

CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

ANDA 77-407

Name: Sodium Chloride Injection USP, 0.9%,
packaged in 5 mL and 10 mL single-dose plastic
ampules.

Sponsor: Taro Pharmaceuticals U.S.A., Inc.

Approval Date: August 11, 2006

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:
ANDA 77-407

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CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 77-407

APPROVAL LETTER

ANDA 77-407

AUG 11 2006

Taro Pharmaceuticals U.S.A., Inc.
U.S. Agent for: Taro Pharmaceuticals Ireland Ltd.
Attention: Kalpana Rao
GVP, Regulatory Affairs (Global)
5 Skyline Drive
Hawthorne, NY 10532

Dear Madam:

This is in reference to your abbreviated new drug application (ANDA) dated November 29, 2004, submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (the Act), for Sodium Chloride Injection USP, 0.9% packaged in 5 mL and 10 mL single-dose plastic ampules.

Reference is also made to your amendments dated January 23, March 3, and May 30, 2006.

We have completed the review of this ANDA and have concluded that the drug is safe and effective for use as recommended in the submitted labeling. Accordingly the ANDA is approved. The Division of Bioequivalence has determined your Sodium Chloride Injection USP, 0.9%, packaged in 5 mL and 10 mL single-dose plastic ampules, to be bioequivalent and, therefore, therapeutically equivalent to the reference listed drug, Sodium Chloride Injection USP, 0.9%, packaged in plastic containers of Hospira Inc.

Under section 506A of the Act, certain changes in the conditions described in this ANDA require an approved supplemental application before the change may be made.

Postmarketing reporting requirements for this ANDA are set forth in 21 CFR 314.80-81 and 314.98. The Office of Generic Drugs should be advised of any change in the marketing status of this drug.

Promotional materials may be submitted to FDA for comment prior to publication or dissemination. Please note that these submissions are voluntary. If you desire comments on proposed launch promotional materials with respect to compliance with applicable regulatory requirements, we recommend you submit, in draft or mock-up form, two copies of both the promotional materials and package insert(s) directly to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising, and Communications
5901-B Ammendale Road
Beltsville, MD 20705

We call your attention to 21 CFR 314.81(b)(3) which requires that all promotional materials be submitted to the Division of Drug Marketing, Advertising, and Communications with a completed Form FDA 2253 at the time of their initial use.

Sincerely yours,

Robert L. Lest for
8/11/2006

Gary Buehler
Director

Office of Generic Drugs
Center for Drug Evaluation and Research

cc: ANDA 77-407
Division File
Field Copy
HFD-610/R. West
HFD-013
HFD-610/Orange Book Staff

Endorsements:

HFD-600/N.Nashed/ *W 8/10/06*
HFD-623/J.Fan/ *Q 8/10/06*
HFD-617/R.Adigun/ *RA 7/20/06*
HFD-613/A.Payne/
HFD-613/J.Grace/

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F/T by

APPROVAL

AP
R. West
8/11/06
Robert West
8/11/2006

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:
ANDA 77-407

LABELING

APPROVAL

AUG 1 1 2006

170MM

170MM

Sodium Chloride Injection USP, 0.9% Rx only Polypropylene Ampule

DESCRIPTION

This preparation is designed solely for parenteral use only after addition of drugs that require dilution or must be dissolved in an aqueous vehicle prior to injection.

Sodium Chloride Injection, USP is a sterile, nonpyrogenic, isotonic solution of sodium chloride and water for injection. Each mL contains sodium chloride 9 mg. It contains no bacteriostat, antimicrobial agent or added buffer and is supplied only in single-dose containers to dilute or dissolve drugs for injection. 0.308 mOsmol/mL (calc.). The solution may contain hydrochloric acid and/or sodium hydroxide for pH adjustment. The pH is 5.3 (4.5 to 7.0).

Sodium Chloride, USP is chemically designated NaCl, a white crystalline compound freely soluble in water.

The blow-fill-sealed polypropylene plastic ampule is transparent/translucent in color with a twist-off top.

CLINICAL PHARMACOLOGY

Sodium chloride in water dissociates to provide sodium (Na^+) and chloride (Cl^-) ions. These ions are normal constituents of the body fluids (principally extracellular) and are essential for maintaining electrolyte balance.

The distribution and excretion of sodium (Na^+) and chloride (Cl^-) are largely under the control of the kidney which maintains a balance between intake and output.

The small volume of fluid and amount of sodium chloride provided by Sodium Chloride Injection USP, 0.9% when used only as an isotonic vehicle for parenteral injection of drugs, is unlikely to exert a significant effect on fluid and electrolyte balance except possibly in neonates and very small infants.

Water is an essential constituent of all body tissues and accounts for approximately 70% of total body weight. Average normal adult daily requirement ranges from two to three liters (1 to 1.5 liters each for insensible water loss by perspiration and urine production).

Water balance is maintained by various regulatory mechanisms. Water distribution depends primarily on the concentration of electrolytes in the body compartments and sodium (Na^+) plays a major role in maintaining physiologic equilibrium.

INDICATIONS AND USAGE

This parenteral preparation is indicated only for diluting or dissolving drugs for intravenous, intramuscular or subcutaneous injection, according to instructions of the manufacturer of the drug to be administered.

PRECAUTIONS

Consult the manufacturer's instructions for choice of vehicle, appropriate dilution or volume for dissolving the drugs to be injected, including the route and rate of injection.

Inspect reconstituted (diluted or dissolved) drugs for clarity (if soluble) and freedom from unexpected precipitation or discoloration prior to administration.

