CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: 020181

CHEMISTRY REVIEW(S)

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DIVISION OF METABOLIC & ENDOCRINE DRUG PRODUCTS

REVIEW OF CHEMISTRY, MANUFACTURING AND CONTROLS

NDA # 20-181
CHEMISTRY REVIEW # 3

DATE REVIEW COMPLETED: 12-24-97

SUBMISSION TYPE	DOCUMENT DATE	CDER DATE	ASSIGNED (Received) DATE
Amendment (AZ)	7-24-97	7-28-97	8-8-97
Amendment (BC)	10-22-97	10-23-97	10-24-97
New Corresp.	10-24-97	10-27-97	10-31-97
Amendment (BC)	10-27-97	11-3-97	11-7-97
Amendment (BC)	11-4-97	11-5-97	11-10-97
Amendment (BC)	11-5-97	11-7-97	11-19-97
Amendment (BC)	11-5-97	11-10-97	11-18-97
Amendment (BC)	11-11-97	11-12-97	11-19-97
Amendment (BC)	12-19-97	12-19-97	12-24-97

Action Performance Goal Date: 1-21-98

NAME AND ADDRESS OF APPLICANT:

Abbott Laboratories
Hospital Products Division
Attention: Thomas P. Sampogna, Manager, Regulatory Affairs
Abbott Park, IL 60064
847-935-3715

DRUG PRODUCT NAME:

Proprietary: Liposyn III 30% Pharmacy Bulk Package
Established: Intravenous Fat Emulsion Pharmacy Bulk Package
Code Name: none
Official: no

ANDA Suitability Petition/DESI/Patent Status: N/A

PHARMACOLOGICAL CATEGORY/INDICATION:

For use as a source of essential fatty acids and calories during extended periods of parenteral nutrition.

Dosage Form: LVP
Strength: 30%
Route of Administration: admixture used intravenously

APPEARS THIS WAY ON ORIGINAL

The Action Performance Goal Date for this 7-24-97 amendment is 1-21-97; the HFD-510 chemistry review due date is 12-21-97. Refer to the previous chemistry review (#2) dated 1-10-97 and to Chemistry Review #1 dated 8-28-91.

The expiration dating period requested for this drug product remains at 18 months.

The reviewing chemist should monitor performed by Abbott on the refined soybean oil received by Abbott from as a raw material.

Conclusions and Recommendations:

This new drug application is now acceptable from the standpoint of the manufacturing & controls with the understanding that the following commitments are in place:

1. The firm has agreed to submit specifications and method(s) of analysis to control the levels of the two major components

of this NDA 20-181. It is anticipated from discussions with the firm that these

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2. Specifications and a validated method for the determination of will be submitted to this file within 60 days of the 10-17-97 telecon with firm (see MEMO telecon). The preliminary dated 7-10-97 was submitted to this NDA in the 10-22-97 amendment.

3.

Updating information has been provided by

Additional information is being requested of to complete the data which we believe should be included in the DMF. Based on circumstances in place at the time of this review, we believe this additional information, if not part of the file at time of NDA approval, may be provided subsequent to NDA approval. is now considered by HFD-325 to be a food processing plant, and the cGMP evaluation request for this plant has been cancelled by HFD-324. We recommend that the DMF continue to be maintained in current status to support the use of the

cc:
Orig NDA 20-181
HFD-510/Div File
HFD-510/DGWu
HFD-510/SMcCort
HFD-510/SKoch
F/T SKoch 12/24/97

APPEARS THIS WAY
ON ORIGINAL

/S/

Stan Koch

/S/ 12/31/97

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DIVISION OF METABOLIC & ENDOCRINE DRUG PRODUCTS JAN 17 1997

REVIEW OF CHEMISTRY, MANUFACTURING AND CONTROLS

NDA # 20-181
CHEMISTRY REVIEW #2 DATE REVIEW COMPLETED: 1-10-97

SUBMISSION TYPE	DOCUMENT DATE	CDER DATE	ASSIGNED DATE
Amendment	3-11-96	3-12-96	4-9-96
Amendment	5-21-96	5-28-96	

NAME AND ADDRESS OF APPLICANT:

Abbott Laboratories
Hospital Products Division
Attention: Frederick A. Gustafson, Director, Regulatory Affairs
Abbott Park, IL 60064

DRUG PRODUCT NAME:

Proprietary: Liposyn III 30% Pharmacy Bulk Package
Established: Intravenous Fat Emulsion Pharmacy Bulk Package
Code Name: none
Official: no

ANDA Suitability Petition/DESI/Patent Status: N/A

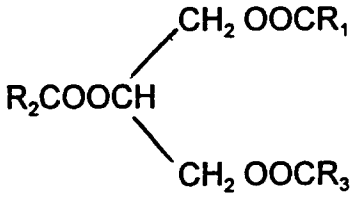
PHARMACOLOGICAL CATEGORY/INDICATION:

For use as a source of essential fatty acids and calories during extended periods of parenteral nutrition.

Dosage Form: LVP
Strength: 30%
Route of Administration: admixture used intravenously

Chemical Name/Structural Formula:

soybean oil - mixture of triglycerides of oleic, linoleic, linolenic, palmitic, and stearic acids.



egg yolk phospholipids - mixture of phospholipids obtained from egg yolk powder, with primary components

phosphatidylcholine and phosphatidylethanolamine.

