CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: 20849

ADMINISTRATIVE DOCUMENTS/CORRESPONDENCE

Division of Metabolic and Endocrine Drug Products, HFD-510

CONSUMER SAFETY OFFICER REVIEW

Application Number: 20-849

Name of Drug: 20% ProSol™ - sulfite free (Amino Acid) Injection

Sponsor: Baxter Healthcare

Material Reviewed

Submission Date(s): August 11, 1998

APPEARS THIS WAY
ON ORIGINAL

Receipt Date(s): August 12, 1998

Background and Summary Description:

Draft labeling dated August 25, 1997 was submitted for review with the original submission for NDA 20-849. As a result of the August 3, 1998, internal meeting in our Division the following labeling revisions to the August 25, 1997 labeling, were Faxed to the Sponsor:

APPEARS THIS WAY
ON ORIGINAL

PACKAGE INSERT:

1. In the **DESCRIPTIONS** section of the package insert, paragraph 2, line 6, the last word that reads "material" should be change to read "materials".

2. In the **INDICATIONS AND USAGE** section,

APPEARS THIS WAY
ON ORIGINAL

   a. The first paragraph line 5 that reads,

   should be changed to read,

   b. **Central Vein Administration** subsection, last sentence which reads,

c. **Peripheral Vein Administration**, subsection, last sentence which reads.

should be bolded.

3. Under the **PRECAUTIONS** section, last paragraph which reads,

should be bolded.

4. Under **PRECAUTIONS** section, the Pediatric Use subsection is unacceptable. The Sponsor needs to make a statement about the safety and efficacy of the product in the pediatric population.

In a August 5, 1998 FAX the Sponsor agreed to items 1, 2b, 2c, and 3. above. They proposed alternate wording to item 2a as follows:

In an August 7, 1998, Fax the sponsor agreed with Dr. Eric Colman, of this Division to include the following wording to the PRECAUTIONS - Pediatric Use subsection of the package insert:

An August 11, 1998, draft labeling was submitted to NDA 20-849 incorporating the changes agreed above.

Review

The August 11, 1998 draft labeling was compared with the August 25, 1997, draft labeling. All the revisions agreed to above have been incorporated in to the August 11, 1998, draft labeling.

No other changes to the August 11, 1998, labeling (package insert, container and over pouch labels) were made by the Sponsor.

Conclusions

RECOMMENDATION:

Pending concurrence of the reviewing staff, the draft labeling dated July 27, 1998 for NDA 20-898 is recommended for approval.

/S/

Eric Colman, M.D.

/S/

Gloria Troendle, M.D.
Medical Team Leader

/S/

Ron Steigerwalt, Ph.D.
Pharmacology Team Leader

/S/

David Lewis, Ph.D.
Chemistry Reviewer

/S/

Duu-Gong Wu
Chemistry Team Leader

/S/

Steve McCort
Project Manager

APPEARS THIS WAY
ON ORIGINAL

/S/

Solomon Sobel, M.D.
Division Director

cc:
Original
HFD-510/Div. Files
HFD-510/SMcCort/EColman/GTroendleRSteigerwalt/DLewis/DWu
HFD-510/Solomon Sobel, M.D.

CSO REVIEW

APPEARS THIS WAY
ON ORIGINAL

DEC 12 1997

MEMORANDUM OF TELECON

DATE: December 12, 1997

APPLICATION NUMBER:NDA 20-849; 20% PROSOL

BETWEEN:

Name: Tamima Itani, Ph.D.
Phone: 847-252-2577
Representing: Baxter Heathcare

APPEARS THIS WAY
ON ORIGINAL

AND

Name: Steve McCort
Division of Metabolic and Endocrine Drug Products, HFD-510

SUBJECT: Fees for Prosol Application

APPEARS THIS WAY
ON ORIGINAL

Based on a E-Mail from Tom Hassell, Review Management, regarding user fees, the Sponsor was called They were told that, while the application qualifies as a 505(b)(2) application, the application requires a fee. This determination was based on:

1. Composition of the product (new quantitative combination of active drug substances- i.e. Amino acids)
2. A new indication "use in fluid restricted patients."
3. The Divisions's determination that "clinical data" consisting of adequate and well controlled studies will be required for approval and therefore will require a fee. The literature supplied in this application for the new indication, "use in fluid restricted patients" fulfills this requirement.

Since the firm has paid of the required fee upfront they were told that they are in arrears for the rest of the fee

APPEARS THIS WAY
ON ORIGINAL

/S/

Steve McCort
Project Manager, HFD-510

APPEARS THIS WAY
ON ORIGINAL

cc: Original NDA 20-849
HFD-510/Div. File
HFD-510/Steve McCort
HFD-510/EGalliers/GTroendle/EColman/S 5/8/98

TELECON

ITEM 14. PATENT CERTIFICATION

Baxter certifies that, to the best of its knowledge, there are no active, competitor patents that claim the drug substance, drug product or method of using the drug product that would affect the marketability of the proposed product.

Certification per section 505(b)(2) of the Food, Drug and Cosmetic Act:

In the opinion, and to the best knowledge of Baxter Healthcare Corporation, there are no patents that claim the drug or drugs on which investigations that are relied upon in this application were conducted or that claim a use of such drug or drugs.

Marcia Marconi (VP) 12/18/97

Marcia Marconi
Vice President
Regulatory Affairs

Date

APPEARS THIS WAY
ON ORIGINAL

ITEM 13. PATENT INFORMATION

The drug product formulation for 20% ProSol™ (Amino Acid) Injection is protected by US Patent Number 5206269. The title of the patent is "Highly Concentrated Amino Acid Solution", invented by Douglas G. Johnson and Josef K. Ludwig of Baxter Healthcare Corporation, dated April 27, 1993. This patent will expire on March 20, 2012.