Pregnancy Category C. Animal reproduction studies have not been conducted with Sodium Chloride Injection USP, 0.9%. It is also not known whether sodium chloride injection containing additives can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Sodium chloride injection containing additives should be given to a pregnant woman

only if clearly needed.

Pediatric Use

Safety and effectiveness have been established in pediatric patients. However, in neonates or very small infants the volume of fluid may affect fluid and electrolyte balance.

Drug Interactions

Some drugs for injection may be incompatible in a given vehicle, or when combined in the same vehicle or in a vehicle containing benzyl alcohol. Consult with pharmacist, if available.

Use aseptic technique for single or multiple entry and withdrawal from all containers.

When diluting or dissolving drugs, mix thoroughly and use promptly.

Do not store reconstituted solutions of drugs for injection unless otherwise directed by the manufacturer of the solute.

Do not use unless the solution is clear and seal intact. Do not reuse single-dose containers, discard unused portion.

ADVERSE REACTIONS

Reactions which may occur because of this solution, added drugs or the technique of reconstitution or administration include febrile response, local tenderness, abscess, tissue necrosis or infection at the site of injection, venous thrombosis or phlebitis extending from the site of injection and extravasation.

If an adverse reaction does occur, discontinue the infusion, evaluate the patient, institute appropriate countermeasures, and if possible, retrieve and save the remainder of the unused vehicle for examination.

OVERDOSAGE

Use only as a diluent or solvent. This parenteral preparation is unlikely to pose a threat of carbohydrate, sodium chloride or fluid overload except possible in neonates or very small infants. In the event these should occur, re-evaluate the patient and institute appropriate corrective measures. See **PRECAUTIONS** and **ADVERSE REACTIONS**.

DOSAGE AND ADMINISTRATION

The volume of the preparation to be used for diluting or dissolving any drug for injection, is dependent on the vehicle concentration, dose and route of administration as recommended by the manufacturer.

Use aseptic technique for entry and withdrawal from container.

This parenteral should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. See **PRECAUTIONS**.

HOW SUPPLIED

Sodium Chloride Injection USP, 0.9% is supplied in 5 mL single-dose (NDC 51672-3019-0) and 10 mL single-dose (NDC 51672-3019-1) polypropylene ampules in cartons containing 20 ampules.

Store at 20°-25°C (68°-77°F) [see USP Controlled Room Temperature].

Mfd. by: Taro Pharmaceuticals Ireland, Ltd., Roscrea Co., Tipperary, Ireland
Dist. by: **Taro Pharmaceuticals U.S.A., Inc.**, Hawthorne, NY 10532

