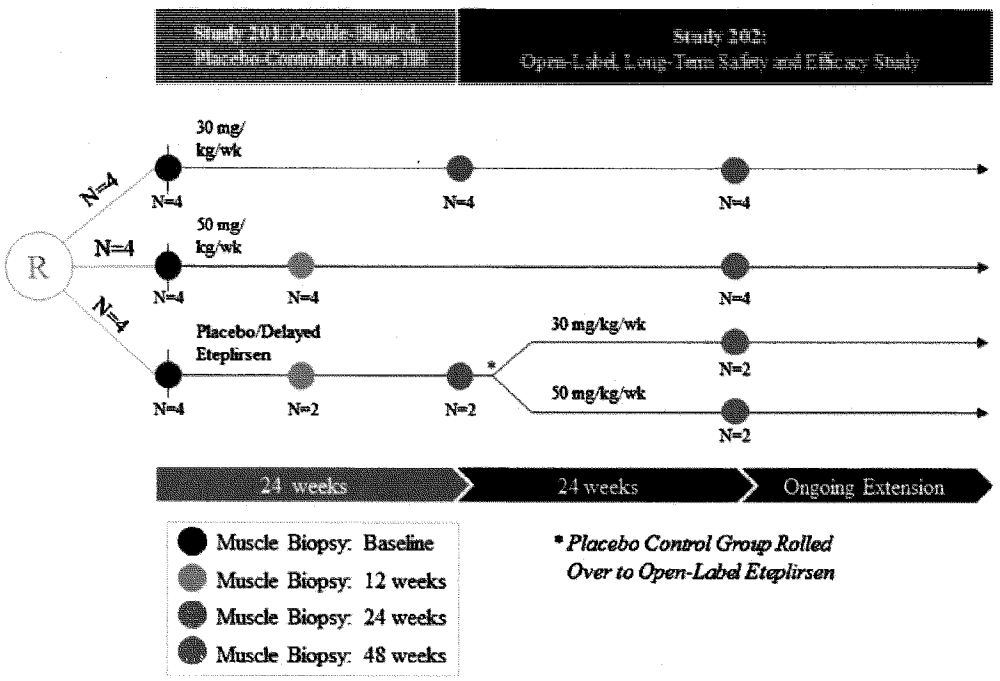


FIGURE 1: Study schema. Twelve Duchenne muscular dystrophy patients were randomized (R) to 1 of 3 cohorts in double-blind, placebo-controlled Study 201: Cohort 1, eteplirsen 30 mg/kg/wk; Cohort 2, eteplirsen 50 mg/kg/wk; and Cohort 3, placebo-treated, referred to as "placebo/delayed." At week 25, placebo/delayed patients in Cohort 3 switched to open-label treatment with either 30 or 50 mg/kg/wk eteplirsen. Patients were maintained on the same dose of eteplirsen under open-label extension Study 202. All patients underwent biceps biopsies at baseline and deltoid biopsies at week 48 for analysis of dystrophin. Additional biceps biopsies were obtained at week 12 (from patients in Cohort 2 and 2 patients in Cohort 3) or week 24 (from patients in Cohort 1 and 2 patients in Cohort 3). The 6-minute walk test was the primary functional outcome measure and was performed pretreatment and post-treatment through week 48 (every 4 weeks through week 36 and then week 48).

cardiac failure in their late teens or early 20s.[2–5] DMD is a universally fatal disease.

Exon skipping,[6–9] a promising disease-modifying approach for DMD, is induced by eteplirsen, a charge-neutral, phosphorodiamidate morpholino oligomer (PMO) that selectively binds to exon 51 of dystrophin pre-mRNA, restoring the open reading frame and enabling production of functional dystrophin. In patients with exon 51 amenable deletions (approximately 13% of DMD patients[10]), eteplirsen yields a truncated in-frame dystrophin protein, like those found in a less severe form of dystrophinopathy, Becker muscular dystrophy.[11,12]

In previous open-label trials, eteplirsen was given as a single intramuscular dose (Study 33[7]) or systemically (Study 28[9]) at doses up to 20 mg/kg/wk for 12 weeks. Although novel dystrophin was identified at the sarcolemma in both studies, Study 28 was not of sufficient duration to assess clinical outcomes. In the current trial, we employed a double-blind placebo-controlled protocol that has not been previously used for testing exon skipping. Regarding outcome measures, we assessed eteplirsen-induced dystrophin production, comparing treated to placebo cohorts; asked whether dystrophin production was affected by longer duration or a higher dose of treatment; and derermined whether the observed percentage of muscle fibers expressing dysttophin was sufficient to result in functional effects on the distance walked in the 6-minute walk test (6MWT).

Patients and Methods

Patients

Boys aged 7 to 13 years with confirmed out-of-frame DMD deletions potentially correctable by skipping exon 51 and the ability to walk 200 to 400 m on the 6MWT were eligible for this study. Patients had to have been on stable glucocorticoids (prednisone or deflazacort) for $\geq$24 weeks to be enrolled, including: 8 DMD boys taking 18–25 mg/day deflazacort; 1 boy on 20 mg/day prednisone, and another 2 boys taking 25 mg/day prednisone. One boy was taking a prednisone weekend dosing regimen of 75 mg on Fridays and 75 mg on Saturdays. Cardiac and pulmonary functions were stable.

Study Design

This trial (Fig 1) was a 24-week, randomized, double-blind, placebo-controlled study (Study 201) consisting of 3 cohorts (placebo, 30 mg/kg/wk, 50 mg/kg/wk) conducted at Nationwide Children's Hospital (NCH), followed by a long-term

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open-label extension study (Study 202) with 2 cohorts (30 or 50 mg/kg/wk) conducted at 10 additional sites throughout the United States through week 48, with the exclusive role of eteplirsen administration. After 24 weeks of double-blind dosing, the placebo-treated patients were crossed over to weekly dosing with eteplirsen and received 30 (n = 2) or 50 mg/kg (n = 2), and were thereafter identified as "placebo/delayed" cohorts.