The undersigned declares that patent number 5206269 covers the formulation, of 20% ProSol™ - sulfite-free (Amino Acid) Injection. This product is the subject of this application for which approval is being sought:

Marcia Marconi (TP) 8/25/97

Marcia Marconi, Vice President
Regulatory Affairs

Date

APPEARS THIS WAY
ON ORIGINAL

EXCLUSIVITY SUMMARY for NDA # 20-898 SUPPL # ____

Trade Name 20% ProSol™ - sulfite free Generic Name Amino Acid Injection In PL 146® in Plastic Container

Applicant Name Baxter Heathcare Corporation HFD-510

Approval Date 8-26-98

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:

_____

_____

APPEARS THIS WAY
ON ORIGINAL

Form OGD-011347 Revised 8/7/95; edited 8/8/95
cc: Original NDA Division File HFD-85 Mary Ann Holovac

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?

_____

IF YOU HAVE ANSWERED "NO" TO ALL OF THE ABOVE QUESTIONS, GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8.

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?

YES /___/ NO /_x__/

If yes, NDA # _____ Drug Name _____

IF THE ANSWER TO QUESTION 2 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8.

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

YES /___/ NO /_x__/

IF THE ANSWER TO QUESTION 3 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8 (even if a study was required for the upgrade).

APPEARS THIS WAY
ON ORIGINAL

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 /_x__/ NO /___/

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

NDA # 17-957 Novamine 15% amino acid solution in glass container

IF THE ANSWER TO QUESTION 1 OR 2 UNDER PART II IS "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8. IF "YES," GO TO PART III.

ADDITIONAL NDAs: Part II #2

NDA 19-438 Aminsyn II 3.5%, 5%, 7%, 8.5% and 10% Amino Acid Solution in Glass Container

NDA 20-041 Aminosyn II 15% Amino Acid Solution in Plastic Container
NDA 19-398 Aminosyn-PF 7% Amino Acid Solution in Glass Container
NDA 19-492 Aminosyn-PF 10% Amino Acid Solution in Glass Container
NDA 19-018 TrophAmine 6% and 10% Amino Acid Solution in Glass Container

PART III THREE-YEAR EXCLUSIVITY FOR NDA'S AND SUPPLEMENTS

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.

Clinical [No right of Reference] to NDA 17-957 Novamine YES /X/ NO /__/

IF "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8.

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 /X/ 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 8:**

_____

_____

(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?

List submitted YES /X/ NO /__/
Statement NOT submitted

(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 /X/

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 /X/

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 # _____

APPEARS THIS WAY
ON ORIGINAL

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 /X/
Investigation #2	YES /___/	NO /X/
~~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 /X/
Investigation #2	YES /___/	NO /X/
~~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 #1, Study # _____

Investigation #2, 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 /X/ Explain _____

_____ _____

_____ _____

Investigation #2 !

YES /___/ Explain _____ ! NO /X/ 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.)

Not applicable YES /___/ NO /___/

If yes, explain: _____

_____

_____

_____

/S/ 5-21-98

Signature Date

Title: Consumer Safety Officer

cmg 8/24/98

/S/ 8-21-98

Signature of Division Director Date

APPEARS THIS WAY
ON ORIGINAL

cc: Original NDA Division File HFD-85 Mary Ann Holovac

PEDIATRIC PAGE

(Complete for all original applications and all efficacy supplements)

NDA/PLA/PMA # 20-849 Supplement # _____ Circle one: SE1 SE2 SE3 SE4 SE5 SE6

2070 PROSOL™ - Sulfite free

HFD-510 Trade and generic names/dosage form: (Amino Acid) Injection Action: (AP) AE NA

Applicant Baxter Therapeutic Class 35

Indication(s) previously approved not applicable

Pediatric information in labeling of approved indication(s) is adequate ___ inadequate ___

Indication in this application ① parenteral nutrition nitrogen balance offset ② use in fluid restricted patients requiring TPN (For supplements, answer the following questions in relation to the proposed indication.)

___ 1. **PEDIATRIC LABELING IS ADEQUATE FOR ALL PEDIATRIC AGE GROUPS.** Appropriate information has been submitted in this or previous applications and has been adequately summarized in the labeling to permit satisfactory labeling for all pediatric age groups. Further information is not required.

___ 2. **PEDIATRIC LABELING IS ADEQUATE FOR CERTAIN AGE GROUPS.** Appropriate information has been submitted in this or previous applications and has been adequately summarized in the labeling to permit satisfactory labeling for certain pediatric age groups (e.g., infants, children, and adolescents but not neonates). Further information is not required.

___ 3. **PEDIATRIC STUDIES ARE NEEDED.** There is potential for use in children, and further information is required to permit adequate labeling for this use.

___ a. A new dosing formulation is needed, and applicant has agreed to provide the appropriate formulation.

___ b. A new dosing formulation is needed, however the sponsor is either not willing to provide it or is in negotiations with FDA.

___ c. The applicant has committed to doing such studies as will be required.
___ (1) Studies are ongoing,
___ (2) Protocols were submitted and approved.
___ (3) Protocols were submitted and are under review.
___ (4) If no protocol has been submitted, attach memo describing status of discussions.

___ d. If the sponsor is not willing to do pediatric studies, attach copies of FDA's written request that such studies be done and of the sponsor's written response to that request.

___ 4. **PEDIATRIC STUDIES ARE NOT NEEDED.** The drug/biologic product has little potential for use in pediatric patients. Attach memo explaining why pediatric studies are not needed.

X 5. **If none of the above apply,** attach an explanation, as necessary.

APPLIES ONLY TO ORIG

ATTACH AN EXPLANATION FOR ANY OF THE FOREGOING ITEMS, AS NECESSARY.