Revised: January, 2006

175 MM

175 MM

DPL 946
20 X 5ml
187 x 34 x 73mm

APPROVED

AUG 11 2006

scaled at 90%



77-407

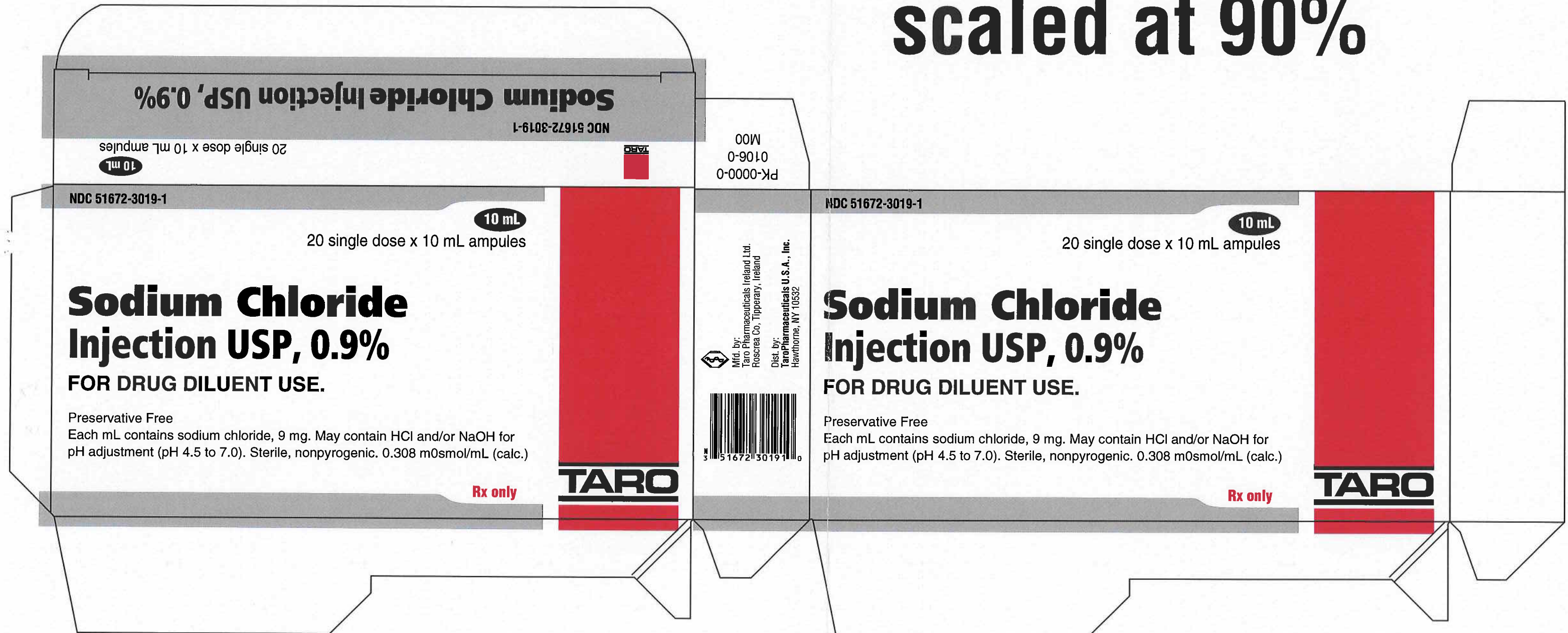
APPROVED

DPL379

ANTIGEN - 20 x 10ml HEPSAL

AUG 11 2006

scaled at 90%



CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 77-407

LABELING REVIEWS

**REVIEW OF PROFESSIONAL LABELING #1
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH**

Filed 11-29-05

ANDA Number: 77-407 Dates of Submission: Nov. 29, 2004 (original)
Applicant's Name: Taro Pharms Ireland
Established Name: Sodium Chloride Injection USP, 9%- 5 mL and 10 mL - SDV ampules

Labeling Deficiencies:

1. We believe you have used an incorrect NDA to model your product labeling after. You used NDA 19-217 (0.9% sodium Chloride Injection USP - in life shield Fliptop Glass vials-Thermoject System). We believe your insert should model NDA 18-803 (0.9% Sodium Chloride Injection USP in fliptop Plastic vials). Please comment on why you chose 19-217 as the reference listed drug. The inserts are very similar and there are not many changes required below.
2. **CONTAINER** (5 mL and 10 mL):
 - a. Include the drug use "FOR DRUG DILUENT USE".
 - b. Please provide a drawing of your ampules and comment on how one would gain access to the product inside the ampules. The reference listed drug uses glass ampules that must be popped at the designated line.
 - c. Please indicate "single dose".
 - d. What is the color of your cap?
3. **CARTON** (20s X 5 mL):
 - a. Place the following in bold print and all caps "FOR DRUG DILUENT USE".
 - b. Revise "ampoules" to read "ampules".
 - c. See comments under CONTAINER.
 - d. Include the pH range.
4. **INSERT:**
 - a. Include the "Rx only" statement so that it follows the title and type of ampule.
 - b. Please include a statement about your ampule composition.
 - c. **CLINICAL PHARMACOLOGY** - Combine the last two sentences so that they become the last paragraph.
 - d. **DOSAGE AND ADMINISTRATION** - Add "Use aseptic technique for entry and withdrawal from container".
 - e. **HOW SUPPLIED** - Describe your containers as single-dose containers. Change the spelling of ampoules.

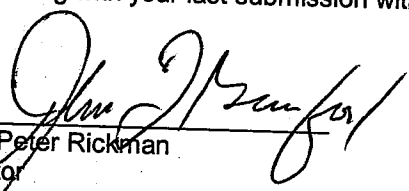
Please revise your labels and labeling, as instructed above, and submit actual sized final printed labels

and labeling. The electronic labeling rule published December 11, 2003, (68 FR 69009) requires submission of labeling content in electronic format effective June 8, 2004. For additional information, consult the following guidance for industry regarding electronic submissions: Providing Regulatory Submissions in Electronic Format — ANDAs (Issued 6/2002) (<http://www.fda.gov/cder/guidance/5004fnl.htm>). The guidance specifies labeling to be submitted in pdf format. To assist in our review, we request that labeling also be submitted in MS Word format.

Prior to approval, it may be necessary to revise your labeling subsequent to approved changes for the reference listed drug. In order to keep ANDA labeling current, we suggest that you subscribe to the daily or weekly updates of new documents posted on the CDER web site at the following address -

<http://www.fda.gov/cder/cdernew/listserv.html> or
<http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm>

To facilitate review of your next submission, and in accordance with 21 CFR 314.94(a)(8)(iv), please provide a side-by-side comparison of your proposed labeling with your last submission with all differences annotated and explained.



Wm. Peter Rickman
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

APPROVAL SUMMARY
REVIEW OF PROFESSIONAL LABELING
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH

ANDA Number 77-407
Date of Submission
Applicant Taro Pharm
Drug Name
Strength(s)

FPL Approval Summary

Container Labels		Submitted
5 ml and 10 mL	XXXXXXXX	vol XX
Package Insert Labeling	#XXXXRev.	vol XX

BASIS OF APPROVAL:

Patent Data For NDA 19-217 should be 18-803

Patent No	Patent Expiration	Use Code	Description	How Filed	Labeling Impact
None	None			PI	

Exclusivity Data For NDA 19-217

Code/sup	Expiration	Description	Labeling impact

Reference Listed Drug

RLD on the 356(h) form NaCl
NDA Number 19-217 should be 18-803
RLD established name Sodium Chloride Injection USP
Firm Abbott
Currently approved PI S-023 should be Y-026
AP Date April 7, 2004 should be 12-17-04

Note: RLD insert is combined with several other diluent products that are not the subject of this application. Y-27 submitted in Dec 2004 with a revision date of 1997 has been superceded by April 7, 2004 revision year 2000.

