CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

19-044 / S-006

Trade Name: Indium In-111 Oxyquinoline

Generic Name:

Sponsor: GE Healthcare

Approval Date: August 8, 1990

Indications: For the substitution of the USP Limulus Amebocyte bacterial endotoxin test for the rabbit pyrogen test.

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APPLICATION NUMBER:

19-044 / S-006

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APPLICATION NUMBER:

19-044 / S-006

APPROVAL LETTER

9.1

NDA 19-044/S-006

AUG 8 1990

Amersham Corporation
2636 South Clearbrook Drive
Arlington Heights, Illinois 60005-4692

Attention: John H. Waterman
Manager, Scientific and Regulatory Affairs

Dear Mr. Waterman:

Reference is made to your supplemental new drug application dated March 22, 1989 submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for indium In 111 oxyquinoline.

The supplemental new drug application provides for the substitution of the USP Limulus Amebocyte Lysate bacterial endotoxin test for the rabbit pyrogen test.

We have completed our review of this supplemental new drug application and it is approved effective on the date of this letter.

We remind you that you must comply with the requirements set forth under 21 CFR 314.80 and 314.81 for an approved NDA.

Sincerely yours,

J Palmer 8-7-90

John F. Palmer, M.D.
Director
Division of Medical Imaging,
Surgical and Dental Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

cc:
NDA 19-044/S-006
HFD-160/Div File
HFD-160/CSO/Lange
HFD-160/Ruby/Sheinin
HFD-160/Stone
R/D Endorsed by:
S. Lange 7.31.90
E. Ruby 8.03.90
E. Sheinin, Ph.D. 8.03.90
W. Rumble 8.06.90
F/T by: RCannon 8.06.90
Wang 0467B
APPROVAL

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

19-044 / S-006

CHEMISTRY REVIEW(S)

APR 4 1990 APR 4 1990 9.1

CHEMIST'S REVIEW | Organization: HFD-160 | NDA Number: 19-044

Name and Address of Applicant
Amersham Corporation
2636 South Clearbrook Dr.
Arlington Heights, IL 60005-4692
(312) 593-6300

AF Number

Supplements
Number Date
S-006 22Mar89

Name of Drug

Non-Proprietary Name
Indium In-111 Oxyquinoline

Supplement Provides For:
Substitution of the USP Limulus Amebocyte Lysate bacterial endotoxin test for the rabbit pyrogen test.

Pharmacological Category	How Dispensed	Related NDA/DMF
diagnostic radiopharmaceutical	Rx	

Dosage Form	Potency
injectable solution	about 1 mCi In-111; and 50 ug 8-hydroxyquinoline

Chemical Name and Structure
complex of 8-hydroxyquinoline and In-111 [redacted] (b) (4)

Comments

A microbiology consult was requested on 09Aug89. The consult was completed 02Apr90, and the reviewing microbiologist recommended approval of the supplement (see microbiologist's review in file).

Conclusions and Recommendations

Approval is recommended.

Reviewer: Eric Ruby, Chemist, HFD-160 — 03Apr90 — Date Completed: 03Apr90

4-4-90

Orig. NDA 19-044/S-006
HFD-160/Div. File
HFD-160/ERuby
HFD-160/FStone
HFD-161/SLange
R/D Init. by: ESheinin/ 4-4-90
F/T by: ERuby

C:\RUBY.03\19044S06.CR1

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

19-044 / S-006

MICROBIOLOGY REVIEW(S)

9.1

APR 2 1990

MICROBIOLOGIST'S REVIEW OF SUPPLEMENT
DIVISION OF MEDICAL IMAGING, SURGICAL AND DENTAL DRUG PRODUCTS
April 2, 1990

NDA/Supplement Number: NDA 19-044/S006

Document Date: March 22, 1989

Amendments and Others: N/A

Name and Address of Applicant: Amersham Corporation
Arlington Heights, IL 60005

Name of Drug: Indium (^{111}In) Oxyquinoline

Supplement Provides For: Use of the LAL 5000 Automated Endotoxin Detection System in lieu of the rabbit pyrogen test as a finished product release test.

Pharmacological Category: Diagnostic radiopharmaceutical - For intravenous use in radiolabeling autologous leukocytes.

Dosage Form: Sterile solution for IV injection. 1.0 ml vials.

Related Documents: ---

Comments:

The subject Supplement provides for use of an automated spectrophotometric LAL test system. The system, LAL 5000, is commercially available and is available from (b)(4) (b)(4). The Supplement is submitted as a "Special Supplement - Changes Being Effected" (21 CFR 314.70 (c)). The Agency LAL guidelines provide for such submissions.

The following items are incorporated into the submission and are part of the testing protocol:

(1) For routine testing the product is diluted 1:200 in phosphate buffer, pH 7.0. The product consists of several inhibiting/enhancing substances (e.g., HEPES buffer, (b)(4)) so that dilution in phosphate buffer was necessary. Product standard curves are run daily.

(2) A product limit of (b)(4) EU/ml has been set. This is within the Agency limit of 5 EU/kilogram based on maximum human dose. The maximum human dose of the drug is the entire contents of a 1.0 ml vial at expiry. Using the 1:200 dilution, the pass/fail limit in the assay is (b)(4) EU/ml in the diluted sample. Three samples from the beginning, middle, and end of a run are pooled prior to dilution for testing. Since the assay is quantitative (i.e., is not performed as a limit test), pooling should not affect the

outcome.

