

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

21-538

PROPRIETARY NAME REVIEW(S)



**Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Surveillance and Epidemiology**

Date: January 17, 2008

To: Mary Parks, M.D., Director
Division of Metabolic and Endocrinology Products

Through: Denise Toyer, Pharm.D., Deputy Director
Carol Holquist, R.Ph., Director
Division of Medication Errors and Technical Support

From: Kristina C. Arnwine, Pharm.D., Acting Safety Evaluator Team Leader

Subject: Final Name Review for Accretropin

Drug Name(s): Somatropin rDNA Origin Injection

Submission Number: NDA #: 21-538

Application Type/Number:

Applicant/sponsor: _____ **b(4)**

OSE RCM #: 2007-2441

*****NOTE: This review contains proprietary and confidential information that should not be released to the public.*****

CONTENTS

EXECUTIVE SUMMARY	1
1 BACKGROUND	1
1.1 Introduction.....	1
1.2 Regulatory History	1
1.3 Product Information	1
2 METHODS AND MATERIALS	1
2.1 Proprietary Name Risk Assessment	2
2.2 Safety Evaluator Risk Assessment of the Proposed Proprietary Name	4
2.3 Label and Labeling Risk Assessment	6
3 RESULTS.....	6
3.1 Database and information sources	6
3.2 CDER Expert panel discussion	7
3.3 Safety evaluator risk assessment.....	7
3.4 Label and Labeling Risk Assessment	7
4 DISCUSSION	7
5 CONCLUSIONS	8
6 Recommendations	9
6.1 Proprietary name:.....	9
6.2 label and Labeling.....	9
7 REFERENCES	9
APPENDICES	1

EXECUTIVE SUMMARY

The results of the Proprietary Name Risk Assessment found that the proposed name, Accretropin, has some similarity to other proprietary and established drug names, but the findings of the FMEA process indicate that the proposed name does not appear to be vulnerable to name confusion that could lead to medication errors. Thus, DMETS has no objections to the use of the proprietary name, Accretropin.

The results of the Label and Labeling Risk Assessment found that the presentation of information and design of the proposed carton and container labels appears to be vulnerable to confusion that could lead to medication errors. DMETS believes the risks we have identified can be addressed and mitigated prior to drug approval, and provides recommendations in Section 6 that aim at reducing the risk of medication errors.

However; if any of the proposed product characteristics as stated in this review are altered prior to approval of the product, DMETS rescinds this Risk Assessment finding, and recommends that the name be resubmitted for review. Additionally, if the product approval is delayed beyond 90 days from the signature date of this review, the proposed name must be resubmitted for evaluation.

1 BACKGROUND

Accretropin is the proprietary name for the proposed product, Somatropin rDNA Origin Injection, to be submitted for DMETS review.

1.1 INTRODUCTION

This review was written in response to a request from the Division of Metabolism and Endocrinology Products (DMEP) to re-evaluate the product for its potential to contribute to medication errors. The proposed proprietary name, Accretropin, is evaluated to determine if the name could be potentially confused with other proprietary or established drug names.

1.2 REGULATORY HISTORY

DMETS completed the first review of the proposed name, Accretropin, in OSE Review #2006-820, dated February 2, 2007, in which DMETS had no objections to the use of the proprietary name. Additionally, label and labeling changes were recommended in this review.

1.3 PRODUCT INFORMATION

Accretropin is a recombinant growth hormone indicated for long-term treatment of growth failure in pediatric patients and treatment of short stature associated with Turner syndrome in pediatric patients. The usual dose of Accretropin is 0.18 mg/kg to 0.36 mg/kg divided into equal doses given six or seven days per week. Accretropin is supplied in a one milliliter multi-dose vial.

2 METHODS AND MATERIALS

FDA's Proprietary Name Risk Assessment considers the potential for confusion between the proposed proprietary name, Accretropin, and the proprietary and established names of drug products existing in the marketplace and those pending IND, NDA, and ANDA products currently under review by the Agency.

For the proprietary name, Accretropin, the medication error staff of DMETS searched a standard set of databases and information sources to identify names with orthographic and phonetic similarity (see Sections 2.1.1 for detail) and held an CDER Expert Panel discussion to gather professional opinions on the safety of the proposed proprietary name (see 2.1.1.2).

The Safety Evaluator assigned to the Proprietary Name Risk Assessment is responsible for considering the collective findings, and provides an overall risk assessment of the proposed proprietary name (see detail 2.1.4). The overall risk assessment is based on the findings of a Failure Modes and Effects Analysis (FMEA) of the proprietary name, and is focused on the avoidance of medication errors. FMEA is a systematic tool for evaluating a process and identifying where and how it might fail.¹ FMEA is used to analyze whether the drug names identified with look- or sound-alike similarity to the proposed name could cause confusion that subsequently lead to medication errors in the clinical setting. DMETS defines a medication error as any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer.² DMETS uses the clinical expertise of the medication error staff to anticipate the conditions of the clinical setting that the product is likely to be used in based on the characteristics of the proposed product.

In addition, the product characteristics provide the context for the verbal and written communication of the drug names and can interact with the orthographic and phonetic attributes of the names to increase the risk of confusion when there is overlap, or, in some instances, decrease the risk of confusion by helping to differentiate the products through dissimilarity. As such, the Staff considers the product characteristics associated with the proposed drug throughout the risk assessment, since the product characteristics of the proposed may provide a context for communication of the drug name and ultimately determine the use of the product in the *usual* clinical practice setting.

Typical product characteristics considered when identifying drug names that could potentially be confused with the proposed drug name include, but are not limited to established name of the proposed product, the proposed indication, dosage form, route of administration, strength, unit of measure, dosage units, recommended dose, typical quantity or volume, frequency of administration, product packaging, storage conditions, patient population, and prescriber population. Because drug name confusion can occur at any point in the medication use process, DMETS considers the potential for confusion throughout the entire U.S. medication use process, including drug procurement, prescribing and ordering, dispensing, administration, and monitoring the impact of the medication.³

2.1 PROPRIETARY NAME RISK ASSESSMENT

2.1.1 Search Criteria

The Medication Error Staff consider the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted as outlined in Appendix A.

For this review, particular consideration was given to drug names beginning with the letter 'A' when searching to identify potentially similar drug names, as 75% of the confused drug names reported by the USP-ISMP Medication Error Reporting Program involve pairs beginning with the same letter.⁴

To identify drug names that may look similar to Accretropin, the Staff also consider the other orthographic appearance of the name on lined and unlined orders. Specific attributes taken into

¹ Institute for Healthcare Improvement (IHI). Failure Modes and Effects Analysis. Boston. IHI:2004.

² National Coordinating Council for Medication Error Reporting and Prevention. <http://www.nccmerp.org/aboutMedErrors.html>. Last accessed 10/11/2007.

³ Institute of Medicine. Preventing Medication Errors. The National Academies Press: Washington DC. 2006.