REVIEW OF PROFESSIONAL LABELING CHECKLIST

Applicant's Established Name	Yes	No	N.A.
Different name than on acceptance to file letter?		x	
Is this product a USP item? If so, USP supplement in which verification was assured. USP 24	x		
Is this name different than that used in the Orange Book?		x	
If not USP, has the product name been proposed in the PF?			x
Error Prevention Analysis			
Has the firm proposed a proprietary name? If yes, complete this subsection.		x	
Do you find the name objectionable? List reasons in FTR, if so. Consider: Misleading? Sounds or looks like another name? USAN stem present? Prefix or Suffix present?			x
Has the name been forwarded to the Labeling and Nomenclature Committee? If so, what were the recommendations? If the name was unacceptable, has the firm been notified?			x
PACKAGING -See applicant's packaging configuration in FTR			
Is this a new packaging configuration, never been approved by an ANDA or NDA for this drug product? If yes, describe in FTR.		X	
Is this package size mismatched with the recommended dosage? If yes, the Poison Prevention Act may require a CRC. [see FTR]		X	
Does the package proposed have any safety and/or regulatory concerns?		X	
If IV product packaged in syringe, could there be adverse patient outcome if given by direct IV injection?			x
Conflict between the DOSAGE AND ADMINISTRATION and INDICATIONS sections and the packaging configuration?		X	
Is the strength and/or concentration of the product unsupported by the insert labeling?		X	
Is the color of the container (i.e. the color of the cap of a mydriatic ophthalmic) or cap incorrect?			x
Individual cartons required? Issues for FTR: Innovator individually cartoned? Light sensitive product which might require cartoning? Must the package insert accompany the product?		x	
Are there any other safety concerns?		X	
LABELING			
Is the name of the drug unclear in print or lacking in prominence? (Name should be the most prominent information on the label).		X	
Has applicant failed to clearly differentiate multiple product strengths?			x
Is the corporate logo larger than 1/3 container label? (No regulation - see ASHP guidelines)		X	
Does RLD make special differentiation for this label? (i.e., Pediatric strength vs Adult; Oral Solution vs Concentrate, Warning Statements that might be in red for the NDA)		X	
Is the Manufactured by/Distributor statement incorrect or falsely inconsistent between labels and		X	

labeling? Is "Jointly Manufactured by..." statement needed?			
Failure to describe solid oral dosage form identifying markings in HOW SUPPLIED?			x
Has the firm failed to adequately support compatibility or stability claims which appear in the insert labeling? Note: Chemist should confirm the data has been adequately supported.		X	
Scoring: Describe scoring configuration of RLD and applicant (p. #) in the FTR			
Is the scoring configuration different than the RLD?			x
Has the firm failed to describe the scoring in the HOW SUPPLIED section?			x
Inactive Ingredients: (FTR: List p. # in application where inactives are listed)			
Does the product contain alcohol? If so, has the accuracy of the statement been confirmed?	X		
Do any of the inactives differ in concentration for this route of administration?			X
Any adverse effects anticipated from inactives (i.e., benzyl alcohol in neonates)?		X	
Is there a discrepancy in inactives between DESCRIPTION and the composition statement?		X	
Has the term "other ingredients" been used to protect a trade secret? If so, is claim supported?		x	
Failure to list the coloring agents if the composition statement lists e.g., Opacode, Opaspray?		x	
Failure to list gelatin, coloring agents, antimicrobials for capsules in DESCRIPTION?			X
Failure to list dyes in imprinting inks? (Coloring agents e.g., iron oxides need not be listed)			X
USP Issues: (FTR: List USP/NDA/ANDA dispensing/storage recommendations)			
Do container recommendations fail to meet or exceed USP/NDA recommendations? If so, are the recommendations supported and is the difference acceptable?[see FTR]		X	
Does USP have labeling recommendations? If any, does ANDA meet them?		X	
Is the product light sensitive? If so, is NDA and/or ANDA in a light resistant container?	X		
Failure of DESCRIPTION to meet USP Description and Solubility information? If so, USP information should be used. However, only include solvents appearing in innovator labeling.		X	
Bioequivalence Issues: (Compare bioequivalency values: insert to study. List Cmax, Tmax, T 1/2 and date study acceptable)			
Insert labeling references a food effect or a no-effect? If so, was a food study done?		X	
Has CLINICAL PHARMACOLOGY been modified? If so, briefly detail where/why.		X	
Patent/Exclusivity Issues: FTR: Check the Orange Book edition or cumulative supplement for verification of the latest Patent or Exclusivity. List expiration date for all patents, exclusivities, etc. or if none, please state. NONE			

NOTE TO CHEMIST:

FOR THE RECORD:

1. MODEL LABELING

This review was based on the labeling for NDA 18803 rather than 19-217. The insert includes glass ampules, plastic vials, plastic syringes for 9% NA Cl, 5% dextrose and SWFI al for use as a drug diluent

2. **PATENTS/EXCLUSIVITIES:** See above. [Vol. A1.1 pg. 10-12]

3. **MANUFACTURING FACILITY OF FINISHED DOSAGE FORM** by taro pharm in Ireland for Taro PhARM USA in Hawthorne, NY [Vol. A1.]

4. **CONTAINER/CLOSURE**

RLD: (19-217) 5 mL, 10 mL, 20 mL SD glass ampul, (18-803) 10 mL, 20 mL, 50 mL SD- and 100 mL single -dose plastic flip-top vials, and Ansyr Plastic syringes.

ANDA: 5 mL and 10 mL SD plastic ampuls.

[Vol. A1.2 pg.]

5. **INACTIVE INGREDIENTS**

The description of the inactive ingredients in the insert labeling appears accurate according to the composition statement. No bacteriostatic, antimicrobial agent or added buffer. [Vol. A1.1 pg. 106 and Vol. A1.2 pg. 532.]

6. **PACKAGING CONFIGURATIONS**

RLD: (19-217) glass vials in cartons of 5s

ANDA: plastic ampules in boxes of 20s

USP: Preserve in single-dose glass or plastic containers, of not larger than 1-L size. Glass containers are preferably of Type I or Type II glass. [Vol.]