/S/ - Medical Officer — 8/20/98

Signature of Preparer and Title — Date

cc: ~~Orig NDA/PLA/PMA~~ # 20-849
HFD-510 /Div File
NDA/PLA Action Package
HFD-006/ SOlmstead (plus, for CDER/CBER APs and AEs, copy of action letter and labeling)

APPLIES ONLY TO ORIG

NOTE: A new Pediatric Page must be completed at the time of each action even though one was prepared at the time of the last action. (revised 3/12/97)

MEMO TO THE FILE

DATE: August 20, 1998

NDA #: 20-849

DRUG: ProSol 20% amino acid injection

RE: Pediatric Page

ProSol 20% Amino Acid Injection was filed as a 505 (b)(2) application. As such, the approval of this product was based primarily on published literature. In keeping with this approach, the Division will request the sponsor to submit, if available, literature that might support the safe and effective use of ProSol in the treatment of pediatric patients.

/S/ 8/20/98
Eric Colman, MD

APPEARS THIS WAY
ON ORIGINAL

Attachment 2

Copy of Debarment Certification

20% ProSol™ - sulfite-free (Amino Acid) Injection
in PL 146® Plastic Container
NDA 20-849
Debarment Certification

APPEARS THIS WAY
ON ORIGINAL

CERTIFICATION PER THE GENERIC DRUG ENFORCEMENT ACT OF 1992

In accordance with section 306(k) of the Federal Food, Drug and Cosmetic Act (21 U.S.C. 335a(k)(1)), Baxter Healthcare Corporation wishes to certify that Baxter Healthcare Corporation did not and will not use in any capacity the services of any person debarred under subsections (a) or (b) [Section 306(a) or (b)], in connection with this application.

In addition, in accordance with section 306(k) of the Act (21 U.S.C. 335a(k) (2)), Baxter Healthcare Corporation wishes to certify that there are no convictions that occurred within 5 years of today's date, for which a person can be debarred, of the applicant and affiliated persons responsible for the development or submission of the application.

Marcia Marconi (TP)
Marcia Marconi, Vice President
Regulatory Affairs

August 25, 1997
Date

M E M O R A N D U M

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

DATE: August 21, 1998

FROM: Steve McCort

SUBJECT: Environmental Assessment

TO: File for NDA 20-849

An environmental impact analysis report was submitted in accordance with 21 CFR 25.31a(a) and FDA's "Guidance for Industry for the Submission of a n Environmental Assessment in Human Drug Applications and Supplements" dated November, 1995.

In Dr. David Lewis's Chemistry Review #1 dated July 14, 1998, page 39, the conclusion was that the submission qualified for a categorical exclusion under 21 CFR 25.31(c) since the ingredients are naturally occurring chemicals.

/S/

Stephen McCort
Project Manager, HFD-510

David Lewis

Duu-Gong Wu, Ph.D.
Chemistry Team Leader
ONDC II, HFD-510

TL for D-G Wu
8-26-98

cc:

NDA 20-181
HFD-510/Division Files
HFD-510/DGWu/SKoch
HFD-510/CSO/McCort

MEMORANDUM OF A MEETING
DIVISION OF METABOLISM AND
ENDOCRINE DRUG PRODUCTS (HFD-510)

MEETING DATE: August 3, 1998 TIME: 10:00 a.m. PLACE: Parklawn Rm 14B-56

DRUG: 20% Prosol - sulfite free (Amino Acid) Injection

NDA: 20-734

TYPE OF MEETING: Labeling meeting

MEETING CHAIR: Eric Colman, Medical Reviewer

MEETING RECORDER: Steve McCort, Project Manager

PARTICIPANTS:

Eric Colman, M.D., Medical Reviewer (HFD-510)
David Lewis, Chemistry Reviewer (HFD-510)
Ron Steigerwalt, Pharmacology Team Leader (HFD-510)
Steve McCort, Project Manager (HFD-510)

MEETING OBJECTIVE: To review the draft labeling

CONCLUSIONS and DECISIONS REACHED:

The following labeling recommendations were to the August 25, 1997, draft labeling:

1. In the **DESCRIPTIONS** section of the package insert, paragraph 2, line 6, the last word that reads "material" should be change to read "materials".

2. In the **INDICATIONS AND USAGE** section,

   a. The first paragraph line 5 that reads,

   should be changed to read,

b. **Central Vein Administration** subsection, last sentence which reads,

should be bolded.

c. **Peripheral Vein Administration**, subsection, last sentence which reads.

should be bolded.

3. Under the **PRECAUTIONS** section, last paragraph which reads,

such, should never be administered undiluted."

4. Under **PRECAUTIONS** section, the Pediatric Use subsection is unacceptable. The Sponsor needs to make a statement about the safety and efficacy of the product in the pediatric population.

ACTION ITEMS:

Item	Responsible Person	Due Date
1. The firm will be Faxed our comments regarding the draft labeling.		

Signature of Minutes Preparer: /S/

Signature of Meeting Chair: /S/

Signature of Division Director: /S/

APPEARS THIS WAY
ON ORIGINAL

cc: NDA 20-849
HFD-510/DivFile
HFD-510/CSO/SMcCort
HFD-510/GTroendle/EColman/SSobel/RSteigerwalt/DWu/DLewis

MEMORANDUM OF TELECON

DATE: August 26, 1998

APPLICATION NUMBER: NDA 20-849: 20% ProSol

BETWEEN:

Names: Tamima Itani, Ph.D., Regulatory Affairs

Phone: (847) 270-2577
Representing: Baxter Healthcare

AND

Names: Steve McCort, Project Manager
Representing: Division of Metabolic and Endocrine Drug Products, HFD-510

SUBJECT: Confirmation of Receipt of Approval letter with labeling

The approval letter for NDA 20-849 with labeling was FAXED to the Sponsor on August 26, 1998. Dr. Tamima Itani of Baxter acknowledged receipt of both the letter and the labeling.

