CENTER FOR DRUG EVALUATION AND RESEARCH

APPROVAL PACKAGE FOR:

APPLICATION NUMBER

21-305

Administrative Documents

NDA/EFFICACY SUPPLEMENT ACTION PACKAGE CHECKLIST

Application Information			
NDA 21-305	Efficacy Supplement Type SE-	Supplement Number Resubmission	
Drug: Sodium Iodide I 131		Applicant: DRAXIMAGE Inc.	
RPM: Renee C. Tyson		HFD-160	Phone (301) 827-7498
Application Type: ( ) 505(b)(1) (X) 505(b)(2)		Reference Listed Drug (NDA #, Drug name):	

❖ Application Classifications:	
• Review priority	(X) Standard ( ) Priority
• Chem class (NDAs only)	3S
• Other (e.g., orphan, OTC)	
❖ User Fee Goal Dates	January 24, 2003
❖ Special programs (indicate all that apply)	(X) None Subpart H ( ) 21 CFR 314.510 (accelerated approval) ( ) 21 CFR 314.520 (restricted distribution) ( ) Fast Track ( ) Rolling Review
❖ User Fee Information	
• User Fee	(X) Paid
• User Fee waiver	( ) Small business ( ) Public health ( ) Barrier-to-Innovation ( ) Other
• User Fee exception	( ) Orphan designation ( ) No-fee 505(b)(2) ( ) Other
❖ Application Integrity Policy (AIP)	
• Applicant is on the AIP	( ) Yes (X) No
• This application is on the AIP	( ) Yes (X) No
• Exception for review (Center Director's memo)	
• OC clearance for approval	
❖ Debarment certification: verified that qualifying language (e.g., willingly, knowingly) was not used in certification and certifications from foreign applicants are co-signed by U.S. agent.	(X) Verified
❖ Patent	
• Information: Verify that patent information was submitted	(X) Verified
• Patent certification [505(b)(2) applications]: Verify type of certifications submitted	21 CFR 314.50(i)(1)(*i*)(A) ( ) I ( ) II ( ) III ( ) IV 21 CFR 314.50(i)(1) ( ) (ii) ( ) (iii)
• For paragraph IV certification, verify that the applicant notified the patent holder(s) of their certification that the patent(s) is invalid, unenforceable, or will not be infringed (certification of notification and documentation of receipt of notice).	( ) Verified
❖ Exclusivity Summary (approvals only)	X
❖ Administrative Reviews (Project Manager, ADRA) *(indicate date of each review)*	November 25, 2002

General Information	
❖ Actions	
• Proposed action	(X) AP ( ) TA ( ) AE ( ) NA
• Previous actions (specify type and date for each action taken)	NA
• Status of advertising (approvals only)	(X) Materials requested in AP letter ( ) Reviewed for Subpart H
❖ Public communications	Pending
• Press Office notified of action (approval only)	( ) Yes ( ) Not applicable
• Indicate what types (if any) of information dissemination are anticipated	(X) None ( ) Press Release ( ) Talk Paper ( ) Dear Health Care Professional Letter
❖ Labeling (package insert, patient package insert (if applicable), MedGuide (if applicable)	Pending
• Division's proposed labeling (only if generated after latest applicant submission of labeling)	Pending
• Most recent applicant-proposed labeling	X
• Original applicant-proposed labeling	X
• Labeling reviews (including DDMAC, Office of Drug Safety trade name review, nomenclature reviews) and minutes of labeling meetings *(indicate dates of reviews and meetings)*	Vial and carton Consult Pending
• Other relevant labeling (e.g., most recent 3 in class, class labeling)	N/A
❖ Labels (immediate container & carton labels)	Pending
• Division proposed (only if generated after latest applicant submission)	Pending
• Applicant proposed	X
• Reviews	X
❖ Post-marketing commitments	Pending
• Agency request for post-marketing commitments	Pending
• Documentation of discussions and/or agreements relating to post-marketing commitments	Pending
❖ Outgoing correspondence (i.e., letters, E-mails, faxes)	N/A
❖ Memoranda and Telecons	N/A
❖ Minutes of Meetings	
• EOP2 meeting (indicate date)	N/A
• Pre-NDA meeting (indicate date)	March 9, 2000
• Pre-Approval Safety Conference (indicate date; approvals only)	N/A
• Other	N/A
❖ Advisory Committee Meeting	N/A
• Date of Meeting	N/A
• 48-hour alert	N/A
❖ Federal Register Notices, DESI documents, NAS, NRC (if any are applicable)	N/A