Biopsies at all time points were done at NCH. Biceps muscle was biopsied from all patients at baseline to evaluate pretreatment dystrophin-positive fibers. To evaluate the effect of eteplirsen dose and treatment duration on dystrophin production, a second biopsy from the opposite biceps was collected at week 12 from the 4 patients in the 50 mg/kg cohort and 2 placebo-treated patients, and at week 24 from the 4 patients in the 30 mg/kg cohort and 2 placebo-treated patients. To evaluate the effect of continued exposure to eteplirsen on dystrophin production, a third biopsy was done on the left deltoid in all 12 patients at week 48.

All functional assessments (Studies 201 and 202), including the 6MWT, were performed at NCH (by the same clinical evaluators, L.P.L. and L.A.). The 6MWT was assessed on 2 consecutive days when muscle biopsies were scheduled (ie, pretreatment and weeks 12, 24, and 48). Single-day assessments were performed on weeks 4, 8, 16, 20, 32, and 36.

Study Drug

Single-use vials of either phosphate-buffered saline (PBS) or eteplirsen[13] (100 mg/ml, PBS) were diluted in 150 ml normal saline and infused over 60 minutes.

Safety and Pharmacokinetic Assessments

Vital signs, physical examinations, monitoring for injection site reactions, electrocardiograms, echocardiograms, and clinical laboratory testing, including serum and urine cystatin C and kidney injury molecule 1, were performed. T-cell responses to novel dystrophin protein were assessed via ELISpots.[14]

Eteplirsen's pharmacokinetic (PK) profile was estimated from plasma and urine collected postinfusion at week 12.

Efficacy Assessments

To evaluate dystrophin-positive fiber levels, immunohistochemical staining was done on 10 μm frozen sections of 3 separate blocks of biopsy tissue separated by at least 200 μm and evaluated by blinded expert muscle pathologists. For dystrophin localization, sections were stained with MANDYS106 NCL, a mouse monoclonal antibody to amino acids 1749–2248,[15,16] using standard immunofluorescence methodology.[9,14] Dystrophin-positive fibers and total fibers were counted, and the percentage of dystrophin-positive fibers was calculated across all samples. Pretreatment dystrophin values, composed of revertant fibers (representing somatic mutations that result in removal of additional exons from mRNA[17,18]), were subtracted from on-treatment values to determine the percentage of dystrophin-positive fibers resulting from eteplirsen treatment.

Dystrophin expression was quantified using BIOQUANT (Nashville, TN) image analysis software on MANDYS106-stained sections. Intensity of fibers expressing dystrophin from eteplirsen-treated patient biopsies was compared to normal control biopsies. Supportive measures were further provided by Western blots prepared from serial sections from the same blocks stained using NCL-Dys1 (Novacastra Laboratories, Newcastle Upon Tyne, UK) mouse monoclonal to amino acids 1181–1388.[17] Immunohistochemical analyses of β- and γ-sarcoglycan and neuronal nitric oxide synthase (nNOS) were also done. Exon skipping was confirmed by reverse transcriptase polymerase chain reaction (RT-PCR).[7]

The 6MWT was administered using the protocol established for DMD.[19] Additional functional measures were assessed at various visits and included the North Star Ambulatory Assessment, quantitative muscle testing, the 9-Hole Peg Test, pulmonary function testing (PFT), timed function tests, and quality of life (data not presented here).

Statistical Analysis

Dystrophin production was the primary endpoint at week 12 for the 50 mg/kg cohort, at week 24 for the 30 mg/kg cohort, and at week 48 for all patients. This design specifically compared dose versus duration of eteplirsen treatment. Changes from baseline at weeks 12 and 24 were compared separately from change from baseline for the combined placebo cohorts using analysis of covariance (ANCOVA) for ranked data, with baseline values and duration of DMD as covariates. Change from baseline at week 48 used a mixed model with treatment as fixed effect, and subject nested within treatment as random effect, with baseline value and time since DMD diagnosis as covariates. Additionally, paired t test was used to compare the on-treatment value with the baseline value.

Mixed model repeated measures (MMRM) was used to evaluate change from baseline in the 6MWT data (the critical functional endpoint) to week 24 and to week 48. Treatment, time, and treatment-by-time interaction terms were used as fixed effects, subject nested within treatment as random effect, and baseline value and time since DMD diagnosis as covariates. If there was strong evidence of deviation from normality, then ANCOVA for ranked data was used. Additionally, data distribution and the impact of outliers on the results were assessed by analyzing the modified intent-to-treat (mITT) population, which excluded ambulatory nonevaluable patients from the intent-to-treat (ITT) population. Type I error correction was not employed for any of these analyses.

SAS version 9.3 (Cary, NC) was used for all statistical analyses.

Results

Patient Characteristics

The patient characteristics are summarized in the Table. Patients in the 30 mg/kg cohort were older, taller, and heavier than the other 2 cohorts. The 12 enrolled patients represented 5 different genotypes, resulting in out-of-frame deletions correctable by exon 51 skipping.

Mean baseline 6MWT distance for all subjects was 381.9m (range = 261–456). The mean distance walked

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A

Cohort (n)	Week 12 Mean Change from BL, SE (p-value) *	Week 24 Mean Change from BL, SE (p-value) *	Week 48 Mean Change from BL, SE (p-value) †
All Eteplirsen (8)	NA	NA	47.3, 3.89 (≤0.001)
Eteplirsen 30mg/kg (4)	ND	22.9, 2.90 (≤0.002)	51.7, 3.54 (≤0.001)
Eteplirsen 50 mg/kg (4)	0.8, 3.55 (NS)	ND	42.9, 6.72 (≤0.008)
Placebo/Delayed Eteplirsen (4) ‡	-4.0, 2.92	-4.0, 2.92	37.7, 6.30 (≤0.009) §
Eteplirsen 30 mg/kg (2)	ND	-7.48, 1.00	33.6, 5.23
Eteplirsen 50 mg/kg (2)	-0.6, 5.16	ND	41.8, 13.30