⁴ Institute for Safe Medication Practices. Confused Drug name List (1996-2006). Available at <http://www.ismp.org/Tools/confuseddrugnames.pdf>

⁵ Kondrack, G and Dorr, B. Automatic Identification of Confusable Drug Names. Artificial Intelligence in Medicine (2005)

consideration include the length of the name (11 letters), upstrokes (capital letter 'A', lower case 't'), downstrokes (lowercase 'p'), cross-strokes ('t'), and dotted letters ('i'). Additionally, several letters in Accretropin may be vulnerable to ambiguity when scripted, including the letter 'A' may appear as 'C' or 'Cl'; lower case 'r' appear as a lower case 'n' or 's'; and 'e' may appear as 'i' and vice versa. As such, the Staff also considers these alternate appearances when identifying drug names that may look similar to Accretropin.

When searching to identify potential names that may look or sound similar to Accretropin, the Medication Error Staff search for names with similar number of syllables (4), stresses (ac-creh-TROH-pin or ac-CREH-troh-pin), and placement of vowel and consonant sounds. DMETS notes that there is no way of testing all variance in phonetic pronunciation that occurs from person to person when the name is spoken (i.e., regional phonetic accents). Additionally, the Sponsor's intended pronunciation of the proprietary name could not be expressly taken into consideration, as this was not provided with the proposed name submission.

The Staff also consider the product characteristics associated with the proposed drug throughout the identification of similar drug names, since the product characteristics of the proposed drug ultimately determine the use of the product in the clinical practice setting. For this review, the Medication Error Staff were provided with the following information about the proposed product: the proposed proprietary name (Accretropin) the established name (Somatropin), proposed indication (growth failure in pediatric patients and short stature in patients with Turner syndrome), strength (5 mg/mL), dose (growth hormone deficiency – 0.18 mg/kg to 0.3 mg/kg, Turner Syndrome – 0.36 mg/kg), frequency of administration (daily), route (subcutaneous) and dosage form of the product (injection). Appendix A provides a more detailed listing of the product characteristics the Medication Error Staff generally take into consideration.

Lastly, the Medication Error Staff also consider the potential for the proposed name to inadvertently function as a source of error for reasons other than look and sound-alike name confusion. Post-marketing experience has demonstrated that proprietary names (or components of the proprietary name) can be a source of error in a variety of ways. As such, these broader safety implications of the name are considered and evaluated throughout this assessment and the Medication Error Staff provide additional comments related to the safety of the proposed name or product based on their professional experience with medication errors.

2.1.2 Data base and information sources

The proposed proprietary name, Accretropin, was provided to the medication error staff of DMETS to conduct a search of the internet, several standard published drug product reference texts, and FDA databases to identify existing and proposed drug names that may sound-alike or look-alike to Accretropin using the criteria outlined in 2.1.1. A standard description of the databases used in the searches is provided in Section 7. To complement the process, the Medication Error Staff use a computerized method of identifying phonetic and orthographic similarity between medication names. The program, Phonetic and Orthographic Computer Analysis (POCA), uses complex algorithms to select a list of names from a database that have some similarity (phonetic, orthographic, or both) to the trademark being evaluated. Lastly, the Medication Error Staff review the USAN stem list to determine if any USAN stems are present within the proprietary name. The findings of the individual Safety Evaluators were then pooled and presented to the Expert Panel.

2.1.3 CDER Expert Panel Discussion

An Expert Panel Discussion was held by DMETS to gather CDER professional opinions on the safety of the product and the proprietary name, Accretropin. Potential concerns regarding drug marketing and promotion related to the proposed names were also discussed. This group is composed of DMETS

Medication Errors Prevention Staff and representatives from the Division of Drug Marketing, Advertising, and Communications (DDMAC).

The pooled results of the medication error staff were presented to the Expert Panel for consideration. Based on the clinical and professional experiences of the Expert Panel members, the Panel may recommend the addition of names, additional searches by the Safety Evaluator to supplement the pooled results, or general advice to consider when reviewing the proposed proprietary name.

2.2 SAFETY EVALUATOR RISK ASSESSMENT OF THE PROPOSED PROPRIETARY NAME

Based on the criteria set forth in Section 2.1.1, the Safety Evaluator Risk Assessment applies their individual expertise gained from evaluating medication errors reported to FDA to conduct a Failure Modes and Effects Analysis and provide an overall risk of name confusion. Failure Mode and Effects Analysis (FMEA) is a systematic tool for evaluating a process and identifying where and how it might fail.⁶ When applying FMEA to assess the risk of a proposed proprietary name, DMETS seeks to evaluate the potential for a proposed name to be confused with another drug name as a result of the name confusion and cause errors to occur in the medication use system. FMEA capitalizes on the predictable and preventable nature of medication errors associated with drug name confusion. FMEA allows the Agency to identify the potential for medication errors due to look- or sound-alike drug names prior to approval, where actions to overcome these issues are easier and more effective than remedies available in the post-approval phase.

In order to perform an FMEA of the proposed name, the Safety Evaluator must analyze the use of the product at all points in the medication use system. Because the proposed product is not yet marketed, the Safety Evaluator anticipates the use of the product in the usual practice settings by considering the clinical and product characteristics listed in Appendix A. The Safety Evaluator then analyzes the proposed proprietary name in the context of the usual practice setting and works to identify potential failure modes and the effects associated with the failure modes.

In the initial stage of the Risk Assessment, the Safety Evaluator compares the proposed proprietary name to all of the names gathered from the above searches, expert panel evaluation, and studies, and identifies potential failure modes by asking: "Is the name Accretropin convincingly similar to another drug name, which may cause practitioners to become confused at any point in the usual practice setting?" An affirmative answer indicates a failure mode and represents a potential for Accretropin to be confused with another proprietary or established drug name because of look- or sound-alike similarity. If the answer to the question is no, the Safety Evaluator is not convinced that the names possess similarity that would cause confusion at any point in the medication use system, and the name is eliminated from further review.

In the second stage of the Risk Assessment, all potential failure modes are evaluated to determine the likely *effect* of the drug name confusion, by asking "Could the confusion of the drug names conceivably result in medication errors in the usual practice setting?" The answer to this question is a central component of the Safety Evaluator's overall risk assessment of the proprietary name. If the Safety Evaluator determines through FMEA that the name similarity would ultimately not be a source of medication errors in the usual practice setting, the name is eliminated from further analysis. However, if the Safety Evaluator determines through FMEA that the name similarity could ultimately cause medication errors in the usual practice setting, the Safety Evaluator will then recommend that an alternate proprietary name be used. In rare instances, the FMEA findings may provide other risk-reduction strategies, such as product reformulation to avoid an overlap in strength or an alternate modifier designation may be recommended as a means of reducing the risk of medication errors resulting from drug name confusion.

⁶ Institute for Healthcare Improvement (IHI). Failure Modes and Effects Analysis. Boston. IHI:2004.