Clinical and Summary Information	
❖ Summary Reviews (e.g., Office Director, Division Director, Medical Team Leader) *(indicate date for each review)*	Pending
❖ Clinical review(s) *(indicate date for each review)*	See 1st Cycle Reviews
❖ Microbiology (efficacy) review(s) *(indicate date for each review)*	See 1st Cycle Reviews
❖ Safety Update review(s) *(indicate date or location if incorporated in another review)*	N/A
❖ Pediatric Page(separate page for each indication addressing status of all age groups)	Pending
❖ Statistical review(s) *(indicate date for each review)*	See 1st Cycle Reviews
❖ Biopharmaceutical review(s) *(indicate date for each review)*	December 2, 2002
❖ Controlled Substance Staff review(s) and recommendation for scheduling *(indicate date for each review)*	N/A
❖ Clinical Inspection Review Summary (DSI)	N/A
• Clinical studies	N/A
• Bioequivalence studies	N/A
CMC Information	
❖ CMC review(s) *(indicate date for each review)*	November 26, 2002
❖ Environmental Assessment	March 30, 2001
• Categorical Exclusion *(indicate review date)*	(1st Cycle Review March 30, 2001)
• Review & FONSI *(indicate date of review)*	N/A
• Review & Environmental Impact Statement *(indicate date of each review)*	N/A
❖ Micro (validation of sterilization & product sterility) review(s) *(indicate date for each review)*	(1st Cycle Review March 30, 2001)
❖ Facilities inspection (provide EER report) N/A	Date completed: (X) Acceptable ( ) Withhold recommendation
❖ Methods validation	(X) Completed ( ) Requested ( ) Not yet requested
Nonclinical Pharm/Tox Information	
❖ Pharm/tox review(s), including referenced IND reviews *(indicate date for each review)*	See 1st Cycle Reviews
❖ Nonclinical inspection review summary	N/A
❖ Statistical review(s) of carcinogenicity studies *(indicate date for each review)*	N/A
❖ CAC/ECAC report	N/A

DRAXIMAGE

Food and Drug Administration

Re: Patent Certification
NDA 21-305 for DRAXIMAGE Sodium Iodide I 131 Solution, USP

Patent Information

The Sponsor, DRAXIMAGE, Inc., Kirkland, Quebec, Canada, makes no claims of exclusivity for Sodium Iodide I 131 Solution USP, Therapeutic Oral, at the proposed concentration of 37 gigabecquerels/mL (1 Ci/mL). No active patents currently exist, nor are future application planned to address the increase in potency relative to this compendial radiopharmaceutical therapy.

Patent Certification

In accordance with the requirements for patent certification related to an NDA filed under 505(b)(2) of the Food Drug & Cosmetic Act, the sponsor DRAXIMAGE, Inc. has reviewed the Orange Book for approved NDAs for Sodium Iodide I 131 Solution USP Therapeutic Oral. Our review of the patent and exclusivity search for the active ingredient Sodium Iodide I 131 solution USP, Therapeutic Oral resulted in the discovery of three products currently approved and marketed in the US. The manufacturers and marketers of Sodium Iodide I 131 Solution USP Therapeutic Oral are Bracco Diagnostics Inc., Princeton, NJ (Iodotope®) application number 010929-002, CIS Bio- International, Bedford MA, application number 017315, and Mallinckrodt Inc., St. Louis MO, application number 016515.

The Orange Book Database reports that there are no active patents or exclusivity statements for any of these products.

In the opinion and to the best knowledge of DRAXIMAGE, Inc., Kirkland, Quebec, Canada, there are no patents that claim the listed drug referred to in this application or that claim a use of this listed drug.

Edward B. per Richard Flanagan

Richard J. Flanagan, Ph. D.
President
Tel: 514-630-7039

Date: December 2, 2002

EXCLUSIVITY SUMMARY for NDA # 21-305 SUPPL #
Trade Name N/A Generic Name Sodium Iodide I 131
Applicant Name DRAXIMAGE, Inc. HFD- 160
Approval Date January 24, 2003

PART I: IS AN EXCLUSIVITY DETERMINATION NEEDED?

1. An exclusivity determination will be made for all original applications, but only for certain supplements. Complete Parts II and III of this Exclusivity Summary only if you answer "YES" to one or more of the following questions about the submission.

   a) Is it an original NDA? YES/X__/ NO /___/

   b) Is it an effectiveness supplement? YES /___/ NO /_X__/

      If yes, what type(SE1, SE2, etc.)?

   c) Did it require the review of clinical data other than to support a safety claim or change in labeling related to safety? (If it required review only of bioavailability or bioequivalence data, answer "NO.")