7. **STORAGE TEMPERATURE RECOMMENDATIONS COMPARISON**

USP:

RLD: CRT.15-30C

ANDA: Store at 20-25C

8. **DISPENSING STATEMENTS COMPARISON**

USP: Label it to indicate that no antimicrobial or other substance has been added, and that it is not suitable for intravascular injection without first having been made approximately isotonic by the addition of a suitable solute.

RLD: same

ANDA (*Insert*): Same

Date of Review: 10/25/05

Date of Submission: Nov. 29, 2004(original)

cc:

ANDA: 77-407
DUP/DIVISION FILE
HFD-613/APayne/JGrace (no cc)
V:\FIRMSNZ\TARO\LTRS&REV\77407NA1.lab.doc
Review digital signature and Date: APayne 10/25/05
Draft e-dr

Done 10/25/05
Jim Grace 11/3/05

**APPROVAL SUMMARY
REVIEW OF PROFESSIONAL LABELING
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH**

ANDA Number	77-407
Date of Submission	23 JAN 2006
Applicant	Taro Pharm
Drug Name	Sodium Chloride Injection USP, 9%-
Strength(s)	5 mL and 10 mL - SDV ampules

FPL Approval Summary

Container Labels	Submitted
5 ml and 10 mL	23 JAN 2006, vol 4.1A
Cartons - 20s	23 JAN 2006, vol 4.1A
Package Insert Labeling	23 JAN 2006, vol 4.1A

BASIS OF APPROVAL:

Patent Data For NDA 19-217 should be 18-803

Patent No	Patent Expiration	Use Code	Description	How Filed	Labeling Impact
None	None			PI	

Exclusivity Data For NDA 19-217

Code/sup	Expiration	Description	Labeling impact

Reference Listed Drug

RLD on the 356(h) form	NaCl
NDA Number	19-217 should be 18-803
RLD established name	Sodium Chloride Injection USP
Firm	Abbott
Currently approved PI	S-023 should be Y-026
AP Date	April 7, 2004 should be 12-17-04

Note: RLD insert is combined with several other diluent products that are not the subject of this application. Y-27 submitted in Dec 2004 with a revision date of 1997 has been superseded by April 7, 2004 revision year 2000.

REVIEW OF PROFESSIONAL LABELING CHECKLIST

Applicant's Established Name	Yes	No	N.A.
Different name than on acceptance to file letter?		x	
Is this product a USP item? If so, USP supplement in which verification was assured. USP 24	x		
Is this name different than that used in the Orange Book?		x	
If not USP, has the product name been proposed in the PF?			x
Error Prevention Analysis			
Has the firm proposed a proprietary name? If yes, complete this subsection.		x	
Do you find the name objectionable? List reasons in FTR, if so. Consider: Misleading? Sounds or looks like another name? USAN stem present? Prefix or Suffix present?			x
Has the name been forwarded to the Labeling and Nomenclature Committee? If so, what were the recommendations? If the name was unacceptable, has the firm been notified?			x
PACKAGING -See applicant's packaging configuration in FTR			
Is this a new packaging configuration, never been approved by an ANDA or NDA for this drug product? If yes, describe in FTR.		X	
Is this package size mismatched with the recommended dosage? If yes, the Poison Prevention Act may require a CRC. [see FTR]		X	
Does the package proposed have any safety and/or regulatory concerns?		X	
If IV product packaged in syringe, could there be adverse patient outcome if given by direct IV injection?			x
Conflict between the DOSAGE AND ADMINISTRATION and INDICATIONS sections and the packaging configuration?		X	
Is the strength and/or concentration of the product unsupported by the insert labeling?		X	
Is the color of the container (i.e. the color of the cap of a mydriatic ophthalmic) or cap incorrect?			x
Individual cartons required? Issues for FTR: Innovator individually cartoned? Light sensitive product which might require cartoning? Must the package insert accompany the product?		x	
Are there any other safety concerns?		X	
LABELING			
Is the name of the drug unclear in print or lacking in prominence? (Name should be the most prominent information on the label).		X	
Has applicant failed to clearly differentiate multiple product strengths?			x
Is the corporate logo larger than 1/3 container label? (No regulation - see ASHP guidelines)		X	
Does RLD make special differentiation for this label? (i.e., Pediatric strength vs Adult; Oral Solution vs Concentrate, Warning Statements that might be in red for the NDA)		X	
Is the Manufactured by/Distributor statement incorrect or falsely inconsistent between labels and		X	

labeling? Is "Jointly Manufactured by...", statement needed?			
Failure to describe solid oral dosage form identifying markings in HOW SUPPLIED?			x
Has the firm failed to adequately support compatibility or stability claims which appear in the insert labeling? Note: Chemist should confirm the data has been adequately supported.		X	
Scoring: Describe scoring configuration of RLD and applicant (p. #) in the FTR			
Is the scoring configuration different than the RLD?			x
Has the firm failed to describe the scoring in the HOW SUPPLIED section?			x
Inactive Ingredients: (FTR: List p. # in application where inactives are listed)			
Does the product contain alcohol? If so, has the accuracy of the statement been confirmed?	X		
Do any of the inactives differ in concentration for this route of administration?			X
Any adverse effects anticipated from inactives (i.e., benzyl alcohol in neonates)?		X	
Is there a discrepancy in inactives between DESCRIPTION and the composition statement?		X	
Has the term "other ingredients" been used to protect a trade secret? If so, is claim supported?		x	
Failure to list the coloring agents if the composition statement lists e.g., Opacode, Opaspray?		x	
Failure to list gelatin, coloring agents, antimicrobials for capsules in DESCRIPTION?			X
Failure to list dyes in imprinting inks? (Coloring agents e.g., iron oxides need not be listed)			X
USP Issues: (FTR: List USP/NDA/ANDA dispensing/storage recommendations)			
Do container recommendations fail to meet or exceed USP/NDA recommendations? If so, are the recommendations supported and is the difference acceptable?[see FTR]		X	
Does USP have labeling recommendations? If any, does ANDA meet them?		X	
Is the product light sensitive? If so, is NDA and/or ANDA in a light resistant container?	X		
Failure of DESCRIPTION to meet USP Description and Solubility information? If so, USP information should be used. However, only include solvents appearing in innovator labeling.		X	
Bioequivalence Issues: (Compare bioequivalency values: insert to study. List Cmax, Tmax, T 1/2 and date study acceptable)			
Insert labeling references a food effect or a no-effect? If so, was a food study done?		X	
Has CLINICAL PHARMACOLOGY been modified? If so, briefly detail where/why.		X	
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NOTE TO CHEMIST:

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2. PATENTS/EXCLUSIVITIES: See above. [Vol. A1.1 pg. 10-12]

3. MANUFACTURING FACILITY OF FINISHED DOSAGE FORM by taro pharm in Ireland for Taro PhARM USA in Hawthorne, NY [Vol. A1.]

4. CONTAINER/CLOSURE

RLD: (19-217) 5 mL, 10 mL, 20 mL SD glass ampul, (18-803) 10 mL, 20 mL, 50 mL SD- and 100 mL single -dose plastic flip-top vials, and Ansyr Plastic syringes.
ANDA: 5 mL and 10 mL SD plastic ampuls.

[Vol. A1.2 pg.]

5. INACTIVE INGREDIENTS

The description of the inactive ingredients in the insert labeling appears accurate according to the composition statement. No bacteriostatic, antimicrobial agent or added buffer. [Vol. A1.1 pg. 106 and Vol. A1.2 pg. 532.]

6. PACKAGING CONFIGURATIONS

RLD: (19-217) glass vials in cartons of 5s

ANDA: plastic ampules in boxes of 20s

USP: Preserve in single-dose glass or plastic containers, of not larger than 1-L size. Glass containers are preferably of Type I or Type II glass. [Vol.]

7. STORAGE TEMPERATURE RECOMMENDATIONS COMPARISON

USP:

RLD: CRT.15-30C

ANDA: Store at 20-25C

8. DISPENSING STATEMENTS COMPARISON

USP: Label it to indicate that no antimicrobial or other substance has been added, and that it is not suitable for intravascular injection without first having been made approximately isotonic by the addition of a suitable solute.

RLD: same

ANDA (Insert): Same

Date of Review: 2/01/06

Date of Submission: 23 JAN 2006,

cc:

ANDA: 77-407

DUP/DIVISION FILE

HFD-613/APayne/JGrace (no cc)

V:\FIRMSNZ\TARO\LTRS&REV\77407ap1.lab.doc

Review digital signature and Date: APayne 2/01/06

No document just handwritten

Done 2/01/06
John H. 2, 10, 2006

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 77-407

CHEMISTRY REVIEWS

ANDA 77- 407

Sodium Chloride Injection USP, 0.9%, 5 mL ampoules

Taro Pharmaceuticals Ireland Ltd.

Nashed E. Nashed, Ph.D.

Chemistry Division 1

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CHEMISTRY REVIEW

Chemistry Review Data Sheet

Chemistry Review Data Sheet

1. ANDA: 77- 407 (First Generic)
2. REVIEW #: 1
3. REVIEW DATE: 4/6/05
Revised: 5/4/05
4. REVIEWER: Nashed E. Nashed, Ph.D.
5. PREVIOUS DOCUMENTS:

Previous Documents

N/A

Document Date

N/A

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed

Original Submission

Acceptable for filing

New Correspondence

New Correspondence

Document Date

11/29/04

11/30/04

11/30/04

1/13/05

7. NAME & ADDRESS OF APPLICANT:

Name: Taro Pharmaceuticals Ireland Ltd.

Address: Lourdes Road, Roscrea, Co. Tipperary, Ireland

Representative: Taro Pharmaceuticals U.S.A., Inc.
5 Skyline Drive, Hawthorne, NY 10532
Kalpana Rao

Telephone: 914-345-9001

8. DRUG PRODUCT NAME/CODE/TYPE:

a) Proprietary Name: N/A

b) Non-Proprietary Name (USAN): Sodium Chloride Injection, USP

CHEMISTRY REVIEW

Chemistry Review Data Sheet

9. LEGAL BASIS FOR SUBMISSION:

The firm has provided a Paragraph I Certification.
Taro certifies, in its opinion and to the best of its knowledge, that there are no patents listed in the Approved Drugs Products with Therapeutic Equivalence that claim the drug referred to in this application.
Taro certifies that in its opinion and to the best of its knowledge, there are no unexpired Exclusivities for Sodium Chloride Injection USP, 0.9% in plastic container.
The Reference Listed Drug is Sodium Chloride Injection USP, 0.9% in Plastic Container, NDA 19-217, manufactured by Hospira Ltd. and labeled for Abbott Laboratories.

10. PHARMACOL CATEGORY:

Electrolyte Replenishment, LVI

11. DOSAGE FORM: Solution for Injection

12. STRENGTH/POTENCY: 0.9% w/v (9 mg/mL)

13. ROUTE OF ADMINISTRATION: Injectable; Injection

14. Rx/OTC DISPENSED: XX__Rx __OTC

15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):

____SPOTS product – Form Completed

XX Not a SPOTS product

16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:

Empirical formula is NaCl and Molecular weight is 58.44.