/S/

Steve McCort
Project Manager, HFD-510

cc: Original 20-849
HFD-510/Div. File
HFD-510/Steve McCort

TELECON

DA 20-849

axter Healthcare Corporation
V. Systems Division
ttention: Marcia Marconi
ice President, Regulatory Affairs
oute 120 and Wilson Road
OUND LAKE, IL 60073

SEP 2 1997

APPEARS THIS WAY
ON ORIGINAL

ear Ms. Marconi:

We have received your new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for the following:

Name of Drug Product: 20% ProSol™ - sulfite free (Amino Acid) Injection in PL 146® Plastic Container

Therapeutic Classification: Standard

Date of Application: August 25, 1997

APPEARS THIS WAY
ON ORIGINAL

Date of Receipt: August 27, 1997

Our Reference Number: 20-849

APPEARS THIS WAY
ON ORIGINAL

Unless we notify you within 60 days of our receipt date that the application is not sufficiently complete to permit a substantive review, this application will be filed under section 505(b) of the Act on October 26, 1997, in accordance with 21 CFR 314.101(a).

If you have any questions, please contact Steve McCort, Consumer Safety Officer, at (301) 827-6415.

Please cite the NDA number listed above at the top of the first page of any communications concerning this application.

Sincerely yours,

/S/ 9/2/97

Enid Galliers
Chief, Project Mangement Staff
Division of Metabolic
and Endocrine Drug Products, HFD-510
Office of Drug Evaluation II
Center for Drug Evaluation and Research

FOR DRUG
EC'D
.1 1997
D-510
SEARCH

I.V. Systems Division
Regulatory Affairs

Baxter Healthcare Corporation
Route 120 & Wilson Road
Round Lake, Illinois 60073-0490

847.546.6311
Fax: 847.270.4668

Baxter

August 11, 1998

Steve McCort
Consumer Safety Officer
Office of Drug Evaluation II
Division of Metabolism and Endocrine Drug Products
Center for Drug Evaluation and Research, Room 14B-04
Food and Drug Administration
5600 Fishers Lane - HFD-510
Rockville, MD 20857

Re: NDA 20-849: 20% ProSol™ - sulfite-free (Amino Acid) Injection in PL 146® Plastic Container

Minor Amendment – Final Draft Labeling

Dear Sir or Madam:

Per telephone request from Mr. Steve McCort, we are submitting an archival copy and a review copy of the direction insert, the container labels and the overpouch labels for the above-referenced product. The direction insert reflects all amendments agreed to with the Agency through August 7, 1998. A paper copy of formatted labeling appears in **Attachment 1**. An electronic copy of the labeling on a 3 1/2 diskette formatted in Microsoft® Word97, as well as a paper copy of the unformatted labeling are provided in **Attachment 2**.

Thank you for incorporating this information into the file. If you have questions or comments, please contact me, or Tamima Itani, Ph.D. at (847) 270-2577.

Sincerely,

Marcia Marconi (TI)

Marcia Marconi
Vice President
Regulatory Affairs
(847) 270-4637
(847) 270-4668 (Fax)

I.V. Systems Division
Regulatory Affairs

Baxter Healthcare Corporation
Route 120 & Wilson Road
Round Lake, Illinois 60073-0490

847.546.6311
Fax: 847.270.4668

Baxter

August 10, 1998

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation II
Division of Metabolism and Endocrine
Drug Products, HFD-10
Document Room, 14B-19
5600 Fishers Lane
Rockville, MD 20857

RE: NDA 20-849: 20% ProSol™ - sulfite-free (Amino Acid) Injection in PL 146® Plastic Container

Response to Agency's Labeling Recommendations

--- MINOR AMENDMENT ---

Dear Sir or Madam:

Attached is the modified Direction Insert for the referenced drug product which incorporates the Agency's August 4, 1998 recommendations as well as subsequent changes that were agreed upon by Baxter and the Agency.

Thank you for incorporating this information into the file. If you have questions or comments, please contact me, or Tamima Itani, Ph.D. at (847) 270-2577.

Sincerely,

Marcia Marconi (RC)

ORIGINAL

Marcia Marconi
Vice President
Regulatory Affairs
(847) 270-4637
(847) 270-4668 (Fax)

I.V. Systems Division
Regulatory Affairs

Baxter Healthcare Corporation
Route 120 & Wilson Road
Round Lake, Illinois 60073-0490

847.546.6311
Fax: 847.270.4668

C

Baxter

August 3, 1998

Steve McCort
Consumer Safety Officer
Office of Drug Evaluation II
Division of Metabolism and Endocrine Drug Products
Center for Drug Evaluation and Research, Room 14B-04
Food and Drug Administration
5600 Fishers Lane - HFD-510
Rockville, MD 20857

APPEARS THIS WAY

Re: NDA 20-849: 20% ProSol™ - sulfite-free (Amino Acid) Injection in PL 146® Plastic Container

Desk Copy of Requested Information

APPEARS THIS WAY ON ORIGINAL

Dear Mr. McCort:

Per our telephone conversation this morning, I have attached a copy of the safety results previously submitted in Item 8.VI. of NDA 20-849.

Please do not hesitate to contact me if I can be of further assistance.

Sincerely,

Tamima Itani

Tamima Itani, Ph.D.
Associate Director
Regulatory Affairs
(847) 270-2577
(847) 270-4668 (Fax)

8-13-98

I.V. Systems Division
Regulatory Affairs

Baxter Healthcare Corporation
Route 120 & Wilson Road
Round Lake, Illinois 60073-0490

847.546.6311
Fax. 847.270.4668

Baxter

July 14, 1998

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation II
Division of Metabolic and Endocrine
Drug Products, HFD-10
Document Room. 14B-19
5600 Fishers Lane
Rockville, MD 20857

APPEARS THIS WAY
ON ORIGINAL

Re: NDA 20-849: 20% ProSol™ - sulfite-free (Amino Acid) Injection in PL 146® Plastic Container

Request for Categorical Exclusion

--- MINOR AMENDMENT ---

Dear Sir or Madam:

Per 21 CFR 25.31(c), Baxter Healthcare Corporation is requesting categorical exclusion from the requirements of 21 CFR 25 (Environmental Impact Considerations) for the above-referenced NDA. The active moieties that comprise the new drug product, all of which are amino acids, are naturally occurring substances and are not expected to alter significantly the concentration or distribution of amino acids, their metabolites, or degradation products in the environment as a result of approval of this NDA. Furthermore, to the best of our knowledge, we do not believe that there are any extraordinary circumstances, as defined in 21 CFR 25.15(d), that would indicate that the approval of this new drug product could affect the quality of the human environment.