      YES /_X__/ NO /___/

      If your answer is "no" because you believe the study is a bioavailability study and, therefore, not eligible for exclusivity, EXPLAIN why it is a bioavailability study, including your reasons for disagreeing with any arguments made by the applicant that the study was not simply a bioavailability study.

      If it is a supplement requiring the review of clinical data but it is not an effectiveness supplement, describe the change or claim that is supported by the clinical data:

   d) Did the applicant request exclusivity?

      YES /___/ NO /_X__/

If the answer to (d) is "yes," how many years of exclusivity did the applicant request?

e) Has pediatric exclusivity been granted for this Active Moiety?

YES /___/ NO /_X__/

IF YOU HAVE ANSWERED "NO" TO ALL OF THE ABOVE QUESTIONS, GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9.

2. Has a product with the same active ingredient(s), dosage form, strength, route of administration, and dosing schedule previously been approved by FDA for the same use? (Rx to OTC Switches should be answered No - Please indicate as such).

YES /___/ NO /_X__/

If yes, NDA # _____ Drug Name

IF THE ANSWER TO QUESTION 2 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9.

3. Is this drug product or indication a DESI upgrade?

YES /_X__/ NO /___/

IF THE ANSWER TO QUESTION 3 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9 (even if a study was required for the upgrade).

PART II: FIVE-YEAR EXCLUSIVITY FOR NEW CHEMICAL ENTITIES
(Answer either #1 or #2, as appropriate)

1. Single active ingredient product.

Has FDA previously approved under section 505 of the Act any

drug product containing the same active moiety as the drug under consideration? Answer "yes" if the active moiety (including other esterified forms, salts, complexes, chelates or clathrates) has been previously approved, but this particular form of the active moiety, e.g., this particular ester or salt (including salts with hydrogen or coordination bonding) or other non-covalent derivative (such as a complex, chelate, or clathrate) has not been approved. Answer "no" if the compound requires metabolic conversion (other than deesterification of an esterified form of the drug) to produce an already approved active moiety.

YES /___/ NO /___/

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA #

NDA #

NDA #

2. Combination product.

If the product contains more than one active moiety (as defined in Part II, #1), has FDA previously approved an application under section 505 containing any one of the active moieties in the drug product? If, for example, the combination contains one never-before-approved active moiety and one previously approved active moiety, answer "yes." (An active moiety that is marketed under an OTC monograph, but that was never approved under an NDA, is considered not previously approved.)

YES /___/ NO /___/

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA #

NDA #

NDA #

IF THE ANSWER TO QUESTION 1 OR 2 UNDER PART II IS "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9. IF "YES," GO TO PART III.

PART III: <u>THREE-YEAR EXCLUSIVITY FOR NDA'S AND SUPPLEMENTS</u>

To qualify for three years of exclusivity, an application or supplement must contain "reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant." This section should be completed only if the answer to PART II, Question 1 or 2, was "yes."

1. Does the application contain reports of clinical investigations? (The Agency interprets "clinical investigations" to mean investigations conducted on humans other than bioavailability studies.) If the application contains clinical investigations only by virtue of a right of reference to clinical investigations in another application, answer "yes," then skip to question 3(a). If the answer to 3(a) is "yes" for any investigation referred to in another application, do not complete remainder of summary for that investigation.

YES /___/ NO /___/

IF "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9.

2. A clinical investigation is "essential to the approval" if the Agency could not have approved the application or supplement without relying on that investigation. Thus, the investigation is not essential to the approval if 1) no clinical investigation is necessary to support the supplement or application in light of previously approved applications (i.e., information other than clinical trials, such as bioavailability data, would be sufficient to provide a basis

for approval as an ANDA or 505(b)(2) application because of what is already known about a previously approved product), or 2) there are published reports of studies (other than those conducted or sponsored by the applicant) or other publicly available data that independently would have been sufficient to support approval of the application, without reference to the clinical investigation submitted in the application.

For the purposes of this section, studies comparing two products with the same ingredient(s) are considered to be bioavailability studies.

(a) In light of previously approved applications, is a clinical investigation (either conducted by the applicant or available from some other source, including the published literature) necessary to support approval of the application or supplement?

YES /___/ NO /___/

If "no," state the basis for your conclusion that a clinical trial is not necessary for approval **AND GO DIRECTLY TO SIGNATURE BLOCK ON Page 9:**

(b) Did the applicant submit a list of published studies relevant to the safety and effectiveness of this drug product and a statement that the publicly available data would not independently support approval of the application?