DMETS will object to the use of proposed proprietary name when the one or more of the following conditions are identified in the Safety Evaluator's Risk Assessment:

1. DDMAC finds the proposed proprietary name misleading from a promotional perspective, and the review Division concurs with DDMAC's findings. The Federal Food, Drug, and Cosmetic Act provides that labeling or advertising can misbrand a product if misleading representations are made or suggested by statement, word, design, device, or any combination thereof, whether through a trade name or otherwise. [21 U.S.C 321(n); see also 21 U.S.C. 352(a) & (n)].
2. DMETS identifies that the proposed proprietary name is misleading because of similarity in spelling or pronunciation to another proprietary or established name of a different drug or ingredient [CFR 201.10.(C)(5)].
3. FMEA identifies potential for confusion between the proposed proprietary name and other proprietary or established drug names, and demonstrates that medication errors are likely to result from the drug name confusion under the conditions of usual clinical practice.
4. The proposed proprietary name contains an USAN stem, particularly in a manner that is contradictory to the USAN Council's definition.
5. Medication Error Staff identify a potential source of medication error within the proposed proprietary name. The proprietary name may be misleading, or inadvertently introduce ambiguity and confusion that leads to errors. Such errors may not necessarily involve confusion between the proposed drug another drug product.

In the event that DMETS objects to the use of the proposed proprietary name, based upon the potential for confusion with another proposed (but not yet approved) proprietary name, DMETS will provide a contingency objection based on the date of approval: whichever product is awarded approval first has the right to the use the name, while DMETS will recommend that the second product to reach approval seek an alternative name.

If none of these conditions are met, then DMETS will not object to the use of the proprietary name. If any of these conditions are met, then DMETS will object to the use of the proprietary name. The threshold set for objection to the proposed proprietary name may seem low to the Sponsor; however, the safety concerns set forth in criteria 1 through 5 are supported either by FDA Regulation or by external healthcare authorities, including the IOM, WHO, JCAHO, and ISMP, all who have examined medication errors resulting from look- or sound-alike drug names and called for Regulatory Authorities to address the issue prior to approval.

Furthermore, DMETS contends that the threshold set for the Proprietary Name Risk Assessment is reasonable because proprietary drug name confusion is a predictable and preventable source of medication error that, in many instances, can be identified and remedied prior to approval to avoid patient harm.

Additionally, post-marketing experience has demonstrated that medication errors resulting from drug name confusion are notoriously difficult to remedy post-approval. Educational efforts and so on are low-leverage strategies that have proven to have limited effectiveness at alleviating the medication errors involving drug name confusion. Higher-leverage strategies, such as drug name changes, have been undertaken in the past; but at great financial cost to the Sponsor, and at the expense of the public welfare, not to mention the Agency's credibility as the authority responsible for the approving the error-prone proprietary name. Moreover, even after Sponsor's have changed a product's proprietary name in the post-approval phase, it is difficult to eradicate the original proprietary name from practitioner's vocabulary, and as such, the Agency has continued to receive reports of drug name confusion long after a name change in some instances. Therefore, DMETS believes that post-approval efforts at reducing name

confusion errors should be reserved for those cases in which the potential for name confusion could not be predicted prior to approval (see limitations of the process).

If DMETS objects to a proposed proprietary name on the basis that drug name confusion could lead to medication errors, the FMEA process is used to identify strategies to reduce the risk of medication errors. DMETS is likely to recommend that the Sponsor select an alternative proprietary name and submit the alternate name to the Agency for DMETS to review. However, in rare instances FMEA may identify plausible strategies that could reduce the risk of medication error of the currently proposed name, and so DMETS may be able to provide the Sponsor with recommendations that reduce or eliminate the potential for error would render the proposed name acceptable.

2.3 LABEL AND LABELING RISK ASSESSMENT

The label and labeling of a drug product are the primary means by which practitioners and patients (depending on configuration) interact with the pharmaceutical product. The carton and container labels communicate critical information including proprietary and established name, strength, form, container quantity, expiration, and so on. The insert labeling is intended to communicate to practitioners all information relevant to the approved uses of the drug, including the correct dosing and administration.

Given the critical role that the label and labeling has in the safe use of drug products, it is not surprising that 33 percent of medication errors reported to the USP-ISMP Medication Error Reporting Program may be attributed to the packaging and labeling of drug products, including 30 percent of fatal errors.⁷

Because DMETS staff analyze reported misuse of drugs, DMETS staff are able to use this experience to identify potential errors with all medication similarly packaged, labeled or prescribed. DMETS uses FMEA and the principles of human factors to identify potential sources of error with the proposed product labels and insert labeling, and provided recommendations that aim at reducing the risk of medication errors.

For this product the Sponsor submitted on April 23, 2007 and March 27, 2007 the following labels and insert labeling for DMETS review (see Appendix D and E for images):

- Container: 1 mL vial
- Carton
- Prescribing Information

3 RESULTS

3.1 DATABASE AND INFORMATION SOURCES

DMETS conducted a search of the internet, several standard published databases and information sources (see Section 7 References) for existing drug names which sound-alike or look-alike to Accretropin to a degree where potential confusion between drug names could occur and result in medication errors in the usual clinical practice settings. In total, 11 names were identified as having some similarity to the name Accretropin.

Seven of the eleven names were thought to look like Accretropin, which include: Accuretic, Homatropine, Accutane, Accolate, Genotropin, Acetaminophen, and Acitretin. Three of the eleven names were thought to sound like Accretropin, which include: Protoprin, Oxaprozin, and Acrivastine. The remaining name, Atropine, was thought to look and sound similar to Accretropin.

⁷ Institute of Medicine. Preventing Medication Errors. The National Academies Press: Washington DC. 2006. p275.

3.2 CDER EXPERT PANEL DISCUSSION

The Expert Panel reviewed the pool of names identified by DMETS staff (see section 3.1 above), and did not note any additional names thought to have both orthographic and phonetic similarity to Accretropin.

DDMAC had no concerns regarding the proposed name from a promotional perspective, and did not offer any additional comments relating to the proposed name.

3.3 SAFETY EVALUATOR RISK ASSESSMENT

Independent searches by the primary Safety Evaluator identified one additional name, Acapodene***, thought to look or sound similar to Accretropin and represent a potential source of drug name confusion. As such, a total of 12 names (Accuretic, Homatropine, Accutane, Accolate, Genotropin, Acetaminophen, Acapodene***, Acitretin, Oxaprozin, Acrivastine, Protropin, and Atropine) were analyzed to determine if the drug names could be confused with Accretropin, and if the drug name confusion would likely result in a medication error.

Further analysis determined that the name similarity between Accretropin and one name, Protropin, was unlikely to result in medication errors since Protropin has been discontinued and no generic equivalents are available.

The remaining eleven names were analyzed to determine if the similar appearance and/or sound of the drug name could lead to confusion with Accretropin and if the drug name confusion would likely result in a medication error. Two of the eleven names were eliminated because it was determined that medication errors were unlikely to occur because the products do not overlap in strength or dosage with Accretropin and have limited orthographic and/or visual similarity to Accretropin (Appendix B). The other nine names underwent further evaluation in the FMEA process but analysis of the failure mode did not determine that the effect of this similarity would result in medication errors in the usual practice setting (see Appendix E).