B

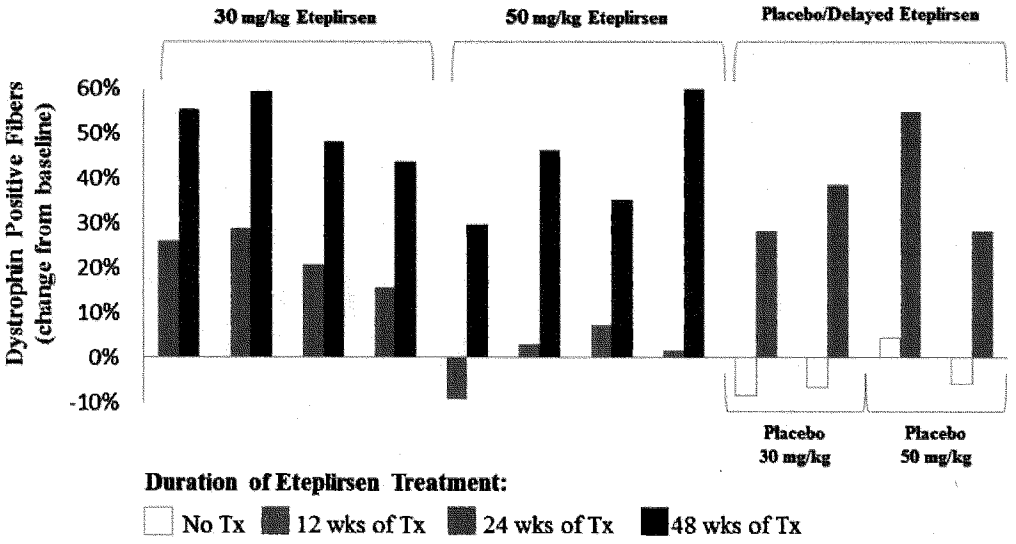


FIGURE 2: Dystrophin-positive muscle fibers after 12, 24, and 48 weeks of eteplirsen. (A) Mean absolute change from baseline in the percentage of dystrophin-positive fibers by treatment cohort; *p* values are for comparison between eteplirsen and placebo using the combined results from weeks 12 and 24, and are based on an analysis of covariance model for ranked data, with treatment as a fixed effect and baseline value and time since Duchenne muscular dystrophy diagnosis as covariates. Mean changes shown are based on descriptive statistics. †Probability values are from a paired *t* test comparing the week 48 value to baseline. ‡Results from the placebo-treated patients biopsied at weeks 12 and 24 are combined. *Placebo/delayed eteplirsen patients began receiving eteplirsen at week 25 and had received a total of 24 doses at week 48. BL = Baseline; NA = not applicable; ND = not done; NS = not significant; SE = standard error. (B) Change from baseline in dystrophin-positive fibers are shown by cohort and by duration of treatment with eteplirsen (Tx). The first biopsies (blue) at 12 weeks (50 mg/kg cohort) showed little or no dystrophin beyond expected numbers from revertant fibers. At 24 weeks (army green), there was a definite increase in dystrophin positive fibers. At 48 weeks (purple) the 30 and 50 mg/kg cohorts both showed significant dystrophin production. The placebo/delayed group biopsied at 12 weeks (blanks) showed only minimal fibers (could be fewer than baseline depending on the number of revertant fibers). By 48 weeks, the placebo/delayed group had been treated for 24 weeks and now showed significant dystrophin-positive fibers.

by the 30 mg/kg cohort was approximately 40 m less than that of the 2 other cohorts. Mean distances on the 6MWT at baseline were similar to those in other DMD studies.[20,21]

Safety and Pharmacokinetic Profile

Through week 48, eteplirsen was well tolerated, with no treatment-related adverse events (Supplementary Materials). No changes were observed in vital signs or physical examination, including injection site reactions. Electrocardiograms, echocardiograms, and PFTs remained stable, and no changes were observed in chemistries, hematology, coagulation, or renal or liver function. Mild and transient proteinuria was observed in a single placebo-treated patient. Dystrophin-induced T-cell responses were not observed.

Week 12 PK parameters revealed dose-proportional exposure and similar plasma clearance. The mean half-

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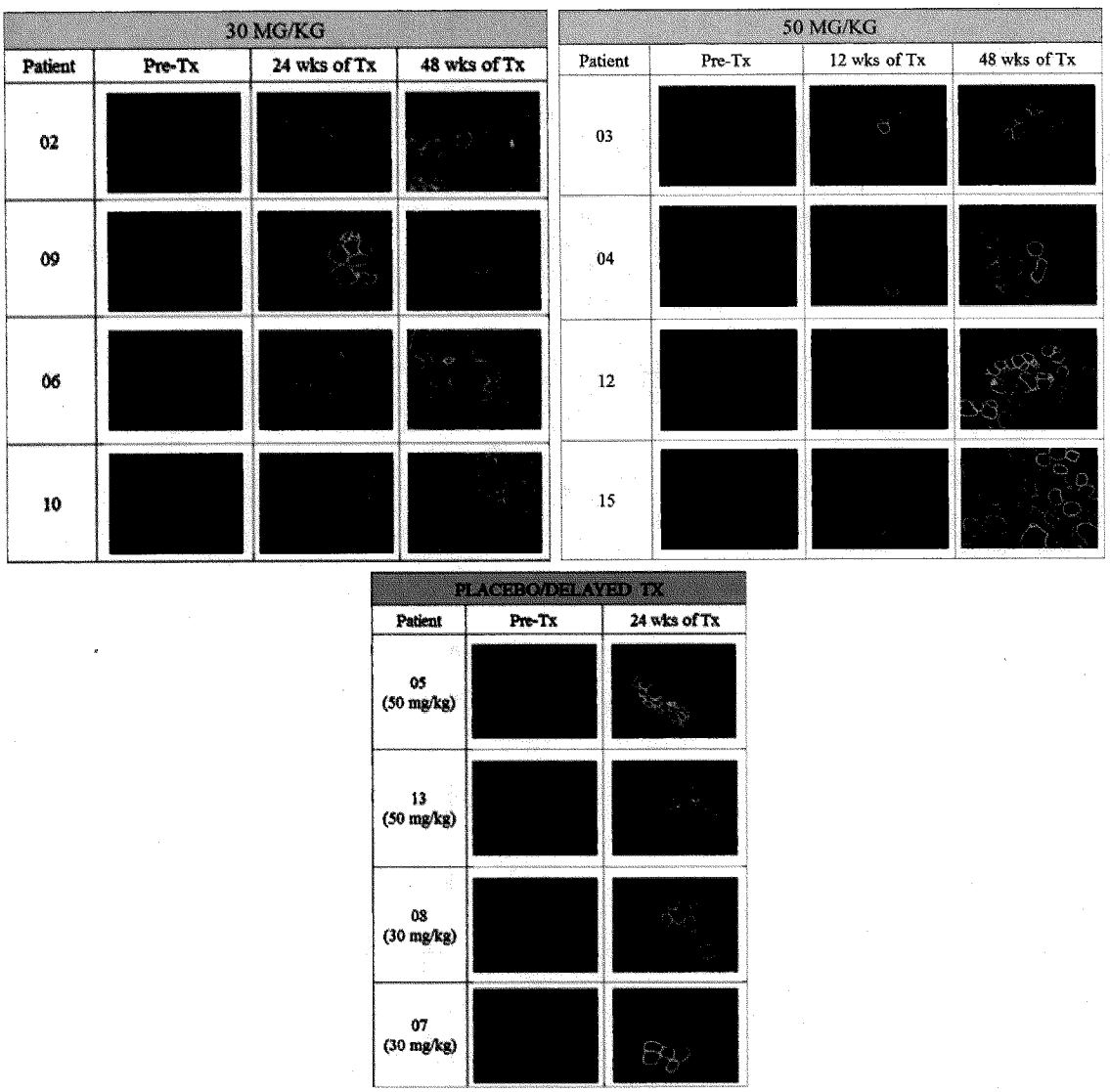