YES /___/ NO /___/

(1) If the answer to 2(b) is "yes," do you personally know of any reason to disagree with the applicant's conclusion? If not applicable, answer NO.

YES /___/ NO /___/

If yes, explain:

(2) If the answer to 2(b) is "no," are you aware of published studies not conducted or sponsored by the applicant or other publicly available data that could independently demonstrate the safety and effectiveness of this drug product?

YES /___/ NO /___/

If yes, explain:

(c) If the answers to (b)(1) and (b)(2) were both "no," identify the clinical investigations submitted in the application that are essential to the approval:

Investigation #1, Study #

Investigation #2, Study #

Investigation #3, Study #

3. In addition to being essential, investigations must be "new" to support exclusivity. The agency interprets "new clinical investigation" to mean an investigation that 1) has not been relied on by the agency to demonstrate the effectiveness of a previously approved drug for any indication and 2) does not duplicate the results of another investigation that was relied on by the agency to demonstrate the effectiveness of a previously approved drug product, i.e., does not redemonstrate something the agency considers to have been demonstrated in an already approved application.

(a) For each investigation identified as "essential to the approval," has the investigation been relied on by the agency to demonstrate the effectiveness of a previously approved drug product? (If the investigation was relied on only to support the safety of a previously approved drug, answer "no.")

Investigation #1 YES /___/ NO /___/

Investigation #2 YES /___/ NO /___/

Investigation #3 YES /___/ NO /___/

If you have answered "yes" for one or more investigations, identify each such investigation and the NDA in which each was relied upon:

NDA # _____ Study #
NDA # _____ Study #
NDA # _____ Study #

(b) For each investigation identified as "essential to the approval," does the investigation duplicate the results of another investigation that was relied on by the agency to support the effectiveness of a previously approved drug product?

Investigation #1 YES /___/ NO /___/

Investigation #2 YES /___/ NO /___/

Investigation #3 YES /___/ NO /___/

If you have answered "yes" for one or more investigations, identify the NDA in which a similar investigation was relied on:

NDA # _____ Study #

NDA # _____ Study #

NDA # _____ Study #

(c) If the answers to 3(a) and 3(b) are no, identify each "new" investigation in the application or supplement that is essential to the approval (i.e., the investigations listed in #2(c), less any that are not "new"):

Investigation #__, Study #

Investigation #__, Study #

Investigation #__, Study #

4. To be eligible for exclusivity, a new investigation that is essential to approval must also have been conducted or sponsored by the applicant. An investigation was "conducted or sponsored by" the applicant if, before or during the conduct of the investigation, 1) the applicant was the sponsor of the IND named in the form FDA 1571 filed with the Agency, or 2) the applicant (or its predecessor in interest) provided substantial support for the study. Ordinarily, substantial support will mean providing 50 percent or more of the cost of the study.

(a) For each investigation identified in response to question 3(c): if the investigation was carried out under an IND, was the applicant identified on the FDA 1571 as the sponsor?

Investigation #1	
IND # _____ YES /___/	NO /___/ Explain:
Investigation #2	
IND # _____ YES /___/	NO /___/ Explain:

(b) For each investigation not carried out under an IND or for which the applicant was not identified as the sponsor, did the applicant certify that it or the applicant's predecessor in interest provided substantial support for the study?

Investigation #1	
YES /___/ Explain _____	NO /___/ Explain _____
_____	_____
_____	_____
Investigation #2	
YES /___/ Explain _____	NO /___/ Explain _____
_____	_____
_____	_____

(c) Notwithstanding an answer of "yes" to (a) or (b), are there other reasons to believe that the applicant should not be credited with having "conducted or sponsored" the study? (Purchased studies may not be used as the basis for exclusivity. However, if all rights to the drug are purchased (not just studies on the drug), the applicant may be considered to have sponsored or conducted the studies sponsored or conducted by its predecessor in interest.)

YES /___/ NO /___/

If yes, explain: _____

_____

_____

_____

Signature of Preparer Date
Title:

Signature of Office or Division Director Date

cc:
Archival NDA
HFD- /Division File
HFD- /RPM
HFD-093/Mary Ann Holovac
HFD-104/PEDS/T.Crescenzi

Form OGD-011347
Revised 8/7/95; edited 8/8/95; revised 8/25/98, edited 3/6/00

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

/s/

Sally Loewke
5/14/03 09:56:04 AM
THis product was approved in Januaray 2003, however, this form was inadvertently left out of the DFS entry.

PEDIATRIC EXCLUSIVITY DETERMINATION CHECKLIST

PART I - TO BE COMPLETED BY THE REVIEWING DIVISION.