3.4 LABEL AND LABELING RISK ASSESSMENT

Review of the carton and container labels and package insert labeling identified several potential sources of medication error. We noted the use of _____ statement and the manner in which the net volume and product strength are presented may lead to confusion.

b(4)

The proposed carton and package insert labeling include reference to ' _____'; however Accretropin is dosed in milligrams, _____. We also noted that the net volume is presented in close proximity (directly above) the product strength which may lead to confusion between these two values. Furthermore, the manner in which the product strength is presented in parentheses may lead practitioners to mistake the product strength as simply the milligram per milliliter concentration, when it is in fact the product strength.

4 DISCUSSION

The results of the Proprietary Name Risk Assessment found that the proposed name, Accretropin, has some similarity to other proprietary and established drug names, but the findings of the FMEA process indicate that the proposed name does not appear to be vulnerable to name confusion that could lead to medication errors.

NOTE: This review contains proprietary and confidential information that should not be released to the public.

The findings of the Proprietary Name Risk Assessment are based upon current understanding of factors that contribute to medication errors involving name confusion. Although we believe the findings of the Risk Assessment to be robust, our findings do have limitations. First, because our assessment involves a limited number of practitioners, it is possible that the analysis did not identify a potentially confusing name. Also, there is some possibility that our Risk Assessment failed to consider a circumstance in which confusion could arise once the product is commercially marketed. However, DMETS believes that these limitations are sufficiently minimized by the use of an Expert Panel.

Our risk assessment also faces limitations beyond the control of the Agency. First, our risk assessment is based on current health care practices and drug product characteristics, future changes to either could increase the vulnerability of the proposed name to confusion. Since these changes cannot be predicted for or accounted by the current Proprietary Name Risk Assessment process, such changes limit our findings. To help counterbalance this impact, DMETS recommends that the proprietary name be re-submitted for review if approval of the product is delayed beyond 90 days.

The results of the Label and Labeling Risk Assessment found that the presentation of information on the carton and package insert labeling appear to be vulnerable to confusion that could lead to medication errors. Postmarketing evidence demonstrates that incongruent units of measure _____, lead to dosing errors. There is no need for reference to _____ in the labels and labeling of Accretropin since the product is dosed in milligrams. Furthermore, the presentation of the net volume appears in close proximity to the product strength and appears in a format that is usually used when discussing the total drug content. By placing '1 mL' prior to '5 mg/mL' more prominence is given to the number '1' which distracts the practitioners eye to this number-first. As a result this may be misinterpreted to mean the total drug amount in the vial (i.e. 1 mg rather than 5 mg). This positioning sets practitioners up for failure that may result in preparation and administration of an overdose or underdose. A miscalculation in dosing with this product could lead to adverse events such as hypoglycemia. Relocating the net quantity and removing the parentheses from the strength would likely decrease this risk.

b(4)

5 CONCLUSIONS

The Proprietary Name Risk Assessment findings indicate that the proposed name, Accretropin, does not appear to be vulnerable to name confusion that could lead to medication errors. As such, DMETS does not object to the use of the proprietary name, Accretropin, for this product. Additionally, DDMAC does not object to the proposed name, Accretropin, from a promotional perspective. However, if any of the proposed product characteristics as stated in this review are altered prior to approval of the product; DMETS rescinds this Risk Assessment finding, and recommends that the name be resubmitted for review. If the event that our Risk Assessment finding is rescinded, the evaluation of the name on resubmission is independent of the previous Risk Assessment, and as such, the conclusions on re-review of the name are subject to change. Additionally, if the product approval is delayed beyond 90 days from the date of this review, the proposed name must be resubmitted for evaluation.

The Label and Labeling Risk Assessment findings indicate that the presentation of information on the proposed carton and package insert labeling introduce vulnerability to confusion that could lead to medication errors. DMETS believes the risks we have identified can be addressed and mitigated prior to drug approval, and provides recommendations in Section 6 that aim at reducing the risk of medication errors.

Overall, our Risk Assessment is limited by our current understanding of medication errors and causality. The successful application of Failure Modes and Effect Analysis depends upon the learning gained for a spontaneous reporting program. It is quite possible that our understanding of medication error causality would benefit from unreported medication errors; and, that this understanding could have enabled the Staff to identify vulnerability in the proposed name, packaging, and labeling that was not identified in this assessment.

6 RECOMMENDATIONS

6.1 PROPRIETARY NAME:

- 6.1.1 DMETS finds the proprietary name acceptable.
- 6.1.2 If any of the proposed product characteristics as stated in this review are altered prior to approval of the product, DMETS rescinds this Risk Assessment finding, and recommends that the proposed name be resubmitted for review.
- 6.1.3 If the product approval is delayed beyond 90 days from the date of this review, the proposed name must be resubmitted for evaluation.

6.2 LABEL AND LABELING

- 6.2.1 _____ **b(4)**
- 6.2.2 Relocate the net volume so that it is not presented in close proximity to the product strength.
- 6.2.3 Remove the parentheses from around the product strength so it reads '5 mg/mL'.

7 REFERENCES

1. *Adverse Events Reporting System (AERS)*

AERS is a database application in CDER FDA that contains adverse event reports for approved drugs and therapeutic biologics. These reports are submitted to the FDA mostly from the manufactures that have approved products in the U.S. The main utility of a spontaneous reporting system that captures reports from health care professionals and consumers, such as AERS, is to identify potential postmarketing safety issues. There are inherent limitations to the voluntary or spontaneous reporting system, such as underreporting and duplicate reporting; for any given report, there is no certainty that the reported suspect product(s) caused the reported adverse event(s); and raw counts from AERS cannot be used to calculate incidence rates or estimates of drug risk for a particular product or used for comparing risk between products.

2. *Micromedex Integrated Index (<http://weblern/>)*

Contains a variety of databases covering pharmacology, therapeutics, toxicology and diagnostics.

3. *Phonetic and Orthographic Computer Analysis (POCA)*

As part of the name similarity assessment, proposed names are evaluated via a phonetic/orthographic algorithm. The proposed proprietary name is converted into its phonemic representation before it runs through the phonetic algorithm. Likewise, an orthographic algorithm exists which operates in a similar fashion. This is a database which was created for DMETS, FDA.

4. *Drug Facts and Comparisons, online version, St. Louis, MO (<http://weblern/>)*

Drug Facts and Comparisons is a compendium organized by therapeutic Course; contains monographs on prescription and OTC drugs, with charts comparing similar products.

5. *AMF Decision Support System [DSS]*

DSS is a government database used to track individual submissions and assignments in review divisions.

6. *Division of Medication Errors and Technical Support proprietary name consultation requests*

This is a list of proposed and pending names that is generated by DMETS from the Access database/tracking system.

7. *Drugs@FDA (<http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm>)*

Drugs@FDA contains most of the drug products approved since 1939. The majority of labels, approval letters, reviews, and other information are available for drug products approved from 1998 to the present. Drugs@FDA contains official information about FDA approved brand name and generic drugs and therapeutic biological products; prescription and over-the-counter human drugs and therapeutic biologicals, discontinued drugs and “Chemical Type 6” approvals.