FIGURE 3: Effects of eteplirsen on the dystrophin-associated glycoprotein complex. Representative examples of time-dependent increases in dystrophin-positive fibers can be seen in relation to treatment for all participating study patients.

life was 3.3 and 3.2 hours for the 30 and 50 mg/kg cohorts, respectively. Renal clearance accounted for approximately 65 to 70% of total systemic clearance.

Dystrophin

Treatment with 50 mg/kg for 12 weeks resulted in no increases in percentage of dystrophin-positive fibers compared to pretreatment, and the change from baseline (mean = 0.8%, range = −9.3 to 7.4%) was not statistically different compared to the placebo cohorts (Fig 2). At week 24 (12 additional weeks of treatment with eteplirsen), the 30 mg/kg dose resulted in a 22.9% (range = 15.9–29.0%) increase from pretreatment ($p \leq 0.002$) compared to the combined placebo group. These data suggest that at least 12 weeks of treatment with eteplirsen is needed to produce perceptible increases in dystrophin production in muscle biopsies.

The within-cohort comparison of the percentage of dystrophin-positive fibers (eg, week 12 vs baseline for the 50 mg/kg cohort, and week 24 vs baseline for the 30mg/kg cohort) resulted in a statistically significant difference for the 30 mg/kg cohort ($p \leq 0.004$) but not fot the week 12, 50 mg/kg, or combined placebo cohorts.

At week 48 (see Fig 2), the 30 and 50 mg/kg cohorts showed significant increases ($p \leq 0.001$) in percentage of dystrophin-positive fibers (mean = 47.3%, range = 29.8–60.3%). The 4 patients in the placebo/delayed cohort taking 30 mg/kg (n = 2) and 50 mg/kg (n = 2) of eteplirsen also showed significant increases ($p \leq 0.008$, mean = 37.7%, range = 28.4–55.1%). The

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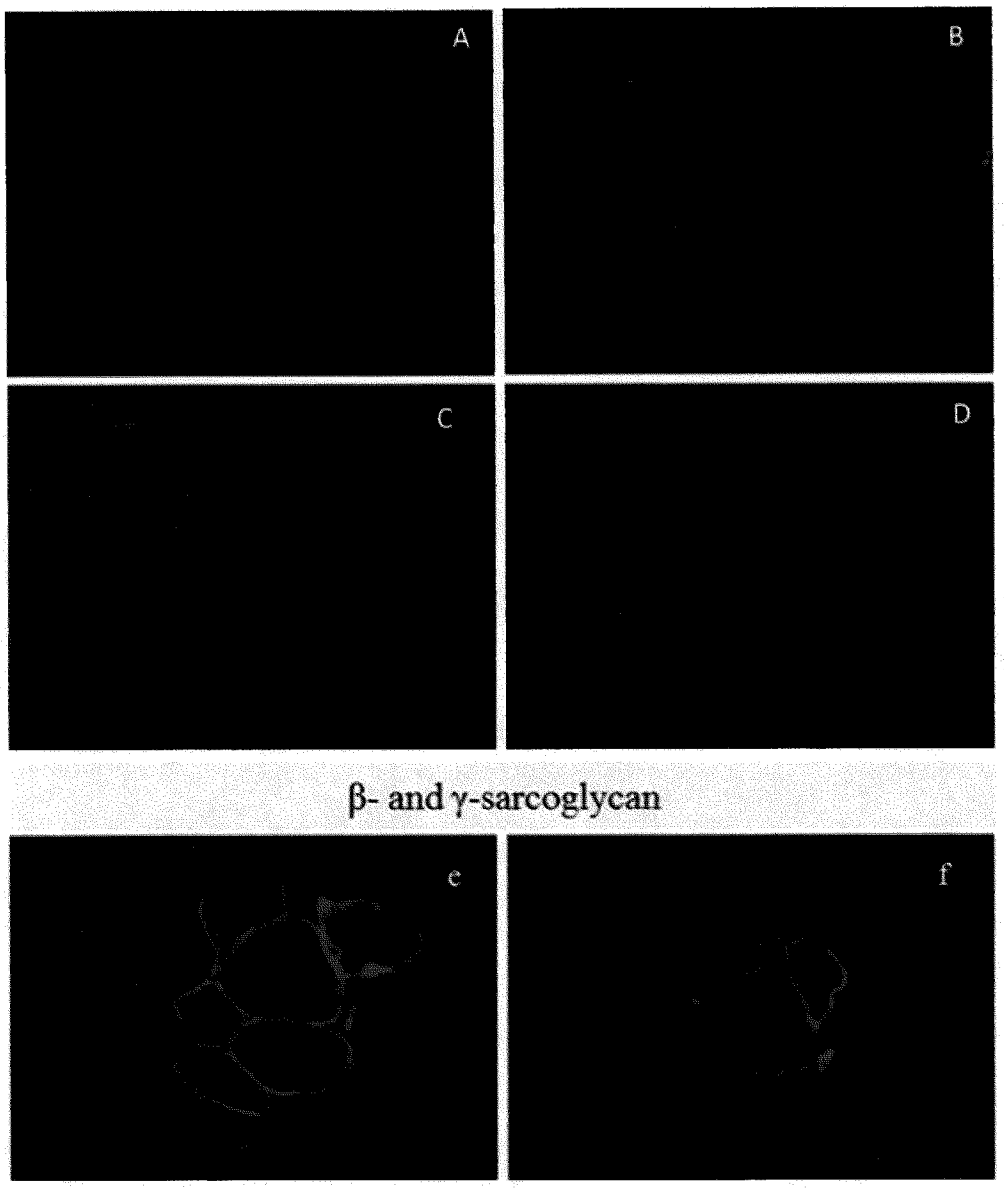