APPEARS THIS WAY
ON ORIGINAL

An amended **Item 3.IV** is attached.

A field copy of this amendment was submitted to the Chicago District office on today's date. Baxter certifies that the field copy is a true copy of this amendment.

20% ProSol™ - sulfite-free (Amino Acid) Injection
in PL 146® Plastic Container
NDA 20-849
Minor Amendment

Baxter

APPEARS THIS WAY
ON ORIGINAL

Please contact me, or Tamima Itani, Ph.D. at (847) 270-2577 if you have comments or questions regarding this amendment. Thank you for your time and consideration in its review.

Sincerely,

Marcia Marconi

Marcia Marconi
Vice President
Regulatory Affairs
(847) 270-4637
(847) 270-4668 (Fax)

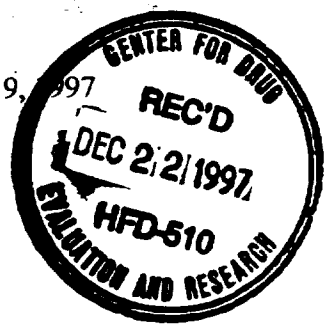
I.V. Systems Division
Regulatory Affairs

Baxter Healthcare Corporation
Route 120 & Wilson Road
Round Lake, Illinois 60073-0490

847-546-6531
Fax 847-270-4668

ORIGINAL
AMENDMENT

Baxter



December 19, 1997

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation II
Division of Metabolism and Endocrine
Drug Products, HFD-10
Document Room, 14B-19
5600 Fishers Lane
Rockville, MD 20857

Re: NDA 20-849: 20% ProSol™ - sulfite-free (Amino Acid) Injection in PL 146® Plastic Container

Response to Request for Additional Information

— MINOR AMENDMENT —

Dear Sir or Madam:

This letter is in response to the telephone conversation between David Lewis, Ph.D. and Tamima Itani, Ph.D. on December 4, 1997. The additional information requested by Dr. Lewis is provided below.

Information regarding extractables of the container system

The 20% ProSol™ solution is packaged in a PL 146® plastic container, which is

The following container extractives were monitored during the NDA stability studies: calcium, zinc and DEHP. The extractive data were provided as part of the stability data in Item 3.II. **Addendum 5** of NDA 20-849. The choice to monitor these extractives is based on Baxter's extensive experience with the PL 146® container.

Baxter Healthcare Corporation introduced the PL 146® plastic container in 1970, when it was first approved for 6% Dextran 70 and 0.9% Sodium Chloride Injection (NDA 16-607). Since then, the PL 146® container system has been

Baxter

approved for over 65 NDAs, including NDAs for amino acid products: NDA 18-931 for 5.5% and 8.5% Travasol® Injections; NDA 19-520 for Amino Acid and Dextrose Injections in Dual Chamber Containers; NDA 20-107 for Novamine® 15% Injection; NDA 20-173 for 5.5% and 8.5% Travasol® with Electrolytes; NDA 20-177 for 3.5% Travasol® with Electrolytes; and NDA 20-147 for Amino Acid with Electrolytes and Dextrose Injections.

Extractives from a container system fall into either of two categories, particulate or soluble. The accumulation of extractables from the container system is assessed by tests designed to evaluate the extractives in each of these categories. Suitable particle counting methodologies are used to evaluate particulate-type extractives present in the solution above their intrinsic solubility.

3 PAGES REDACTED

CONTAINED TRADE SECRETS and/or CONFIDENTIAL/ COMMERCIAL INFORMATION

Baxter

Please contact me, or Tamima Itani, Ph.D. at (847) 270-2577 if you have comments or questions regarding this application. Thank you for your time and consideration in its review.

Sincerely,

Marcia Marconi (TI)

Marcia Marconi
Vice President
Regulatory Affairs
(847) 270-4637

REVIEWS COMPLETED	
CSO ACTION: ☐ LETTER ☐ N.A.I. ☐ MEMO	
CSO INITIALS	DATE

APPEARS THIS WAY
ON ORIGINAL

I.V. Systems Division
Regulatory Affairs

Baxter Healthcare Corporation
Route 120 & Wilson Road
Round Lake, Illinois 60073-0490

A18807N

ORIGINAL

NEW CORRESP
NEW AMENDMENT

Baxter

December 19, 1997

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation II
Division of Metabolism and Endocrine
Drug Products, HFD-10
Document Room, 14B-19
5600 Fishers Lane
Rockville, MD 20857

Re: NDA 20-849: 20% ProSol™ - sulfite-free (Amino Acid) Injection in PL 146® Plastic Container

— MINOR AMENDMENT —

Dear Sir or Madam:

Per a previous telephone conversations between Mr. Steve McCort and Tamima Itani, Ph.D., we are amending NDA 20-849 to provide patent certification per section 505(b)(2) of the Federal Food, Drug and Cosmetic Act. An amended **Item 14** is appended to this correspondence.

Please contact me, or Tamima Itani, Ph.D. at (847) 270-2577 if you have comments or questions regarding this application. Thank you for your time and consideration in its review.