8. *Electronic online version of the FDA Orange Book (<http://www.fda.gov/cder/ob/default.htm>)*

Provides a compilation of approved drug products with therapeutic equivalence evaluations.

9. *WWW location <http://www.uspto.gov>.*

Provides information regarding patent and trademarks.

10. *Clinical Pharmacology Online (<http://weblern/>)*

Contains full monographs for the most common drugs in clinical use, plus mini monographs covering investigational, less common, combination, nutraceutical and nutritional products. Provides a keyword search engine.

11. *Data provided by Thomson & Thomson's SAEGIS™ Online Service, available at www.thomson-thomson.com*

The Pharma In-Use Search database contains over 400,000 unique pharmaceutical trademarks and tradenames that are used in about 50 countries worldwide. The data is provided under license by IMS HEALTH.

12. *Natural Medicines Comprehensive Databases (<http://weblern/>)*

Contains up-to-date clinical data on the natural medicines, herbal medicines, and dietary supplements used in the western world.

13. *Stat!Ref (<http://weblern/>)*

Contains full-text information from approximately 30 texts. Includes tables and references. Among the database titles are: Handbook of Adverse Drug Interactions, Rudolphs Pediatrics, Basic Clinical Pharmacology and Dictionary of Medical Acronyms Abbreviations.

14. *USAN Stems (<http://www.ama-assn.org/ama/pub/category/4782.html>)*

List contains all the recognized USAN stems.

15. *Red Book Pharmacy's Fundamental Reference*

Contains prices and product information for prescription, over-the-counter drugs, medical devices, and accessories.

16. *Lexi-Comp (www.pharmacist.com)*

A web-based searchable version of the Drug Information Handbook.

17. *Medical Abbreviations Book*

Contains commonly used medical abbreviations and their definitions.

APPENDICES

Appendix A:

The Medication Error Staff consider the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted. DMETS also compare the spelling of the proposed proprietary name with the proprietary and established name of existing and proposed drug products because similarly spelled names may have greater likelihood to sound similar to one another when spoken or look similar to one another when scripted. The Medication Error Staff also examine the orthographic appearance of the proposed name using a number of different handwriting samples. Handwritten communication of drug names has a long-standing association with drug name confusion. Handwriting can cause similarly *and* dissimilarly spelled drug name pairs to appear very similar to one another and the similar appearance of drug names when scripted has lead to medication errors. The Medication Error Staff apply their expertise gained from root-cause analysis of such medication errors to identify sources of ambiguity within the name that could be introduced when scripting (e.g. “T” may look like “F,” lower case ‘a’ looks like a lower case ‘u,’ etc), along with other orthographic attributes that determine the overall appearance of the drug name when scripted (see detail in Table 1 below). Additionally, since verbal communication of medication names is common in clinical settings, the Medication Error Staff compare the pronunciation of the proposed proprietary name with the pronunciation of other drug names. If provided, DMETS will consider the Sponsor’s intended pronunciation of the proprietary name. However, because the Sponsor has little control over how the name will be spoken in practice, DMETS also considers a variety of pronunciations that could occur in the English language.

Table 1. Criteria used to identify drug names that look- or sound-similar to a proposed proprietary name

Type of similarity	Considerations when searching the databases		
	Potential causes of drug name similarity	Attributes examined to identify similar drug names	Potential Effects
Look-alike	Similar spelling	Identical prefix Identical infix Identical suffix Length of the name Overlapping product characteristics	<ul style="list-style-type: none"> Names may appear similar in print or electronic media and lead to drug name confusion in printed or electronic communication Names may look similar when scripted and lead to drug name confusion in written communication
	Orthographic similarity	Similar spelling Length of the name Upstrokes Downstrokes Cross-strokes Dotted letters	<ul style="list-style-type: none"> Names may look similar when scripted, and lead to drug name confusion in written communication

		Ambiguity introduced by scripting letters Overlapping product characteristics	
Sound-alike	Phonetic similarity	Identical prefix Identical infix Identical suffix Number of syllables Stresses Placement of vowel sounds Placement of consonant sounds Overlapping product characteristics	<ul style="list-style-type: none"> Names may sound similar when pronounced and lead to drug name confusion in verbal communication

Appendix B: Products with no numerical overlap in strength and dose.

Accretropin (Somatotropin)		5 mg/mL, 1 mL vial	0.18 mg/kg to 0.36 mg/kg divided into equal daily doses given six or seven times per week.
Product name with potential for confusion	Similarity to Proposed Proprietary Name	Strength	Usual Dose (if applicable)
Acetaminophen	Look	80 mg, 160 mg, 325 mg, 500 mg	80 mg to 650 mg every 4 to 6 hours
Oxaprozin	Look	600 mg	1200 mg by mouth once daily

Appendix C: Potentially confusing name with numerical overlap in strength or dose

Accretropin (Somatropin)	5mg/mL, 1 mL vial	Usual dose: 0.18 mg/kg to 0.36 mg/kg divided into equal daily doses given six or seven times per week.
Failure Mode: Name confusion	Causes (could be multiple)	Effects
Accuretic	<p>Orthographic similarity (Share Acc- and -ret-)</p> <p>Potential numerical overlap in dose (10 mg, 12.5 mg, 20 mg, and 25 mg)</p>	<p>Medication error unlikely to occur due to orthographic differences and the fact that Accuretic is a combination product. Additionally, the fact that the overlapping weekly dose of Accretropin is divided into daily doses minimizes the likelihood of medication error in the usual practice setting.</p> <p><i>Rationale:</i></p> <p>The risk for medication error is minimized by orthographic differences in the names. Accretropin has a downstroke ‘p’, and appears longer when scripted (eleven letters vs. nine letters) when compared to Accuretic.</p> <p>Since Accuretic is a combination product which is available in three different strengths 10 mg/12.5 mg, 20 mg/12.5 mg, and 20 mg/25 mg, it is necessary for the strength of both active ingredients to be included in prescription orders. The presence of two strengths would most likely preclude Accretropin being dispensed in error for Accuretic. Conversely, the absence of two strengths on a prescription order would most likely preclude Accuretic being dispensed for Accretropin in error.</p> <p>The potential for numerical overlap in dose between Accretropin and one of the active ingredients in Accuretic is based on the total weekly dose of Accretropin. However, that weekly dose will be divided into six or seven daily doses. Usual prescribing practices include a daily dose on prescription orders, rather than a weekly dose that must be then calculated to a daily dose.</p>
Homatropine	<p>Orthographic similarity (-tropin-)</p> <p>Numerical overlap in strengths (5 mg/mL vs. 5%).</p>	<p>Orthographic differences in the names in addition to differing dosage forms and routes of administration minimize the likelihood of medication error in the usual practice setting.</p> <p><i>Rationale:</i></p> <p>The risk for medication error is minimized by the orthographic differences in the names. The beginnings of each name differ (-ccre- vs -oma-) and Homatropine as a letter ‘e’ at the end of the name, unlike Accretropin.</p> <p>Although the products strengths overlap, usual practice does not involve including the product strength in prescription orders for injections. Rather, the order only includes the desired dose (e.g. Accretropin 2 mg subcutaneously daily).</p>