FIGURE 4: (A) Neuronal nitric oxide synthase (nNOS) staining in muscle from Duchenne muscular dystrophy with deletion in exon 52. (B, D) Restoration of nNOS binding site following eteplirsen treatment from Patient 006 at week 48. (C) Normal muscle showing nNOS binding (no treatment). Notice the nNOS binding in normal control is the same intensity as with eteplirsen. (E, F) β-Sarcoglycan (E) and γ-sarcoglycan (F) staining at week 48 (Patient 006), demonstrating restoration of the sarcoglycan complex with eteplirsen.

between-treatment comparisons of all cohorts, including between the combined eteplirsen and the placebo/delayed cohorts, resulted in no significant differences.

In agreement with these findings, eteplirsen significantly increased mean fluorescence signal intensity of muscle fibers expressing MANDYS106 at week 48 in the 30 mg/kg cohort ($p \leq 0.023$), the 50 mg/kg cohort ($p \leq 0.005$), the combined eteplirsen cohort ($p \leq 0.001$), and the placebo/delayed cohort ($p \leq 0.006$).

Figure 3 illustrates eteplirsen's time-dependent effect on the percentage of dystrophin-positive fibers, and Figure 4 illustrates the associated restoration of sarcolemmal nNOS and β- and γ-sarcoglycan. Dystrophin expression and exon skipping were confirmed by RT-PCR and Western blot (representative patient results are shown in Fig 5).

6MWT

The adjusted mean change using the MMRM model for the 6 MWT from baseline to week 24 was −25.8 m (±30.6) for the placebo cohort, and −128.2 m (±31.6) and −0.3 m (±31.2) for the 30 and 50 mg/kg cohorts,

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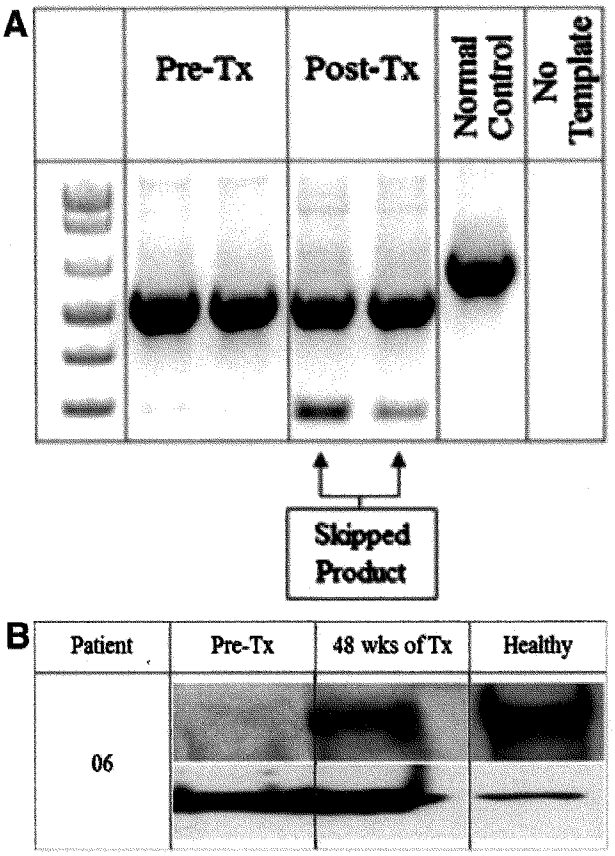


FIGURE 5: (A) Reverse transcriptase polymerase chain reaction shows skipped product (289bp) post-treatment (Tx) in the muscle of Patient 012 (deletions in exons 49–50). (B) Western blot results at baseline and at week 48 (deletion in exon 52) and from healthy control.