Sincerely,

Marcia Marconi (12)

Marcia Marconi
Vice President
Regulatory Affairs
(847) 270-4637

REVIEWS COMPLETED	
CSO ACTION: ☐ LETTER ☐ N.A.I. ☐ MEMO	
CSO INITIALS	DATE

/S/ 12/19/97

I.V. Systems Division
Regulatory Affairs

Baxter Healthcare Corporation
Route 120 & Wilson Road
Round Lake, Illinois 60073-0490

847.546.6311
Fax: 847.270.4668

BB

AMENDMENT

Baxter

ORIGINAL

June 30, 1998

Steve McCort
Consumer Safety Officer
Office of Drug Evaluation II
Division of Metabolism and Endocrine Drug Products
Center for Drug Evaluation and Research, Room 14B-04
Food and Drug Administration
5600 Fishers Lane - HFD-510
Rockville, MD 20857

Re: NDA 20-849: 20% ProSol™ - sulfite-free (Amino Acid) Injection in PL 146® Plastic Container

Request for Bioequivalence Study Raw Data

Dear Mr. McCort:

APPEARS THIS WAY
ON ORIGINAL

In follow-up to our conversation of June 25, 1998, I am providing a disk containing the pharmacokinetic raw data generated in the bioequivalence study conducted on the referenced solution, as requested by Dr. Karen Higgins. The disk contains two files in SAS format, nda.pcl and lab.pcl. These files contain the amino acid concentrations and laboratory results submitted in the August 25, 1997 original NDA in Item 6, Addendum 4, Appendix A, Tables 2 and 3. The data in these files may be viewed using Microsoft Word 6.0 (unformatted) or MS-DOS (formatted).

If there are questions about this correspondence, please contact me or Tamima Itani, Ph.D. at (847) 270-2577.

Sincerely,

Linda Coleman

Linda Coleman
Manager
Regulatory Affairs

Enclosure

APPEARS THIS WAY
ON ORIGINAL

REVIEWS COMPLETED

CSO ACTION:
☐ LETTER ☐ N.A.I. ☐ MEMO

DATE

CSO INITIALS

I.V. Systems Division
Regulatory Affairs

Baxter Healthcare Corporation
Route 120 & Wilson Road
Round Lake, Illinois 60073-0490

847.546.6311
Fax: 847.270.4668

Baxter

November 11, 1997

David Lewis, Ph.D.
Office of Drug Evaluation II
Division of Metabolism and Endocrine Drug Products
Center for Drug Evaluation and Research, Room 14B-04
Food and Drug Administration
5600 Fishers Lane - HFD-510
Rockville, MD 20857

APPEARS THIS WAY
ON ORIGINAL

Re: NDA 20-849: 20% ProSol™ - sulfite-free (Amino Acid) Injection in PL 146® Plastic Container

Dear Dr. Lewis:

APPEARS THIS WAY
ON ORIGINAL

Per your telephone request of Dr. Tamima Itani on November 6, 1997, we are providing you with two samples of empty containers (1000 mL size) for the proposed 20% ProSol™ product (see **Attachment 1**). The containers are not printed with the container label as printing is normally part of the product manufacturing process.

Please do not hesitate to contact me or Tamima Itani at (847) 270-2577.

Sincerely,

Marcia Marconi (pp)

APPEARS THIS WAY
ON ORIGINAL

Marcia Marconi
Vice President
Regulatory Affairs
(847) 270-4637

cc: Mr. Steve McCort, CSO, Division of Metabolism and Endocrine Drug Products, HFD-510, 14B-04 (letter only)

Enclosure

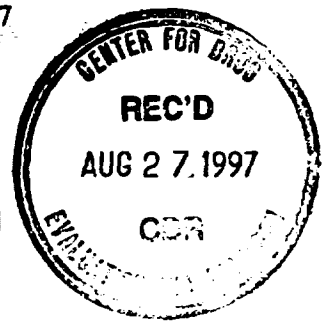
I.V. Systems Division
Regulatory Affairs

Baxter Healthcare Corporation
Route 120 & Wilson Road
Round Lake, Illinois 60073-0490

847.546.6311
Fax: 847.270.4668

Baxter

August 25, 1997



Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation II
Division of Metabolism and Endocrine
Drug Products
Central Document Room
12229 Wilkins Avenue
Rockville, MD 20852

Re: NDA 20-849: 20% ProSol™ - sulfite-free (Amino Acid) Injection in PL 146® Plastic Container

Original New Drug Application

APPEARS THIS WAY
ORIGINAL

Dear Sir or Madam:

Baxter Healthcare Corporation proposes to market a new product, 20% ProSol™ - sulfite-free (Amino Acid) Injection in 500 mL, 1000 mL and 2000 mL PL 146® plastic containers packaged in laminated foil overpouches. 20% ProSol™ - sulfite-free (Amino Acid) Injection is a sterile, nonpyrogenic, hypertonic solution of essential and nonessential amino acids in a Pharmacy Bulk Package. The formulation contains only drug substances already approved in other Baxter amino acid products. The proposed solution, when admixed with concentrated calorie sources, electrolytes, vitamins and minerals and administered parenterally, provides biologically utilizable source material for protein synthesis. 20% ProSol™ - sulfite-free (Amino Acid) Injection is indicated as an adjunct in the offsetting of nitrogen loss or in the treatment of negative nitrogen balance in patients where: (1) the alimentary tract cannot or should not be used, (2) gastrointestinal absorption of protein is impaired, or (3) metabolic requirements for protein are substantially increased, as with extensive burns. Because of its higher concentration (i.e., 20%), this product can supply an amino acid dose equivalent to lower concentration products but in a smaller volume, thereby reducing fluid intake. Given this attribute, 20% ProSol™ is of importance in the clinical management of fluid restricted patients.

APPEARS THIS WAY
ORIGINAL

This cover letter summarizes previous communications with the FDA regarding the proposed products, the submission approach and the applicability of user fees. An overview of the organization of the NDA is also provided.