<p>Accutane</p>	<p>Orthographic similarity (Acc-)</p> <p>Potential numerical overlap in dosage (10 mg, 20 mg, 40 mg).</p>	<p>Orthographic differences in the names and the fact that the overlapping weekly dose of Accretropin is divided into daily doses minimize the likelihood of medication error in the usual practice setting.</p> <p><i>Rationale:</i></p> <p>The risk for medication error is minimized by the orthographic differences in the names. Accretropin has a downstroke introduced by the letter 'p', unlike Accutane. Accretropin appears longer when scripted (11 letters vs. 8 letters).</p> <p>The potential for numerical overlap in dose between Accretropin and Accutane is based on the total weekly dose of Accretropin. However, that weekly dose will be divided into six or seven daily doses. Usual prescribing practices include a daily dose on prescription orders, rather than a weekly dose that must be then calculated to a daily dose.</p>
<p>Accolate</p>	<p>Orthographic similarity (Acc-)</p> <p>Potential numerical overlap in dosage (10 mg, 20 mg)</p>	<p>Orthographic differences in the names and the fact that the overlapping weekly dose of Accretropin will be further divided into daily doses minimize the likelihood of medication error in the usual practice setting.</p> <p><i>Rationale:</i></p> <p>The risk for medication error is minimized by the orthographic differences in the names. Accretropin has a downstroke introduced by the letter 'p', unlike Accolate. Accretropin appears longer when scripted (11 letters vs. 8 letters).</p> <p>The potential for numerical overlap in dose between Accretropin and Accolate is based on the total weekly dose of Accretropin. However, that weekly dose will be divided into six or seven daily doses. Usual prescribing practices include a daily dose on prescription orders, rather than a weekly dose that must be then calculated to a daily dose.</p>
<p>Genotropin</p>	<p>Orthographic similarity (-tropin)</p> <p>Potential numerical overlap in dosage (0.18 mg/kg to 0.36 mg/kg)</p>	<p>Orthographic differences in the names minimize the likelihood of medication error in the usual practice setting.</p> <p><i>Rationale:</i></p> <p>The risk for medication error is minimized by the orthographic differences in the names. The beginning of each name differs (Accre- vs. Geno). Additionally, if Genotropin is scripted with a lower case 'g', the 'g' would introduce a downstroke to the beginning of the name, unlike Accretropin.</p>

Acitretin	<p>Orthographic similarity (Ac-, -ret-)</p> <p>Potential numerical overlap in dosage (10 mg, 25 mg)</p>	<p>Orthographic differences in the names and the fact that the overlapping weekly dose of Accretropin will be further divided into daily doses minimize the likelihood of medication error in the usual practice setting.</p> <p><i>Rationale:</i></p> <p>The risk for medication error is minimized by the orthographic differences in the names. Accretropin has a downstroke introduced by the letter 'p', unlike Acitretin. Accretropin appears longer when scripted (11 letters vs. 9 letters).</p> <p>The potential for numerical overlap in dose between Accretropin and Accolate is based on the total weekly dose of Accretropin. However, that weekly dose will be divided into six or seven daily doses. Usual prescribing practices include a daily dose on prescription orders, rather than a weekly dose that must be then calculated to a daily dose.</p>
Acrivastine	<p>Phonetic similarity (AK-reh-)</p> <p>Potential for overlap in dose (8 mg)</p>	<p>Medication error unlikely to occur due to phonetic differences in the names and the fact that Acrivastine is one active ingredient of a three-ingredient combination product. Additionally, the fact that the dose of Accretropin is divided into daily doses minimizes the likelihood of medication error in the usual practice setting.</p> <p><i>Rationale:</i></p> <p>The risk for medication error is minimized by orthographic differences in the names. The middle and ending portions of each name (-TROH-pin vs. VAS-teen) differ phonetically.</p> <p>Since Acrivastine is one active ingredient in a combination product (Acrivastine/Pseudoephedrine) it is necessary for the strength of both active ingredients to be included in prescription orders. The presence of two strengths would most likely preclude Accretropin being dispensed in error for Acrivastine/Pseudoephedrine. Conversely, the absence of two strengths on a prescription order would most likely preclude Acrivastine/Pseudoephedrine being dispensed for Accretropin in error.</p> <p>The potential for numerical overlap in dose between Accretropin and one of the active ingredients in Acrivastine/Pseudoephedrine is based on the total weekly dose of Accretropin. However, that weekly dose will be divided into six or seven daily doses. Usual prescribing practices include a daily dose on prescription orders, rather than a weekly dose that must be then calculated to a daily dose.</p>

<p>Acapodene***</p>	<p>Phonetic similarity (Ac-, 4 syllables)</p> <p>Potential for numerical overlap in dose (20 mg)</p>	<p>Medication error unlikely to occur due to phonetic differences in the names. Additionally, the fact that the overlapping weekly dose of Accretropin is divided into daily doses minimizes the likelihood of medication error in the usual practice setting.</p> <p><i>Rationale:</i></p> <p>The risk for medication error is minimized by phonetic differences in the names. The middle and ending portions of each name (reh-TROH-pin vs. ah-POH-deen) differ phonetically.</p> <p>The potential for numerical overlap in dose between Accretropin and Acapodene is based on the total weekly dose of Accretropin. However, that weekly dose will be divided into six or seven daily doses. Usual prescribing practices include a daily dose on prescription orders, rather than a weekly dose that must be then calculated to a daily dose.</p>
<p>Atropine</p>	<p>Orthographic and phonetic similarity (-tropin)</p> <p>Potential for numerical overlap in dosage (0.18 mg to 0.6 mg)</p>	<p>Medication error unlikely to occur due to phonetic and orthographic differences in the names.</p> <p><i>Rationale:</i></p> <p>The risk for medication error is minimized by orthographic and phonetic differences in the names. Accretropin has four syllables, unlike Atropine which only has three syllables. Additionally, the beginnings of each name differ phonetically and orthographically (Accre- vs. A-). Moreover, Accretropin contains eleven letters and thus appears longer when scripted compared Atropine which only contains eight letters.</p>

1 Page(s) Withheld

 Trade Secret / Confidential (b4)

 X Draft Labeling (b4)

 Draft Labeling (b5)

 Deliberative Process (b5)

**This is a representation of an electronic record that was signed electronically and
this page is the manifestation of the electronic signature.**

/s/

Kristina Arnwine
1/18/2008 10:27:16 AM
DRUG SAFETY OFFICE REVIEWER

Denise Toyer
1/18/2008 03:26:59 PM
DRUG SAFETY OFFICE REVIEWER
Also signing for Carol Holquist, DMETS Director in her
absence

CONSULTATION RESPONSE

**DIVISION OF MEDICATION ERRORS AND TECHNICAL SUPPORT
OFFICE OF SURVEILLANCE AND EPIDEMIOLOGY
(DMETS; WO22, Mail Stop Room 4447)**