17. RELATED/SUPPORTING DOCUMENTS:

CHEMISTRY REVIEW

Chemistry Review Data Sheet

A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE ¹	STATUS ²	DATE REVIEW COMPLETED	COMMENTS
1	III			4			

¹ Action codes for DMF Table:

1 - DMF Reviewed.

Other codes indicate why the DMF was not reviewed, as follows:

2 - Type 1 DMF

3 - Reviewed previously and no revision since last review

4 - Sufficient information in application

5 - Authority to reference not granted

6 - DMF not available

7 - Other (explain under "Comments")

² Adequate, Inadequate, or N/A (There is enough data in the application, therefore the DMF did not need to be reviewed)

B. Other Documents:

DOCUMENT	APPLICATION NUMBER	DESCRIPTION

18. STATUS:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Microbiology	Pending		
EES	Pending		
Methods Validation	Not required.		
Labeling	Pending		
Bioequivalence	Acceptable		
EA	Acceptable	3/28/05	B. Fabian-Fritsch
Radiopharmaceutical	N/A		

CHEMISTRY REVIEW

Chemistry Review Data Sheet

19. ORDER OF REVIEW

The application submission(s) covered by this review was taken in the date order of receipt. ____ Yes xx No If no, explain reason(s) below:

Transferred from Team 2

**APPEARS THIS WAY
ON ORIGINAL**

CHEMISTRY REVIEW

Executive Summary Section

The Chemistry Review for ANDA 77- 407

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

This application is not approvable due to minor deficiencies.

B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable

N/A

II. Summary of Chemistry Assessments

A. Description of the Drug Product(s) and Drug Substance(s)

The drug product Sodium Chloride Injection USP, 0.9% will be packaged in 5 mL and 10 mL ampoules.

The Reference Listed Drug is Sodium Chloride Injection USP, 0.9% in Plastic Container, NDA 19-217, manufactured by Hospira Ltd. and labeled for Abbott Laboratories.

b(4) The drug substance sodium chloride is a white crystalline powder, colorless crystals or white pearls with empirical formula NaCl and molecular weight is 58.44.

b(4) The firm has submitted blank copy of the master batch record (MBR) for the intended maximum production batch size of ☐ ☐ (both 5 mL and 10 mL ampoules) in Section 3.2.P.3.3.A.

b(4) The firm has provided copies of the exhibit batch records Lot #TP44 (Batch size: ☐ ☐) for the 5 mL Ampoule and Lot #TP47 (Batch size: ☐ ☐) for the 10 mL Ampoule. See Section 3.2.R.1.

b(4) The drug product is ☐ ☐ in accordance with the USP.

CHEMISTRY REVIEW

Executive Summary Section

B. Description of How the Drug Product is Intended to be Used

Sodium Chloride Injection USP, 0.9% is indicated only for diluting or dissolving drugs for intravenous, intramuscular or subcutaneous injection, according to the instructions of the manufacturer of the drug to be administered.

Sodium Chloride Injection USP, 0.9% is supplied in 5 mL and 10 mL polypropylene ampoules in cartons containing 20 ampoules.

The volume of the preparation to be used for diluting or dissolving any drug for injection, is dependent on the vehicle concentration, dose and route of administration as recommended by the manufacturer.

This parenteral should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.

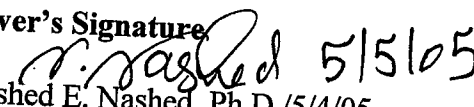
The recommended storage condition is 20° – 25°C (68° – 77°F).

C. Basis for Approvability or Not-Approval Recommendation

The application is not approvable due to minor deficiencies.

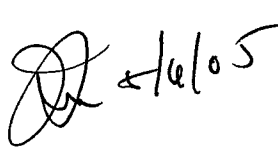
III. Administrative

A. Reviewer's Signature

 5/5/05
Nashed E. Nashed, Ph.D./5/4/05

B. Endorsement Block

James M. Fan

 5/6/05

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of trade secret and/or
confidential commercial
information from

Chemistry Review #1

(b) (4)

CHEMISTRY REVIEW

Chemistry Assessment Section

36. CHEMISTRY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 77- 407

APPLICANT: Taro Pharmaceuticals Ireland Ltd.

DRUG PRODUCT: Sodium Chloride Injection USP, 0.9%, 5 mL

The deficiencies presented below represent MINOR deficiencies.

A. Deficiencies:

1. 

2.

3.

b(4)

4.

5.

6. 

B. In addition to responding to the deficiencies presented above, please note and acknowledge the following comments in your response:

1. The firms referenced in your application should be in compliance with cGMP at the time of approval.
2. Please provide all available drug product room temperature stability data.

CHEMISTRY REVIEW

Chemistry Assessment Section

3. Labeling and microbiology information you have provided is pending review. After the reviews are completed, any deficiencies found will be communicated to you under a separate cover.

Sincerely yours,



Rashmikant M. Patel, Ph.D.

Director

Division of Chemistry I

Office of Generic Drugs

Center for Drug Evaluation and Research

**APPEARS THIS WAY
ON ORIGINAL**

CHEMISTRY REVIEW

Chemistry Assessment Section

cc: ANDA 77-407
ANDA DUP
Division File
Field Copy

Endorsements:

HFD-627/N.Nashed/5/4/05

HFD-627/J.Fan/5/4/05

HFD-617/A.Vu

F/T:ard/5/5/05

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APPEARS THIS WAY
ON ORIGINAL

#2



CHEMISTRY REVIEW



ANDA 77- 407

**Sodium Chloride Injection USP, 0.9%, 5 mL
and 10 mL ampoules**

Taro Pharmaceuticals Ireland Ltd.

Nashed E. Nashed, Ph.D.