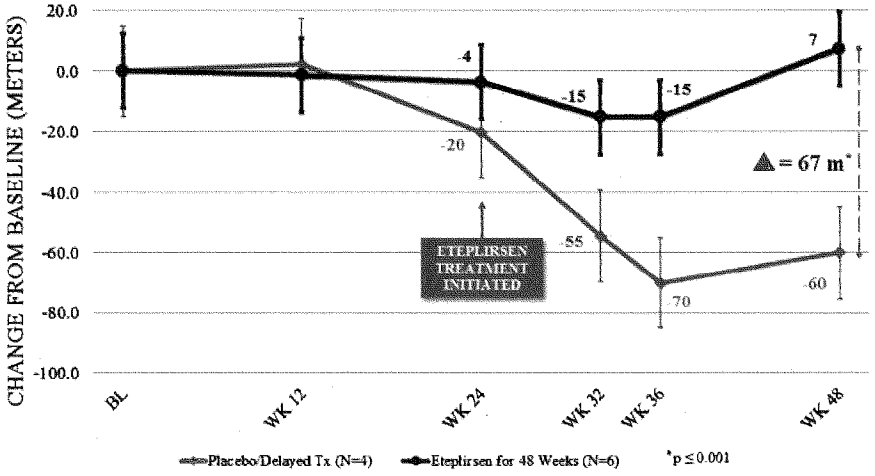


FIGURE 6: Functional efficacy of eteplirsen. The dark purple line shows the change from baseline (BL) in distance walked on the 6-minute walk test (6MWT) over time for the 6 evaluable patients who received eteplirsen from the start of Study 201 (the 2 boys who lost ambulation at or beyond week 24 were excluded from this analysis). The dark gray line shows change from baseline in distance walked on the 6MWT for the 4 patients who received placebo for the first 24 weeks and eteplirsen for the last 24 weeks. It is estimated from dystrophin expression studies and multiple biopsies that significant dystrophin was produced after 12 weeks. This is clearly indicated in the placebo/delayed cohort starting on eteplirsen at week 25 and stabilizing in function at week 36. The eteplirsen-treated cohorts diverged from placebo/delayed patients at week 12, after which they no longer showed significant decline.

respectively. The large decline in the 30 mg/kg cohort was directly attributable to Patients 009 and 010, who showed rapid disease progression immediately after enrollment. When these 2 patients were excluded from the cohort, the adjusted mean change from baseline was 14.2m (±14.4). As data distribution analysis revealed severe violation of normality assumption, the analysis was repeated using ANCOVA for ranked data, showing no significant differences between the 2 eteplirsen and placebo cohorts.

The adjusted mean change from baseline to week 48 on the 6MWT was −68.4 m (±37.6) for the placebo/delayed cohort, and −153.4 m (±38.7) and +21 m (±38.2) for the 30 and 50 mg/kg eteplirsen-treated cohorts, respectively (Fig 6). The large decline in the 30 mg/kg cohort was again due to Patients 009 and 010, and when they were excluded from the 30 mg/kg cohort, the adjusted mean change from baseline was 31.5m (±19.9). As data distribution analysis revealed severe violation of normality assumption, the analysis was repeated using ANCOVA for ranked data, showing no significant differences between the 30 mg/kg and placebo cohorts but a statistically significant difference between the 50 mg/kg and placebo/delayed cohorts ($p \leq 0.016$).

The progressive loss of ambulation is the hallmark of DMD, with most patients becoming wheelchair-dependent by age 10 to 14 years.[2,3] The 6MWT results for the 4 patients in the placebo/delayed cohort was consistent with natural history studies,[21–23] culminating in a loss of almost 70m by week 48. The previously mentioned 2 patients (009 and 010) in the 30 mg/kg cohort showed rapid disease progression evident in more advanced stages of the disease. Patient 009 walked 346m at baseline, but declined by 112m at week 4. When consistent increases in dystrophin-positive fibers were observed, he declined an additional 184m, and became nonambulatory. His identical twin (010) walked 261m at baseline but declined by 213m at week 24. These 2 patients were the tallest and among the oldest of the 12 patients, and had the lowest baseline 6MWT values, placing them at increased risk for imminent loss of ambulation.[21–23] The inclusion of their data in the statistical analysis resulted in severe deviation from normality due to being extreme values (outliers), requiring the use of data transformation for the ITT population (n = 12), which justifies further evaluation of the results after excluding them from the mITT population (n = 10). Both boys remained on eteplirsen with no treatment-related adverse events, maintained stable pulmonary and upper limb function, and showed increases in dystrophin-positive fibers at weeks 24 (20.8% and 15.9%) and 48 (48.3% and 43.6%).

The remaining 6 ambulation-evaluable patients in the 30 (n = 2) and 50 mg/kg (n = 4) cohorts who received eteplirsen for 48 weeks demonstrated stable performance on the 6MWT from baseline to week 48, which was significantly different (67.3m difference; $p \leq 0.001$) compared to the placebo/delayed cohort (see Fig 6). The 50 mg/kg cohort was also significantly different (87.4m difference; $p \leq 0.001$) compared to the placebo/delayed cohort.

Discussion

The data from this trial suggest the potential for eteplirsen as a safe and effective disease-modifying therapy for DMD, whose current management consists primarily of treatment with glucocorticoids.[24]

Eteplirsen resulted in increased dystrophin production in all patients treated for >12 weeks. Increases in dystrophin were observed in all patients following at least 24 weeks of treatment, including those who started eteplirsen at week 25 (placebo/delayed). Dystrophin intensity was accurately measured using BIOQUANT image analysis on the same fibers expressing dystrophin. Confirmation was further demonstrated by Western blots and by the restoration of components of the dystrophin-associated protein complex (eg, sarcoglycans) and the presence of the nNOS-binding site, localized to dystrophin spectrinlike repeats 16/17 of exon 45.

Treatment with eteplirsen for 48 weeks resulted in a 67.3m advantage compared to placebo/delayed treatment on the 6MWT in ambulation-evaluable patients. This difference exceeds the 28 to 44m treatment effects reported in several registration-directed studies,[25–28] as well as in DMD natural history studies.[20–22] Unfortunately, 2 boys (twins) randomized to the 30 mg/kg cohort rapidly lost ambulation and were excluded from the mITT analysis. This is justified on the basis of these patients experiencing a more advanced stage of the disease than the rest of the enrolled patients, although with a small sample size this could indicate variability in response. In a model developed by McDonald et al,[19] height was noted as a key criterion along with age and baseline 6MWT in predicting a more rapid progression to loss of ambulation. That is, the taller and older the subjects are, along with lower baseline 6MWT distance, the higher the predicted percentage of loss of ambulation. These 2 patients were among the oldest (9.8 years old), were the 2 tallest, and had the lowest baseline 6MWT distance among the entire study population. We also have magnetic resonance imaging confirmation of advanced disease in a separate study with DMD patients at a time point between weeks 24 and 28, revealing a severe loss of muscle tissue with replacement of fat and