DATE RECEIVED: November 15, 2006	DESIRED COMPLETION DATE: February 15, 2007	OSE REVIEW #: 2006-820
DATE OF DOCUMENT: May 9, 006	PDUFA DATE: March 10, 2007	

TO: Mary Parks, MD
Director, Division of Metabolism and Endocrinology Products
HFD-510

THROUGH: Linda Kim-Jung, PharmD, Team Leader
Denise Toyer, PharmD, Deputy Director
Carol Holquist, RPh, Director
Division of Medication Errors and Technical Support

FROM: Kristina C. Arnwine, PharmD, Safety Evaluator
Division of Medication Errors and Technical Support

PRODUCT NAME:
Accretropin
(Somatropin rDNA Origin Injection)
15 International Units

NDA#: 21-538

NDA SPONSOR: Cangene Corporation

RECOMMENDATIONS:

1. DMETS has no objections to the use of the proprietary name, Accretropin. This is considered a final decision. If the approval of the NDA is delayed beyond 90 days from the signature date of this document, the name with its associated labels and labeling must be re-evaluated. A re-review of the name before NDA approval will rule out any objections based upon approvals of other proprietary and/or established names from the signature date of this document.
2. DMETS recommends implementation of the label and labeling revisions outlined in section IV of this review to minimize potential errors with the use of this product.
3. DDMAC finds the proprietary name, Accretropin, acceptable from a promotional perspective.

DMETS would appreciate feedback of the final outcome of this consult. We would be willing to meet with the Division for further discussion, if needed. If you have further questions or need clarifications, please contact Nancy Clark, project manager, at 301-796-1187.

**Division of Medication Errors and Technical Support (DMETS)
White Oak Bldg 22, Mail Stop Room 4447
Office of Surveillance and Epidemiology
Center for Drug Evaluation and Research**

PROPRIETARY NAME AND LABEL/LABELING REVIEW

DATE OF REVIEW: December 1, 2006

NDA#: 21-538

NAME OF DRUG: Accretropin
(Somatropin rDNA Origin Injection), 15 International Units

NDA HOLDER: Cangene Corporation

I. INTRODUCTION:

This consult was written in response to a request from the Division of Metabolism and Endocrinology Products (HFD-510), for assessment of the proprietary name, Accretropin, regarding potential name confusion with other proprietary or established drug names. Container labels, carton and insert labeling were provided for review and comment.

PRODUCT INFORMATION

Accretropin is a recombinant growth hormone indicated for long-term treatment of growth failure in pediatric patients and treatment of short stature associated with Turner syndrome in pediatric patients. The usual dose of Accretropin is 0.18 mg/kg to 0.36 mg/kg divided into equal doses given six or seven days per week. Accretropin is supplied in a one milliliter multi-dose vial.

III. RISK ASSESSMENT

The medication error staff of DMETS conducted a search of several standard published drug product reference texts^{1,2} as well as several FDA databases^{3,4} for existing drug names which sound-alike or look-alike to Accretropin to a degree where potential confusion between drug names could occur under the usual clinical practice settings. A search of the electronic online version of the U.S. Patent and Trademark Office's Text and Image Database was also conducted⁵. The Saegis⁶ Pharma-In-Use database was searched for drug names with potential for confusion. An expert panel discussion was conducted to review all findings from the searches. In addition, DMETS conducted three prescription analysis studies consisting of two written prescription studies (inpatient and outpatient) and one

¹ MICROMEDEX Integrated Index, 2007, MICROMEDEX, Inc., 6200 South Syracuse Way, Suite 300, Englewood, Colorado 80111-4740, which includes all products/databases within ChemKnowledge, DrugKnowledge, and RegsKnowledge Systems.

² Facts and Comparisons, online version, Facts and Comparisons, St. Louis, MO.

³ AMF Decision Support System [DSS], the Division of Medication Errors and Technical Support [DMETS] database of Proprietary name consultation requests, New Drug Approvals 98-07, and the electronic online version of the FDA Orange Book.

⁴ Phonetic and Orthographic Computer Analysis (POCA)

⁵ WWW location <http://www.uspto.gov/tmdb/index.html>.

⁶ Data provided by Thomson & Thomson's SAEGIS™ Online Service, available at www.thomson-thomson.com

verbal prescription study, involving health care practitioners within FDA. This exercise was conducted to simulate the prescription ordering process in order to evaluate potential errors in handwriting and verbal communication of the name.

A. EXPERT PANEL DISCUSSION (EPD)

An Expert Panel discussion was held by DMETS to gather professional opinions on the safety of the proprietary name Accretropin. Potential concerns regarding drug marketing and promotion related to the proposed name(s) were also discussed. This group is composed of DMETS Medication Errors Prevention Staff and representation from the Division of Drug Marketing, Advertising, and Communications (DDMAC). The group relies on their clinical and other professional experiences and a number of standard references when making a decision on the acceptability of a proprietary name.

1. DDMAC finds the name, Accretropin, acceptable from a promotional perspective.
2. The Expert Panel identified twelve proprietary names that were thought to have the potential for confusion with Accretropin. Upon further review, one name, Argatroban, warranted further review. See table 1 below for product characteristics. The remaining eleven names will not be reviewed further due to a lack of convincing orthographic and/or phonetic similarity. Additionally the remaining names had differentiating product characteristics such as indication of use, dosage form, product strength, usual dose, and/or dosing frequency. Moreover, two products, Anisotropine and Intropin, have been discontinued from the market. There are no generic equivalents available for Anisotropine. The generic equivalent to Intropin, dopamine, is still available, however, practitioners will most likely order it by the generic name rather than Intropin. Additionally, Ocu-Tropine, is not listed in the Orange Book, Thomson & Thomson, Facts & Comparisons Online, or the Verispan Drug Usage database. Furthermore, Alphatropin is only an ingredient in an over the counter product, not a proprietary or established name, Therefore, Acetaminophen, Alphatropin, Accurbron, Anisotropine, Accuretic, Accutane, Azithromycin, Acitretin, Atropen, Ocu-Tropine, and Intropin will not be reviewed further.

Table 1: Potential Sound-Alike/Look-Alike Names Identified by DMETS Expert Panel

Product Name	Dosage form(s), Established name	Usual adult dose*	Other**
Accretropin	Somatropin (rDNA origin) Injection 5mg (15 International Units)	0.18 mg/kg (0.54 International Units/kg) to 0.36 mg/kg (1.08 International Units/kg) subcutaneously divided in to equal doses given six to seven times per week.	
Argatroban	Argatroban Solution for Injection 100 mg/mL	2 mcg/kg/min to 25 mcg/kg/min until desired activated partial thromboplastin time (aPTT) (usually within one to three hours)	
*Frequently used, not all-inclusive. **L/A (look-alike), S/A (sound-alike)			

B. PRESCRIPTION ANALYSIS STUDIES

1. Methodology:

Three separate studies were conducted within the Centers of the FDA for the proposed proprietary name to determine the degree of confusion of Accretropin with marketed U.S. drug names (proprietary and established) due to similarity in visual appearance with handwritten prescriptions or verbal pronunciation of the drug name. These studies employed a total of 119

health care professionals (pharmacists, physicians, and nurses). This exercise was conducted in an attempt to simulate the prescription ordering process. Two inpatient requisition forms were written, each consisting of a combination of marketed and unapproved drug products and a requisition for Accretropin (see below). These requisitions were optically scanned and one prescription was delivered to a random sample of the participating health professionals via e-mail. In addition, the outpatient orders were recorded on voice mail. The voice mail messages were then sent to a random sample of the participating health professionals for their interpretations and review. After receiving either the written or verbal prescription orders, the participants sent their interpretations of the orders via e-mail to the medication error staff.