AUG 2 5 1997

Baxter

Overview of Past Communications with the Agency

Bioequivalence Study

On April 26, 1993, representatives from the FDA, Baxter Healthcare Corporation met to discuss submission requirements for the proposed product, a 20% amino acid solution.

A draft study protocol was submitted to the Agency on September 9, 1993. Representatives from the FDA, Baxter Healthcare Corporation met again on August 8, 1994. The Agency proposed modifications which were incorporated into the study protocol. A revised draft protocol was submitted to the Agency on February 10, 1995. was then submitted on March 10, 1995. Please note that at the time of IND submission, the intended product brand name was "Travasol®". Based on agency feedback, the brand name was changed to "ProSol™" to differentiate between the new product and existing Baxter amino acid products.

The study started in May, 1995 and was completed in July, 1995. The primary study objective was to compare plasma amino acid concentrations in normal human volunteers at baseline and at a steady state after receiving a peripheral amino acid/dextrose infusion. 20% ProSol™ - sulfite-free (Amino Acid) Injection in PL 146® Plastic Container was compared to Novamine® 15% - sulfite-free (Amino Acid) Injection in PL 146® Plastic Container. The study followed the protocol submitted in the IND on March 10, 1995.

APPEARS THIS WAY
ON ORIGINAL

Copies of all correspondence exchanged with FDA regarding the study protocol appear in Item 6 of this submission.

APPEARS THIS WAY
ON ORIGINAL

[1] In 1993, Clintec Nutrition Company was an independent corporation affiliated with both Baxter Healthcare Corporation On September 30, 1996. was dissolved. Its parenteral nutrition business was integrated into Baxter Healthcare Corporation.

[2] Novamine is a registered trademark of Pharmacia-Upjohn

AUG 2 5 1997

Baxter

Submission Approach

Additional correspondence and communications took place in 1996 and 1997 between Baxter Healthcare Corporation and the FDA regarding the submission approach for this NDA.

A teleconference between Agency and Baxter representatives took place on March 18, 1997. Present from FDA were Drs. Troendle, Coleman and Jones and Mr. McCort. The Agency agreed to the proposed filing approach. Therefore, Baxter Healthcare Corporation is submitting this file as a new drug application under section 505(b)(2) of the Federal Food, Drug and Cosmetic Act, relying on clinical investigations which were not conducted by Baxter and for which Baxter has not obtained a right of reference to demonstrate the safety and efficacy of the proposed drug product. No clinical trials were conducted by Baxter with the purpose of demonstrating safety or efficacy of the proposed product. In Item 8 of this submission, we summarize the published literature that supports the proposed product.

Applicability of User Fees

Subsequent telephone discussions took place between Mr. Thomas Hassall, Office of Policy and Marcia Marconi and Tamima Itani, Baxter, regarding the applicability of user fees. The discussions centered on whether 20% ProSol™ After discussion, Baxter agreed to submit the file and pay applicable user fees at the time of filing. of the applicable will be paid at the time of submission, as required by the regulations.

The opinion that user fees apply because the combination of amino acids that constitute 20% ProSol™ was expressed by FDA. Further, half the fees that would normally apply to a submission with full clinical trials would apply in this situation. Ms. Marconi and Dr. Itani did not concur with the position that the combination of amino acid active ingredients constitutes a new molecular entity and suggested that the traditional framework may not be appropriate for nutritional product intended to provide dietary support. During file review, Baxter will further pursue clarification for the need to pay any user fees for this application.

AUG 2 5 1997

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Submission Contents and Format

The following required items are appended to this cover letter:

- Completed Form 356h
- Completed Form 3397 (User Fee Cover Sheet)
- Information Incorporated by Reference
- Cross Reference Authorization Letters
- Debarment Certification
- Patent Information
- Patent Certification

APPEARS THIS WAY
ON ORIGINAL

The contents of the Archival and Review copies of the NDA are summarized in the table that follows. An additional copy of Item 3, Chemistry, Manufacturing and Controls (CMC), is provided in the Microbiology review binder, for the convenience of the microbiology reviewer. An additional copy of Item 6, Human Pharmacokinetics And Bioavailability, is provided in the Clinical review binder, for the convenience of the medical reviewer.

A field copy of the submission (Cover letter and attachments, Item 1, Index, Item 2, Summary and Item 3, Chemistry, Manufacturing and Controls) was submitted to the Chicago District office on today's date in compliance with 21 CFR §314 (Federal Register, Vol. 58, No. 172, September 8, 1993: "New Drug and Abbreviated Drug Applications; Preapproval Inspection Requirements", Final Rule).

Baxter certifies that the field copies are true copies of the submission.

Please contact Tamima Itani, Ph.D. at (847) 270-2577 if you have comments or questions regarding this application. Thank you for your time and consideration in its review.

Sincerely,

Marcia Marconi (TI)

APPEARS THIS WAY
ON ORIGINAL

Marcia Marconi
Vice President
Regulatory Affairs
(847) 270-4637

AUG 2 5 1997

5

Baxter

	BINDER							
Elements of NDA	Blue Arch	Red Chem	Yellow Pharmcol	Orange Pharmcok	White Micro	Lt. Brown Clinical	Green Stat	Maroon Field
Cover Letter & Attachments	X	X	X	X	X	X	X	X
1. Index to Application	X	X	X	X	X	X	X	X
2. Summary	X	X	X	X	X	X	X	X
3. Chemistry, Mfg. & Controls	X	X			X[1]			X
4. Samples, Methods Validation Draft Labeling (4 copies)	X X	3X X	X			X		
5. Nonclinical Pharmacology & Toxicology	X		X					
6. Human Pharmacokinetics & Bioavailability	X			X		X[2]		
7. Microbiology	X				X			
8. Clinical Information	X					X		
9. Safety Update	X					X		
10. Statistical Data	X					X	X	
11. Case Report Tabulations	X					X		
12. Case Report Forms	X					X		
13. Patent Information (also appended to cover letter)	X	X	X	X	X	X	X	X
14. Patent Certification (also appended to cover letter)	X	X	X	X	X	X	X	X

X Section provided

[1] A complete copy of the Chemistry, Manufacturing and Controls Section is provided in the Microbiology Review Copy for the convenience of the microbiology reviewer.