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TABLE : Baseline Demography and Disease Characteristics

Treatment Arm	Placebo/Delayed Eteplirsen, n = 4	Eteplirsen, 30 mg/kg, n = 4	Eteplirsen, 30 mg/kg, n = 2[a]	Eteplirsen, 50 mg/kg, n = 4
Mutation, No. (%)				
45–50	0	2 (50)	0	1 (25)
48–50	0	1 (25)	1 (50)	0
49–50	3 (75)	0	0	2 (50)
50	1 (25)	0	0	0
52	0	1 (25)	1 (50)	1 (25)
Male gender, No. (%)	4 (100)	4 (100)	2 (100)	4 (100)
Age, yr				
Mean	8.5	9.3	9.5	8.5
SD	1.73	0.50	0.71	1.29
min, max	7, 10	9, 10	9, 10	7, 10
Height, cm				
Mean	119.3	130.5	124.0	121.3
SD	3.40	9.47	9.90	7.85
min, max	116, 124	117, 138	117, 131	117, 133
Weight, kg				
Mean	30.6	34.8	30.0	29.0
SD	6.04	7.05	6.38	6.38
min, max	22.1, 36.2	24.8, 39.8	24.8, 35.1	23.7, 38.3
Race, No. (%)				
Asian	0	1 (25)	1 (50)	0
White	4 (100)	3 (75)	1 (50)	4 (100)
6MWT, m[b]				
Mean	394.5	355.3	407.0	396.0
SD	42.25	74.78	49.50	26.61
min, max	364, 456	261, 442	372, 442	365, 429

[a]Ambulation-evaluable patients.
[b]6MWT results are the maximum observed value of 2 tests administered on 2 consecutive days during screening.
6MWT = 6-minute walk test; min = minimum; max = maximum; SD = standard deviation.

connective tissue that was much more extensive than in all of the other patients (manuscript in preparation: Krista H. Elvire Vandenborne).

The data presented here show a clear relationship between systemic treatment with eteplirsen (an exon-skipping drug; proof of mechanism of action by RT-PCR) and dystrophin production in DMD muscle as demonstrated by percentage of positive fibers, followed by a statistically significant difference in walking ability in treated versus placebo/delayed ambulation-evaluable patients. Eteplirsen's clinical benefit mirrored the time required to produce consistent increases in dystrophin. The majority of the patients in the 30 and 50 mg/kg cohorts maintained a stable walking distance over 48 weeks, whereas the patients in the placebo/delayed cohort stabilized around week 36 (12 weeks after eteplirsen exposure). This observed delay between initiation of eteplirsen and detectable dystrophin production and stabilization in clinical function likely results from an accumulation of novel dystrophin over time, possibly due

to its long half-life[29–32] and the need to achieve a steady state of dystrophin to optimize diffusion across the muscle. Furthermore, because splice switching oligomers do not target skeletal muscle specifically, their uptake is partly dependent on local events such as muscle perfusion, damage, and inflammation.[33] Because dystrophic muscle undergoes accelerated cycles of degeneration and regeneration, with some cells having less stable membranes than others at any time point, it is likely that some muscle fibers take up more drug than others, allowing them to respond more robustly. Over repeated doses, eteplirsen accesses more muscle fibers, thus allowing for more dystrophin-positive fiber production over time.

The benefits seen with eteplirsen in treating the underlying cause of DMD in patients amenable to skipping exon 51 should encourage the development of PMO technology to treat other genotypes amenable to exon skipping to potentially treat an estimated 70 to 80% of all DMD patients with dystrophin gene deletions.[10,33]

APPENDIX

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Acknowledgment

This study was funded by Sarepta Therapeutics and was registered on ClinicalTrials.gov under identification number NCT01396239. The Muscular Dystrophy Association and Parent Project Muscular Dystrophy provided funds for patient travel. Support was also provided by NCRR/NIH (UL1 RR024992) and NIH Roadmap for Medical Research to Anne Connolly, MD. We gratefully acknowledge the patients and their families for their participation in this study. We thank the members of the Eteplirsen Study Group (see Supplementary Appendix) and their supporting staff who were instrumental in the conduct of this study and collection of the data. We also thank Professor Francesco Muntoni, MD. (University College London) and Craig McDonald, MD. (University of California Davis School of Medicine) for their input on study design and data analysis. We also thank the following Sarepta employees Kate Haviland, MBA and Bo Cumbo for important assistance with data interpretation and editing of this manuscript; and Charlene Brathwaite, BA for assistance with clinical trial management.

Potential Conflicts of Interest

Kate Melia, Peter Sazani, Jay B. Saoud, and Ed Kaye are employed at Sarepta Therapeutics. The study data was generated at Nationwide Children's Hospital and they were not involved in that process.

References

1. Mendell JR, Shilling C, Leslie ND, et al. Evidence-based path to newborn screening for Duchenne muscular dystrophy. Ann Neurol 2012;71:304–313.
2. McDonald CM, Abresch RT, Carter GT, et al. Profiles of neuromuscular diseases. Duchenne muscular dystrophy. Am J Phys Med Rehabil 1995;74:S70–S92.
3. Bushby K, Finkel R, Birnkrant DJ, et al. Diagnosis and management of Duchenne muscular dystrophy, part 1: diagnosis, and pharmacological and psychosocial management. Lancet Neurol 2010;9:77–93.
4. Kohler M, Clarenbach CF, Böni L, et al. Quality of life, physical disability and respiratory impairment in Duchenne muscular dystrophy. Am J Respir Crit Care Med 2005;172:1032–1036.
5. Passamano L, Taglia A, Palladino A, et al. Improvement of survival in Duchenne muscular dystrophy: retrospective analysis of 835 patients. Acta Myol 2012;31:121–125.
6. van Deutekom JC, Janson AA, Ginjaar IB, et al. Local dystrophin restoration with antisense oligonucleotide PRO051. N Engl J Med 2007;357:2677–2686.
7. Kinali M, Arechavala-Gomeza V, Feng L, et al. Local restoration of dystrophin expression with the morpholino oligomer AVI-4658 in Duchenne muscular dystrophy: a single-blind, placebo-controlled, dose-escalation, proof-of-concept study. Lancet Neurol 2009;8:918–928.
8. Goemans NM, Tulinius M, van den Akker JT, et al. Systemic administration of PRO051 in Duchenne's muscular dystrophy. N Engl J Med 2011;364:1513–1522.
9. Cirak S, Arechavala-Gomeza V, Guglieri M, et al. Exon skipping and dystrophin restoration in patients with Duchenne muscular dystrophy after systemic phosphorodiamidate morpholino oligomer treatment: an open-label, phase 2, dose-escalation study. Lancet 2011;378:595–605.