HANDWRITTEN PRESCRIPTION	VERBAL PRESCRIPTION			
<p>Requisition #1:</p> <table border="1" style="width: 100%; border-collapse: collapse;"> <tr> <td style="width: 20%; text-align: center;">2</td> <td style="width: 20%; text-align: center;">81</td> <td style="width: 60%; text-align: center;">accretropin</td> </tr> </table>	2	81	accretropin	<p>“That’s for Accretropin, 2 vials.”</p>
2	81	accretropin		
<p>Requisition #2:</p> <table border="1" style="width: 100%; border-collapse: collapse;"> <tr> <td style="width: 20%; text-align: center;">2</td> <td style="width: 20%; text-align: center;">81</td> <td style="width: 60%; text-align: center;">accretropin 2 vials</td> </tr> </table>	2	81	accretropin 2 vials	
2	81	accretropin 2 vials		

2. Results:

None of the interpretations of the proposed name overlap, sound similar, or look similar to any currently marketed U.S. product. See appendix A for the complete listing of interpretations from the verbal and written studies.

C. SAFETY EVALUATOR RISK ASSESSEMEMNT

In reviewing the proprietary name Accretropin, the primary concern relating to look-alike and sound-alike confusion with Accretropin are Argatroban.

Additionally, DMETS conducted prescription studies to simulate the prescription ordering process. In this case, there was no confirmation that the proposed name could be confused with any of the aforementioned names. The majority of misinterpretations were misspelled/phonetic variations of the proposed name, Accretropin. However, negative findings are not predicative as to what may occur once the drug is widely prescribed, as these studies have limitations primarily due to a small sample size.

Argatroban is discussed in detail below.

Argatroban was identified as a name that sounds and looks similar to Accretropin. Argatroban is a synthetic thrombin inhibitor indicated for prophylaxis or treatment of heparin-induced thrombocytopenia.

The phonetic similarities of this name pair can be attributed to the fact that both names begin with the letter ‘A’, and both names contain four syllables, of which, the last two syllables (‘tropin’ vs. ‘troban’) sound similar. However, the beginning two syllables, apart from the letter ‘A’ sound different (ACK-REH vs. AHR-GA). Orthographically, both names begin with the letter ‘A’ and end with the letter ‘n’. Additionally, both names are similar in length (eleven letters vs. ten letters) and

both names contain a downstroke ('p' vs. 'g'). However the downstrokes are presented in different positions in each name (ninth position vs. third position), which helps to distinguish the two names from each other.

With regard to product characteristics, Accretropin and Argatroban are both injections. However, Argatroban must be diluted 100-fold to a final 1 mg/mL concentration, unlike Accretropin which is given undiluted. Furthermore, due to the final volume of Argatroban to be administered, the drug must be administered through either an intravenous bolus or a continuous intravenous drip whereas Accretropin is administered subcutaneously. Accretropin is given once daily for an extended period of time, which may exceed one year, however, Argatroban, is usually given acutely as a continuous infusion only to treat or prevent heparin-induced thrombocytopenia. Additionally, Argatroban will generally be administered on an inpatient basis whereas Accretropin will generally be administered on an outpatient basis. Furthermore, the usual doses of Accretropin and Argatroban differ as well (0.18 mg/kg to 0.36 mg/kg per week given in six or seven equally divided doses vs. 2 mcg/kg/min to 25 mcg/kg/min continuous infusion). Moreover, Accretropin is only indicated for use in children, and will likely only be prescribed by specialists (e.g. endocrinologists). On the other hand, Argatroban does not have any specifically targeted age groups like Accretropin. Overall, the differing beginnings of each name coupled with the differing product characteristics decrease the potential for confusion between this pair.

III. LABELING, PACKAGING, AND SAFETY RELATED ISSUES:

In the review of the container labels, carton and insert labeling of Accretropin, DMETS has focused on safety issues relating to medication errors. DMETS has identified the following areas of improvement, which will minimize potential user error.

A. General Comments

1. Revise the route of administration to read, "For subcutaneous use only".
2. Relocate the net volume so that it is not presented in close proximity to the product strength (see below).
3. _____ Since Accretropin is dosed on a milligram per kilogram basis, all references to other dosing units should be removed from labeling in order to prevent dosing errors. **b(4)**

b(4)

B. Container Label

1. See General Comments A-1 through A-3.
2. Revise the order in which the information is presented on the principal display panel as follows.

Accretropin
[Somatropin (rDNA origin) Injection]
5 mg/mL
For Subcutaneous Use Only

3. Increase the prominence of the proprietary name. As presented, the established name is more prominent than the proprietary name (see below).

b(4)

5. Relocate the “Rx Only” statement to the principal display panel.

6. Revise the statement _____ to read “Usual Dose: See package insert.” b(4)

C. Carton Labeling

1. See General Comments A-1 through A-3 and comments B-5 and B-6.
2. Clarify what is meant by _____. If these are Inactive ingredients, revise as such and present both qualitatively and quantitatively. b(4)

D. Insert Labeling

1. See General Comment A-3.
2. Dosage and Administration Section, Line 386 – Revise the established name to read [somatropin (rDNA origin) injection]. The product is supplied as an injection, not “for injection”.

Attachment 1

Inpatient Written	Outpatient Written	Verbal
Accretropin	accretiopin	Aceatropin
Accretropin	Accretiopin	Aceatropin
Accretropin	Accretiropin	Aceotropin
Accretropin	Accretizosin	Acitropin
Accutropin	Accretrapin	Acetropin
Accutropin	Accretriapan	Asetropin
Accutropin	Accretriopin	Asotropin
Accutropin	Accretropin	Aysfertropin
Accutropin	Accretropin	
	Accretropin	
	Accretropin	
	Accretrozin	
	Accretuopin	
	Accretuopin	
	Accretupin	
	Accretuzsin	

**This is a representation of an electronic record that was signed electronically and
this page is the manifestation of the electronic signature.**

/s/

Kristina Arnwine
2/2/2007 10:19:11 AM
DRUG SAFETY OFFICE REVIEWER

Linda Kim-Jung
2/2/2007 10:25:26 AM
DRUG SAFETY OFFICE REVIEWER

Denise Toyer
2/2/2007 12:57:41 PM
DRUG SAFETY OFFICE REVIEWER
Also signing for Carol Holquist, DMETS Director, in her
absence