Date of Written Request from FDA __/__/__. Application Written Request was made to: NDA/IND#_____
Timeframe Noted in Written Request for Submission of Studies __/__/__.
NDA# _21-305_____ Supplement #_Resubmission Choose one: SE1 SE2 SE3 SE4 SE5 SE6 SE7 SE8 SLR
Sponsor ___DraxImage Inc._____
Generic Name ____Sodium Iodide I 131 solution USP ___ Trade Name _____
Strength _____ Dosage Form/Route__ _____
Date of Submission of Reports of Studies __/__/__.
Pediatric Exclusivity Determination Due Date (60 or 90 days from date of submission of studies) __/__/__.

Was a formal Written Request made for the pediatric studies submitted?	Y ___	N _X__
Were the studies submitted after the Written Request?	Y ___	N _X__
Were the reports submitted as a supplement, amendment to an NDA, or NDA?	Y ___	N _X__
Was the timeframe noted in the Written Request for submission of studies met?	Y ___	N _X__
If there was a written agreement, were the studies conducted according to the written agreement? OR If there was no written agreement, were the studies conducted in accord with good scientific principles?	Y ___	N _X__
Did the studies fairly respond to the Written Request?	Y ___	N _X__

SIGNED_____ **DATE**_____
(Reviewing Medical Officer)

Do not enter in DFS - FORWARD TO PEDIATRIC EXCLUSIVITY BOARD, HFD-960.

PART II - TO BE COMPLETED BY THE PEDIATRIC EXCLUSIVITY BOARD

Pediatric Exclusivity **___Granted** **___ Denied**

Existing Patent or Exclusivity Protection:

NDA/Product #	Eligible Patents/Exclusivity	Current Expiration Date

SIGNED _____ **DATE**_____

DRAXIMAGE

Food and Drug Administration

Re: Debarment Certification Statement
NDA 21-305 for DRAXIMAGE Sodium Iodide I 131 Solution, USP

This information is submitted in accordance with Section 306 (k)(1) of the federal Food, Drug and Cosmetic Act.

I certify that Draximage Inc. did not and will not use in any capacity the service of any person debarred under section 306 of the Federal Food, Drug and Cosmetic Act in connection with this Abbreviated New Drug Application for DRAXIMAGE Sodium Iodide I 131 Solution, USP, NDA 21-305.

Edward Burns per Richard J. Flanagan

Richard J. Flanagan, Ph. D.
President
Tel: 514-630-7039

Date: December 2, 2002

DIVISION DIRECTOR MEMORANDUM TO THE FILE

NDA:	21-305
DRUG:	Sodium iodide I-131 Solution USP
ROUTE:	Oral Solution for preparation of capsules
MODALITY:	Therapeutic Radiopharmaceutical
INDICATION:	Treatment of Hyperthyroidism and Selected Thyroid Cancers
SPONSOR:	DraxImage Inc.
RECEIVED:	August 29, 2002 (Dated August 24, 2003)
FDUFA DATE:	January 24, 2003
COMPLETED:	January 20, 2003

RELATED DRUGS: Approved in lower concentrations of sodium I-131 oral solutions and capsules:
Iodotope® (Bracco Diagnostics, Inc.)
Sodium iodide I-131 Solution USP, Therapeutic Oral (Mallinckrodt Medical Inc.)
Sodium iodide I-131 Solution-For Oral Therapeutic Use (CIS US Bio International)

RELATED REVIEWS:

Chemistry:	M Salazar, PhD 04/06/01 and 12/13/02; E Leutzinger, PhD 11/26/02
Clinical:	R Raman, MD (team leader) 05/24/01
	N Arnstein, MD 05/24/01
Clinical Pharmacology:	A Sancho, PhD 04/06/01; Christy John, PhD, 12/02/03
Microbiology:	D Hussong, PhD 01/18/01
Pharmacology-toxicology:	T Kokate, PhD 02/12/01
Statistics:	M Sobhan, PhD 02/22/01
Project Manager:	Renee Tyson, MA

BACKGROUND:

On August 29, 2002 DraxImage resubmitted its application for the Kit for the preparation of Sodium Iodide I-131 capsules and solution. Sodium iodide has been used in the treatment of a thyroid disorders for 30-50 years. Several approved products are marketed for the diagnosis and treatment of hyperthyroidism and thyroid cancer. DraxImage has developed a higher strength sodium iodide I-131 solution that is proposed for use in preparing the final dosing form. This higher strength formulation of 1000 mCi/ml is intended to decrease the number of capsules or total volume of solution ingested to deliver the required therapeutic dose. The higher strength formulation will be processed into the final dosage form at the clinical site and should result in a smaller number of capsules for patient dosing.