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10. Aartsma-Rus A, Fokkema I, Verschuuren J, et al. Theoretic applicability of antisense-mediated exon skipping for Duchenne muscular dystrophy mutations. Hum Mutat 2009;30:293–299.

11. Muntoni F, Torelli S, Ferlini A. Dystrophin and mutations: one gene, several proteins, multiple phenotypes. Lancet Neurol 2003; 2:731–740.

12. Bushby KM, GardnerMedwin D. The clinical, genetic and dystrophin characteristics of Becker muscular dystrophy. I. Natural history. J Neurol 1993;240:98104.

13. Arechavala-Gomeza V, Graham IR, Popplewell LJ, et al. Comparative analysis of antisense oligonucleotide sequences for targeted skipping of exon 51 during dystrophin pre-mRNA splicing in human muscle. Hum Gene Ther 2007;18:798–810.

14. Mendell JR, Campbell K, Rodino-Klapac L, et al. Dystrophin immunity revealed by gene therapy in Duchenne muscular dystrophy. N Engl J Med 2010;363:1429–1437.

15. Nguyen TM, Morris GE. Use of epitope libraries to identify exon-specific monoclonal antibodies for characterization of altered dystrophins in muscular dystrophy. Am J Hum Genet 1993;52:1057–1066.

16. Arechavala-Gomeza V, Kinali M, Feng L, et al. Immunohistological intensity measurements as a tool to assess sarcolemma-associated protein expression. Neuropathol Appl Neurobiol 2010;36:265–274.

17. Klein CJ, Coovert DD, Bulman DE, et al. Somatic reversion/suppression in Duchenne muscular dystrophy (DMD): evidence supporting a frame-restoring mechanism in rare dystrophin-positive fibers. Am J Hum Genet 1992;50:950–959.

18. Winnard AV, Mendell JR, Prior TW, et al. Frameshift deletions of exons 3–7 and revertant fibers in Duchenne muscular dystrophy: mechanisms of dystrophin production. Am J Hum Genet 1995;56: 158–166.

19. McDonald CM, Henricson EK, Han JJ, et al. The 6-minute walk test as a new outcome measure in Duchenne muscular dystrophy. Muscle Nerve 2010;41:500–510.

20. Mazzone E, Vasco G, Sormani MP, et al. Functional changes in Duchenne muscular dystrophy: a 12-month longitudinal cohort study. Neurology 2011;77:250–256.

21. McDonald CM, Henricson EK, Han JJ, et al. The 6-minute walk test in Duchenne/Becker muscular dystrophy: longitudinal observations. Muscle Nerve 2010;42:966–974.

22. McDonald CM, Henricson EK, Abresch RT, et al. The 6-minute walk test and other clinical endpoints in severe dystrophinopathy: reliability, concurrent validity, and minimal clinically important differences from a multicenter study. Muscle Nerve 2013; May 14. [Epub ahead of print].

23. McDonald CM, Henricson, EK, Abresch, RT, et al. The 6-minute walk test and other endpoints in nonsense-mutation-mediated dystrophinopathy: longitudinal natural history observations in a multicenter study. Muscle Nerve 2013 May 16. [Epub ahead of print].

24. Strober JB. Therapeutics in Duchenne muscular dystrophy. NeuroRx 2006;3:225–234.

25. Muenzer J, Wraith JE, Beck M, et al. A phase II/III clinical study of enzyme replacement therapy with idursulfase in mucopolysaccharidosis II (Hunter syndrome). Genet Med 2006;8:456–473.

26. Rubin LJ, Badesch DB, Barst RJ, et al. Bosentan therapy for pulmonary arterial hypertension. N Engl J Med 2002;346:896–903; erratum 1258.

27. van der Ploeg AT, Clemens PR, Corzo D, et al. A randomized study of alglucosidase alfa in late onset Pompe's disease. N Engl J Med 2010;362:1396–1406.

28. du Bois RM, Weycker D, Albera C, et al. Six-minute-walk test in idiopathic pulmonary fibrosis: test validation and minimal clinically important difference. Am J Respir Crit Care Med 2011;183:1231–1237.

29. Ahmad A, Brinson M, Hodges BL, et al. Mdx mice inducibly expressing dystrophin provide insights into the potential of gene therapy for Duchenne muscular dystrophy. Hum Mol Genet 2000; 9:2507–2515.

30. Hoffman EP, Bronson A, Levin AA, et al. Restoring dystrophin expression in Duchenne muscular dystrophy muscle: progress in exon skipping and stop codon read through. Am J Pathol 2011; 179:12–22.

31. Fletcher S, Honeyman K, Fall AM, et al. Morpholino oligomer-mediated exon skipping averts the onset of dystrophic pathology in the mdx mouse. Mol Ther 2007;15:1587–1592.

32. Yokota T, Lu QL, Partridge T, et al. Efficacy of systemic morpholino exon-skipping in Duchenne dystrophy dogs. Ann Neurol 2009;65:667–676.

33. Aartsma-Rus A, Janson AA, Kaman WE, et al. Antisense-induced multiexon skipping for Duchenne muscular dystrophy makes more sense. Am J Hum Genet 2004;74:83–92.

16.1.12 Important Publications Referenced in Report

Refer to Section 15 in the Clinical Study Report.

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