[2] A complete copy of the Human Pharmacokinetics and Bioavailability Section is provided in the Clinical Review Copy for the convenience of the medical reviewer.

AUG 2 5 1997

6

20% ProSol™ - sulfite-free (Amino Acid) Injection
in PL 146® Plastic Container
NDA 20-849
Confidentiality Statement

APPEARS THIS WAY
ON ORIGINAL

Baxter Healthcare Corporation

New Drug Application

20% ProSol™ - sulfite-free (Amino Acid) Injection
in PL 146® Plastic Container

August 25, 1997

This NDA contains information regarding the components, qualitative formulas and manufacturing methods and controls for the proposed product. This information is deemed to be trade secret and, as such, is fully protected from disclosure under 21 CFR §20 and §314.430.

Baxter requests that this file be considered confidential. We request that this submission not be disclosed without the express written consent of Baxter Healthcare Corporation, except to persons employed by the Food and Drug Administration who require access to this information in the performance of their duties. Should it be your view that any of this information is not entitled to confidential treatment or that the stated grounds for this request are not adequate, we request specific notice of your interpretation. Please notify Baxter Healthcare Corporation of any requests for such information prior to its disclosure.

APPEARS THIS WAY
ON ORIGINAL

I.V. Systems Division
Regulatory Affairs

Baxter Healthcare Corporation
Route 120 & Wilson Road
Round Lake, Illinois 60073-0490

847.546.6311
Fax: 847.270.4668

Baxter

February 7, 1997

Attention: Mr. Steve McCort
Consumer Safety Officer
Office of Drug Evaluation II
Division of Metabolism and Endocrine Drug Products
Center for Drug Evaluation and Research, HFD-510
Document Control Room, 14B-04
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

Re: 20% Amino Acid Injection in PL 146® Plastic Container Submission Approach

Dear Mr. McCort:

Baxter Healthcare Corporation is requesting a meeting with Division representatives to discuss the submission approach for its proposed 20% Amino Acid Injection in PL 146® Plastic Container product.

The proposed product has the same qualitative active ingredient composition as Pharmacia-Upjohn's Novamine® 11.4% and 15% (Amino Acid) Injections in Glass Container, approved by FDA on August 9, 1982 and November 28, 1986, respectively, under NDA 17-957. We are proposing to submit a new drug application under section 505(b)(2) of the Act, using NDA 17-957 as a reference. Our previous conversations on this topic lead us to believe that the agency would consider this an acceptable approach.

We would like to explore this filing approach in a meeting with medical and chemistry representatives at the agency, and the type of information that would be expected in support of an NDA under 505(b)(2). We will forward a pre-meeting package to the Division at the end of February that will outline what we have to date, in support of such an application.

Baxter

At this time, the following persons plan to participate in the meeting from: Marcia Marconi, Vice President, Regulatory Affairs, Tamima Itani, Ph.D., Associate Director, Regulatory Affairs, John Wesley, M.D., Vice President and Medical Director and Hugh Tucker, Ph.D., Consultant.

If you have any questions, please contact Dr. Itani at (847) 270-2577.

Sincerely,

Marcia Marconi (Li)

Marcia Marconi
Vice President
Regulatory Affairs

APPEARS THIS WAY
ON ORIGINAL

I.V. Systems Division

Baxter Healthcare Corporation
Route 120 & Wilson Road
Round Lake, Illinois 60073-0490

847.546.6311

Baxter

November 20, 1996

Attention: Mr. Steve McCort
Consumer Safety Officer
Office of Drug Evaluation II
Division of Metabolism and Endocrine Drug Products
Center for Drug Evaluation and Research, HFD-510
Document Control Room, 14B-19
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

APPEARS THIS WAY
ON ORIGINAL

Re: 20% Amino Acid Injection in PL 146® Plastic Container Submission Approach

APPEARS THIS WAY
ON ORIGINAL

Dear Mr. McCort:

As a follow-up to our letter addressed to Dr. Sobel and dated October 10, 1996 and subsequent telephone conversations between you and Tamima Itani, Ph.D., Baxter Healthcare Corporation is requesting feedback on an alternate submission approach for its proposed 20% Amino Acid Injection in PL 146® Plastic Container.

The proposed product has the same qualitative active ingredient composition as Pharmacia-Upjohn's Novamine® 11.4% and 15% (Amino Acid) Injections in Glass Container, approved by FDA on August 9, 1982 and November 28, 1986, respectively, under NDA 17-957. We are proposing to submit a new drug application under section 505(b)(2) of the Act, using NDA 17-957 as a reference. Our previous conversations on this topic lead us to believe that the agency would consider this an acceptable approach. **Attachment 1** provides a comparison between our proposed 20% Amino Acid Injection and Pharmacia-Upjohn's Novamine® 11.4% and 15% (Amino Acid) Injections.

We would like to explore this filing approach in a teleconference with medical and chemistry representatives at the agency, and the type of information that would be expected in support of an NDA under 505(b)(2). The following persons will be participating in the teleconference from Baxter: Marcia Marconi, Vice President, Regulatory Affairs, Tamima Itani, Ph.D., Associate

Baxter

Director, Regulatory Affairs, Dennis Ocwieja, Consultant and a representative from our Medical Affairs group.

Tamima Itani will follow up with you within the next week. If you have any questions, please contact me or Dr. Itani at (847) 270-2577.

Sincerely,

Marcia Marconi (TI)

Marcia Marconi
Vice President
Regulatory Affairs

APPEARS THIS WAY
ON ORIGINAL

Attachment

s:\pnda\20%aa\61114tia