The original 505(b)(2)NDA was submitted on August 31, 2000 and received an approvable letter on June 20, 2001. At that time the major deficiencies focused on the chemistry and manufacturing controls.

These deficiencies have been reviewed by the chemists, microbiologist, and clinical pharmacologists that recommend approval with labeling revisions.

Additionally, during the original NDA review there was considerable discussion about the additional use request for patients under the age of 30. Currently approved products contain a labeled warning against treatment of patients less than 30 years of age. The original DraxImage submission, proposed labeling for adolescents and pediatric patients. Although, the application lacked sufficient information to establish the full range of ages, preliminarily there was information for adolescents and young adults. In the resubmission, however, the sponsor has withdrawn these new populations and seeks the indications that are approved in other products.

Labeling has been reviewed and revised by all disciplines and the Office of Drug Safety. The sponsor has agreed to the proposed changes.

ACTION: Approval with revised labeling

APPEARS THIS WAY
ON ORIGINAL

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

/s/

Patricia Love
1/27/03 12:08:29 PM
MEDICAL OFFICER

T-Con Record

Date: 19-Nov-2002
From: Milagros Salazar, Ph.D., Review Chemist, HFD-820
To: Charles Vachon, M.Sc., Regulatory Affairs Manager, Draximage, Inc.
Re: Labeling of NDA 21-304/ NaI-131 Solution & Capsules

I called Mr. Vachon to clarify the following labeling issues in the package insert:

1. Is there a typographical error in the statement regarding the carrier free preparation?
   Response: yes, it is a typographical error. The preparation is a non-carrier added one. A revised label will be submitted by fax amendment and as an official amendment.
2. Would you update the section "Directions for the Patient Preparation" to specify the type (i.e., plastic, lead, etc) of containers to be used during storage?
   Response: yes. A revised version of this information will be submitted by fax and as an official amendment.
3. Do you have stability data for the NaI-131 capsules stored as described in the "Directions for the Patient preparation" to support the 7 days expiration proposed in this section of the label.
   Response: yes, there is stability data for 3 lots of capsules manufactured by Draximage and stored as described not only for 7 days but for up to 28 days after preparation. Data will be submitted by fax and as an official amendment.

APPEARS THIS WAY
ON ORIGINAL

MEMORANDUM OF TELECON

DATE: September 23, 2002

APPLICATION NUMBER: NDA 21-305, I-131 Sodium Iodide

BETWEEN:

Name: Dr. Gayle R. Dolecek,
Phone: 301-838-3120
Representing: Draximage Inc.

AND

Name: Patricia A. Stewart, Regulatory Project Manager
Division of Medical Imaging and Radiopharmaceutical Drug Products,
HFD-160

SUBJECT: Unacceptable for Filing Letter dated September 6, 2002.

The sponsor was informed that the Unacceptable to File letter does not apply in the case of an amendment to an application, only to new applications or supplements. He was told that the submission dated July 25, 2002, was under review and to disregard the letter sent by the Agency September 6, 2002. However, even though the submission was under review the sponsor was still responsible for paying the User Fee.

/S/

Patricia A. Stewart
Regulatory Project Manager

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

/s/

Patricia Stewart
9/23/02 05:03:19 PM
CSO

NDA 21-305

DATE: 11/26/02

FROM; Eldon E. Leutzinger, Ph.D.
DNDCII, Office of New Drug Chemistry

RE: Chemistry Review #2

Chemistry Review #2 of NDA 21-305 awaits some rewording for clarity in the evaluation of the firm's response to our question (I.B.5.b) in the action letter (6/29/01), and some minor editorial corrections before it is ready for DFS. These final revisions will be completed when Milagros returns on 12/13/02. Otherwise, Review #2 is complete. Based on Review #2, it is concluded that Draximage, Inc. has satisfactorily responded to all deficiencies identified in Chemistry Review #1 (4/6/01); I concur.

There were two reviews of [redacted] DMF # [redacted] the second of which (10/18/02) concludes that it is acceptable in support of the NDA. There are no remaining issues in the DMF that adversely impact the approvability of NDA 21-305. However, there are some minor comments that are being communicated to [redacted] under separate cover, as an Information Request letter, regards their routine stability protocol for Sodium Iodide I-131. There are no CGMP inspection issues. Microbiology recommended approval of the application on 01/04/2001.

A recommendation of APPROVAL of NDA 21-305 is made in Review #2, based on chemistry, manufacturing and controls. I concur with that recommendation, and will make formal sign-off on the review after the above indicated revisions are complete and the review is in DFS. There are some revisions recommended to labeling described in Review #2, and I will provide those revisions electronically for the scheduled labeling meetings.