Remarks:

This drug product will be supplied in 500 ml glass Abbovac containers intended for use as a Pharmacy Bulk Package (PBP). This package is indicated for use in the preparation of sterile, IV nutrient admixtures in the pharmacy. The qualitative composition is identical to that of the Liposyn III products with an increase in fat concentration and Liposyn III 30% is identical to the Liposyn III 20% formulation except for a proportional increase in soybean oil concentration from 20% to 30% and in egg phosphatide concentration from 12 mg/ml to 18 mg/ml.

This BC amendment dated 3-11-96 contains information concerning the chemistry deficiencies conveyed to the firm in the Agency's 11-29-91 N/A letter. All aspects of the N/A letter were not addressed in this submission. Thus, PDUFA time accounting did not begin until the 9/24/96 amendment was received on 9/26/96.

The expiration dating period requested for this drug product remains at 18 months.

Information regarding the status of this application with reference to Abbott Laboratories as the NDA Applicant and as the egg yolk phospholipid supplier discussed with Anne Kelly, a CSO in the Chicago District Office, on (initially) 1-6-97. Anne is scheduled to investigate these facilities (North Chicago and Waukegan, IL resp.) for CGMP regulation compliance and conformance with NDA commitments. Anne alerted to specific particulate concerns with both Lot 47-356-JE and Lot 89-0373D. I also spoke with Sharon Thoma in the Minneapolis District Office on (initially) 12-18-96 regarding her assignment to inspect the facility in [Based upon telecon with Minneapolis District Office inspector on 1-7-97, the s facility in has not provided assurances in the inspection just completed that the product supplied to is produced in a registered and sanctioned drug manufacturing facility. We are informed that an Official Action Indicated Notification for will likely follow.]

Conclusions and Recommendations:

This new drug application remains inadequate from the standpoint of the manufacturing and controls.

Formal response from HFD-324 regarding CGMP establishment evaluations forthcoming. The EA report was submitted and evaluated as satisfactory in the original submission of this application; in the absence of additional information which indicates otherwise, this issue will not be revisited. The 7-8-96 microbiology review of the 5-21-96 amendment [responding to the Agency's FAX of 12-3-96] finds this application acceptable from the standpoint of sterility assurance.

APPEARS THIS WAY
ON ORIGINAL

/S/

Stan Koch HFD-510

cc:
Orig NDA 20-181
HFD-510/Div File
HFD-510/DGWu
HFD-510/SMcCort
HFD-510/SKoch
F/T SKoch 1/10/97

/S/ 1/17/97

APPEARS THIS WAY
ON ORIGINAL

APPEARS THIS WAY
ON ORIGINAL

DIVISION OF RADIOPHARMACEUTICAL, SURGICAL AND DENTAL DRUG PRODUCTS

REVIEW OF CHEMISTRY, MANUFACTURING AND CONTROLS

NDA # 20-181
CHEMISTRY REVIEW #1

DATE REVIEW COMPLETED: 8-28-91
DATE REVIEW REVISED: 10-7-91

SUBMISSION TYPE	DOCUMENT DATE	CDER DATE	ASSIGNED DATE
original	4-10-91	4-22-91	5-3-91

NAME AND ADDRESS OF APPLICANT:

OCT - 8

Abbott Laboratories
Hospital Products Division
Attention: Frederick A. Gustafson, Director, Regulatory Affairs
Abbott Park, IL 60064

DRUG PRODUCT NAME:

Proprietary: Liposyn III 30% Pharmacy Bulk Package
Established: Intravenous Fat Emulsion Pharmacy Bulk Package
Code Name: none
Official: no

ANDA Suitability Petition/DESI/Patent Status: N/A

PHARMACOLOGICAL CATEGORY/INDICATION:

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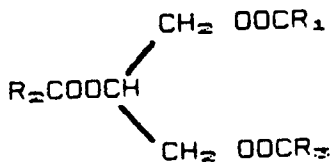

egg yolk phospholipids - mixture of phospholipids obtained from egg yolk powder, with primary components phosphatidylcholine and phosphatidylethanolamine.

Supporting & Related Documents:

Remarks:

This drug product will be supplied in 500 ml and 1000 ml glass Abbovac containers intended for use as a Pharmacy Bulk Package (PBP). This package is indicated for use in the preparation of sterile, IV nutrient admixtures in the pharmacy with automated compounding devices. The qualitative composition is identical to that of the Liposyn III products

for an increase in fat concentration and an increase in the egg phosphatide content, e.g., Liposyn III 30% is identical to the Liposyn III 20% formulation except for a proportional increase in soybean oil concentration from 20% to 30% and in egg phosphatide concentration from 12 mg/ml to 18 mg/ml.

The new drug substances are named as both soybean oil and egg phosphatides.

Conclusions and Recommendations:

This new drug application is not approvable from the standpoint of the manufacturing and controls.

APPEARS THIS WAY
ON ORIGINAL

/S/

Stan Koch HFD-160

cc:
Orig NDA 20-181
HFD-160/Div File
HFD-160/JKenealy, JWilson, PCooney, SKoch
HFD-161/SMcCort
HFD-160/ESheinin
HFD-102/CKumkumian
R/D init by ESheinin
F/T SKoch
pc

/S/

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APPEARS THIS WAY
ON ORIGINAL