(3) Laboratory qualification is performed.

(4) Operator qualification is performed.

(5) The potency of the Control Standard Endotoxin (CSE) in relation to the Lysate used is determined.

(6) Inhibition/enhancement testing has been carried out. Product standard curves are carried out each day.

Acceptance criteria for the automated detection system appear to comply with all aspects of the Agency guidelines (e.g., correlation coefficient in standard curves at least (b) (4), slope of curve between (b) (4), product negative control to contain less than (b) (4) of the endotoxin concentration represented by the lowest point on the standard curve, etc.). There is, therefore, no objection to the use of this test.

Conclusions and Recommendations: Recommend approval of use of the LAL test as described.

Name: Peter H. Cooney, PhD
Supervisory Microbiologist, HFD-160

Signature: Peter H Cooney 4/2/90

Date Completed: April 2, 1990

cc: NDA 19-044
HFD-160/Cooney/Stone/Ruby

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

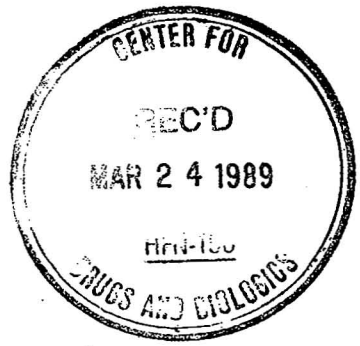
19-044 / S-006

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

Amersham Corporation
2636 South Clearbrook Drive
Arlington Heights, Illinois 60005-4692
(312) 593-6300

NDA NO. 19-044 REF. NO. 006
NDA SUPPL FOR SCS

Amersham



March 22, 1989

Food and Drug Administration
Division of Oncology and
Radiopharmaceutical Drug Products [HFN-150]
5600 Fishers Lane
Rockville, MD 20857

Re: NDA 19-044
Indium (^{111}In) Oxyquinoline
Special Supplement - Changes Being Effected

Gentlemen:

Please refer to our approved Application, identified above.

The purpose of this Supplement is to provide for substitution of the U.S.P. *Limulus Amebocyte* Lysate pyrogen test for the currently employed rabbit pyrogen test as a finished product release test for this product.

Validation of this method was conducted according to the Agency's guideline "Validation of the Limulus Amebocyte Lysate test as an end-product endotoxin test for human and animal parenteral drugs, biological products, and medical devices," published December, 1987. That guideline specifically provides for supplementing approved Applications in accordance with 21 CFR 314.70(c) [guideline page 4].

In support of this Supplement, the following data are supplied:

- Report — Validation of the LAL 5000 Automated Endotoxin Detection System
- Report — Validation of the LAL 5000 Automated Endotoxin Detection System as an End-product Test for Indium Oxyquinoline In-111
- Standard Operating Procedure — Automated Endotoxin Detection Using LAL 5000

In addition, those sections of our approved Application affected by this changes will be updated to reflect this new procedure, as appropriate.

Batches of Indium (^{111}In) Oxyquinoline manufactured on and after March 23, 1989 will be tested for pyrogens according to this method.

We appreciate your continued interest in our Application. Please contact me should you have any questions or comments concerning this Supplement.

Yours truly,

Jack Waterman

John H. Waterman
Manager, Scientific and Regulatory Affairs

W:ths

Amersham Corporation

NDA 19-044
Indium (^{111}In) Oxyquinoline
Special Supplement - Changes Being Effected

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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

Date March 24,1989

NDA No. 19-044

Amersham Corporation
2636 S. Clearbrook Drive
Arlington Heights, IL 60005
Attn: John H. Waterman
Manager, Scientific and Regulatory Affairs

Dear Sir/Madam:

We acknowledge receipt of your supplemental application for the following:

Name of Drug: Indium (111 In) Oxyquinoline Solution

NDA Number: 19-044

Supplement Number: S-006

Date of Supplement: March 23,1989

Date of Receipt: March 24,1989

All communications concerning this NDA should be addressed as follows:

National Center for Drugs and Biologics(HFN-150)
Attention: Document Control Room 17B-28
5600 Fishers Lane
Rockville, MD 20857

Sincerely Yours,

A. Thomas

For R.G. Scully
Supervisory Consumer Safety Officer
Division of Oncology and Radiopharmaceutical
Drug Products
National Center for Drugs and Biologics

FORM FDA 3217e (6/83)

☆ GPO : 1983 O - 408-424

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 10-044/S-006

SEP 18 1989

Amersham
2636 South Clearbrook Drive
Arlington Heights, Illinois
60005-4692

Attention: J.H Waterman
Manager,
Scientific & Regulatory Affairs

Gentlemen:

We acknowledge receipt of your supplemental application(s) for the following:

Name of Drug: Indium III In Oxyquinoline Solution

NDA Number: 19-044

Supplement Number: S-006/Controls

Date of Supplement: September 15, 1989

Date of Receipt: September 19, 1989

File Date: November 20, 1989

All communications concerning this NDA should be addressed as follows:

Center for Drug Evaluation and Research, HFD-160
Attention: Document Control Room 18B-03
5600 Fishers Lane
Rockville, MD 20857

Sincerely Yours,

Regina D. Joyce

Regina D. Joyce
Acting Supervisory Consumer Safety Officer
Division of Medical Imaging,
Surgical and Dental Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research