CONSULTATION RESPONSE

DIVISION OF MEDICATION ERRORS AND TECHNICAL SUPPORT
OFFICE OF DRUG SAFETY
(DMETS; HFD-420)

DATE RECEIVED: December 2, 2002	**DUE DATE:** January 24, 2003	**ODS CONSULT #:** 02-0217

TO: Patricia Y. Love, M.D., M.B.A.
Director, Division of Medical Imaging and Radiopharmaceutical Drug Products
HFD-160

THROUGH: Renee Tyson
Project Manager
HFD-160

PRODUCT NAME: **Sodium Iodide I-131** (Sodium Iodide I-131 Solution, USP) **NDA#: 21-305**	**NDA SPONSOR:** DraxImage Inc.

SAFETY EVALUATOR: Tia M. Harper-Velazquez, Pharm.D.

SUMMARY: In response to a consult request from the Division of Medical Imaging and Radiopharmaceutical Drug products (HFD-160), the Division of Medication Errors and Technical Support (DMETS) conducted a review of the labels and labeling for possible interventions that may help minimize medication errors.

DMETS RECOMMENDATION:

DMETS recommends implementation of the labeling revisions outlined in Section II of this review.

/S/

Carol Holquist, R.Ph.
Deputy Director
Division of Medication Errors and Technical Support
Office of Drug Safety
Phone: (301) 827-3242 Fax: (301) 443-9664

/S/

Jerry Phillips, R.Ph.
Associate Director
Office of Drug Safety
Center for Drug Evaluation and Research
Food and Drug Administration

Division of Medication Errors and Technical Support (DMETS)
Office of Drug Safety
HFD-420; Parklawn Rm. 6-34
Center for Drug Evaluation and Research

LABEL AND LABELING REVIEW

DATE OF REVIEW: January 10, 2003

NDA# 21-305

NAME OF DRUG: **Sodium Iodide I-131**
(Sodium Iodide I-131 Solution, USP)

NDA HOLDER: **DraxImage Inc.**

I. INTRODUCTION:

This consult was written in response to a request from the Division of Medical Imaging and Radiopharmaceutical Drug Products (HFD-160), for a review of the labels and labeling for Sodium Iodide I-131 Solution, USP. A tradename review was not conducted for this review since the sponsor has not proposed a tradename.

PRODUCT INFORMATION

Sodium Iodide I-131 is a radiopharmaceutical drug product containing Sodium Iodide I-131 in an aqueous solution for patient specific compounding of a therapeutic oral solution or capsule. Therapeutic doses of Sodium Iodide I-131 are indicated for the treatment of hyperthyroidism and selected cases of carcinoma of the thyroid. The recommended dosage for orally administered Sodium Iodide I-131 is based on the thyroid uptake as well as the size of the gland. For antihyperthyroid therapy, doses can range from 4 millicuries to 10 millicuries. For antineoplastic therapy the dose can range from 30 millicuries to 100 millicuries (thyroid tissue) and 100 millicuries to 150 millicuries (metastases). Sodium Iodide I-131 will be supplied as a kit containing a blister package of five or ten small hard gelatin capsules. Sodium Iodide I-131 solution will be available in a vial containing approximate 250 millicuries or 500 millicuries in 0.25 mL or 0.50 mL respectively, of Sodium Iodide I-131 at the time of calibration.

II. LABELING, PACKAGING, AND SAFETY RELATED ISSUES:

In review of the vial label, carton label, and package insert labeling, DMETS has focused on safety issues relating to possible medication errors. We have identified the following areas of possible improvement in the interest of minimizing potential user error.

A. CONTAINER LABEL

1. Include the product expiration date.

2. Include the radionuclidic concentration.

B. CARTON LABELING

Please add the "Rx only" statement to the labeling.

C. INSERT LABELING

Directions for Patient Dose Preparation

1. Because the instructions for preparation are cumbersome, please provide pictorial illustrations in conjunction with the text.

2. We note that labels were not provided for the final dosage form (capsules or oral solution). The finished product should have a label that identifies the active ingredient, space to insert radionuclidic concentration, lot number, and expiration date.

3. We note that the 2 capsules are identical in color and similar in size. Once removed from the labeled canister it will be difficult to determine which one contains the dibasic sodium phosphate. Please consider revising one of the capsule's color to avoid possible confusion.

4. We note that vial fill volume is expressed with a terminal zero (0.50 mL). Postmarketing experience has demonstrated that the presence of a terminal zero can lead to errors in interpretation of prescriptions. Please remove the terminal zero from the fill volume accordingly.

III. RECOMMENDATIONS:

DMETS recommends implementation of the labeling revisions outlined in Section II of this review.

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 Sammie Beam, Project Manager, at 301-827-7847.

/S/

Tia M. Harper-Velazquez, Pharm.D.
Safety Evaluator
Division of Medication Errors and Technical Support
Office of Drug Safety

Concur:

/S/

Alina Mahmud, R.Ph.
Team Leader
Division of Medication Errors and Technical Support
Office of Drug Safety

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/s/

Tia Harper-Velazquez
1/23/03 03:26:15 PM
PHARMACIST

Alina Mahmud
1/24/03 07:19:52 AM
PHARMACIST

Carol Holquist
1/24/03 07:36:06 AM
PHARMACIST

Jerry Phillips
1/24/03 08:11:24 AM
DIRECTOR

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

REQUEST FOR CONSULTATION

TO Office of Drug Safety
Division Of Medication Errors and Technical Support

FROM: HFD-160 (Division of Medical Imaging and Radiopharmaceutical Drug Products)
Renee C. Tyson, Project Manager

DATE:	IND NO.:	NDA NO.	TYPE OF DOCUMENT :	DATE OF DOCUMENT:
November 20, 2002		21-305	Labeling Review	July 26,2002

NAME OF DRUG:	PRIORITY CONSIDERATION:	CLASSIFICATION OF DRUG:	DESIRED COMPLETION DATE:
Sodium Iodide I-131 Solution USP	Standard	3S Therapeutic Radiopharmaceutical	January 13, 2003

NAME OF FIRM: DraxImage Inc.

REASON FOR REQUEST

I. GENERAL

- ☐ NEW PROTOCOL
- ☐ PROGRESS REPORT
- ☐ NEW CORRESPONDENCE
- ☐ DRUG ADVERTISING
- ☐ ADVERSE REACTION REPORT
- ☐ MANUFACTURING CHANGE/ADDITION
- ☐ MEETING PLANNED BY
- ☐ PRE–NDA MEETING
- ☐ END OF PHASE II MEETING
- ☐ RESUBMISSION
- ☐ SAFETY/EFFICACY
- ☐ PAPER NDA
- ☐ CONTROL SUPPLEMENT
- ☐ RESPONSE TO DEFICIENCY LETTER
- ☐ FINAL PRINTED LABELING
- ☐ LABELING REVISION
- ☐ ORIGINAL NEW CORRESPONDENCE
- ☐ FORMULATIVE REVIEW
- ☐ OTHER *(SPECIFY BELOW)*:
  Review of vial and packaging labeling

II. BIOMETRICS

STATISTICAL EVALUATION BRANCH	STATISTICAL APPLICATION BRANCH
☐ TYPE A OR B NDA REVIEW ☐ END OF PHASE II MEETING ☐ CONTROLLED STUDIES ☐ PROTOCOL REVIEW ☐ OTHER:	☐ CHEMISTRY REVIEW ☐ PHARMACOLOGY ☐ BIOPHARMACEUTICS ☐ OTHER:

III. BIOPHARMACEUTICS

- ☐ DISSOLUTION
- ☐ BIOAVAILABILTY STUDIES
- ☐ PHASE IV STUDIES
- ☐ DEFICIENCY LETTER RESPONSE
- ☐ PROTOCOL-BIOPHARMACEUTICS
- ☐ IN-VIVO WAIVER REQUEST

IV. DRUG EXPERIENCE

- ☐ PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL
- ☐ DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES
- ☐ CASE REPORTS OF SPECIFIC REACTIONS (List below)
- ☐ COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP
- ☐ REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY
- ☐ SUMMARY OF ADVERSE EXPERIENCE
- ☐ POISON RISK ANALYSIS

V. SCIENTIFIC INVESTIGATIONS

☐ CLINICAL ☐ PRECLINICAL

COMMENTS/SPECIAL INSTRUCTIONS: This is a Multi-Discipline Amendment in response to our NA deficiency letter dated June 29, 2002. The sponsor did not propose a trade name. Therefore, a trade name review not necessary. However, we are close to an approval action and would like a review of the vial labeling and the package labeling.

cc: Original , HFD-160/Div. Files

SIGNATURE OF REQUESTER:	METHOD OF DELIVERY (Check one): ☐ MAIL ☒ HAND X
SIGNATURE OF RECEIVER:	SIGNATURE OF DELIVERER:

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/s/

Renee Tyson
11/21/02 10:37:01 AM