Chemistry Division 1

ANDA 77- 407

Sodium Chloride Injection USP, 0.9%, 5 mL ampoules

Taro Pharmaceuticals Ireland Ltd.

Nashed E. Nashed, Ph.D.

Chemistry Division 1

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II. Summary of Chemistry Assessments.....	7
A. Description of the Drug Product(s) and Drug Substance(s).....	7
B. Description of How the Drug Product is Intended to be Used	8
C. Basis for Approvability or Not-Approval Recommendation	8
III. Administrative.....	8
A. Reviewer's Signature	8
B. Endorsement Block	8
Chemistry Assessment	9

APPEARS THIS WAY
ON ORIGINAL

Chemistry Review Data Sheet

1. ANDA: 77- 407 (First Generic)
2. REVIEW #: 2
3. REVIEW DATE: 9/19/05
Revised: 12/29/05
4. REVIEWER: Nashed E. Nashed, Ph.D.
5. PREVIOUS DOCUMENTS:

Previous Documents

N/A

Document Date

N/A

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed

Original Submission

Acceptable for filing

New Correspondence

New Correspondence

Minor Amendment

Gratuitous Amendment

Document Date

11/29/04

11/30/04

11/30/04

1/13/05

7/28/05

9/22/05

7. NAME & ADDRESS OF APPLICANT:

Name: Taro Pharmaceuticals Ireland Ltd.

Address: Lourdes Road, Roscrea, Co. Tipperary, Ireland

Taro Pharmaceuticals U.S.A., Inc.

Representative: 5 Skyline Drive, Hawthorne, NY 10532
Kalpana Rao

Telephone: 914-345-9001

8. DRUG PRODUCT NAME/CODE/TYPE:

a) Proprietary Name: N/A

b) Non-Proprietary Name (USAN): Sodium Chloride Injection, USP

CHEMISTRY REVIEW

Chemistry Review Data Sheet

9. LEGAL BASIS FOR SUBMISSION:

The firm has provided a Paragraph I Certification.
Taro certifies, in its opinion and to the best of its knowledge, that there are no patents listed in the Approved Drugs Products with Therapeutic Equivalence that claim the drug referred to in this application.
Taro certifies that in its opinion and to the best of its knowledge, there are no unexpired Exclusivities for Sodium Chloride Injection USP, 0.9% in plastic container.
The Reference Listed Drug is Sodium Chloride Injection USP, 0.9% in Plastic Container, NDA 19-217, manufactured by Hospira Ltd. and labeled for Abbott Laboratories.

10. PHARMACOL CATEGORY:

Electrolyte Replenishment, LVI

11. DOSAGE FORM: Solution for Injection

12. STRENGTH/POTENCY: 0.9% w/v (9 mg/mL)

13. ROUTE OF ADMINISTRATION: Injectable; Injection

14. Rx/OTC DISPENSED: XX__Rx __OTC

15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):

____SPOTS product – Form Completed

XX Not a SPOTS product

16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:

Empirical formula is NaCl and Molecular weight is 58.44.

17. RELATED/SUPPORTING DOCUMENTS:

CHEMISTRY REVIEW

Chemistry Review Data Sheet

A. DMFs:

b(4)

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE ¹	STATUS ²	DATE REVIEW COMPLETED	COMMENTS
[]	III	[]	[]	4			

¹ Action codes for DMF Table:

1 – DMF Reviewed.

Other codes indicate why the DMF was not reviewed, as follows:

2 – Type 1 DMF

3 – Reviewed previously and no revision since last review

4 – Sufficient information in application

5 – Authority to reference not granted

6 – DMF not available

7 – Other (explain under "Comments")

² Adequate, Inadequate, or N/A (There is enough data in the application, therefore the DMF did not need to be reviewed)

B. Other Documents: N/a

DOCUMENT	APPLICATION NUMBER	DESCRIPTION

18. STATUS:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Microbiology	Pending		
EES	Pending		
Methods Validation	Not required.		
Labeling	Deficient	11/30/05	A. Payne
Bioequivalence	Acceptable	3/28/05	B. Fabian-Fritsch
EA	Acceptable		
Radiopharmaceutical	N/A		

19. ORDER OF REVIEW

The application submission(s) covered by this review was taken in the date order of receipt. ____ Yes xx No If no, explain reason(s) below:

The application is Minor

**APPEARS THIS WAY
ON ORIGINAL**

The Chemistry Review for ANDA 77- 407

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

CMC is approvable – Micro and EER are Pending. Labeling is deficient 11/30/05.

B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable

N/A

II. Summary of Chemistry Assessments

A. Description of the Drug Product(s) and Drug Substance(s)

The drug product Sodium Chloride Injection USP, 0.9% will be packaged in 5 mL and 10 mL ampoules.

The Reference Listed Drug is Sodium Chloride Injection USP, 0.9% in Plastic Container, NDA 19-217, manufactured by Hospira Ltd. and labeled for Abbott Laboratories.

The drug substance sodium chloride is a white crystalline powder, colorless crystals or white pearls with empirical formula NaCl and molecular weight is 58.44.

b(4)

The firm has submitted blank copy of the master batch record (MBR) for the intended maximum production batch size of [] (both 5 mL and 10 mL ampoules) in Section 3.2.P.3.3.A.

b(4)

The firm has provided copies of the exhibit batch records Lot #TP44 (Batch size: [] for the 5 mL Ampoule and Lot #TP47 (Batch size: [] for the 10 mL Ampoule. See Section 3.2.R.1.

b(4)

The drug product is [] in accordance with the USP.

CHEMISTRY REVIEW

Executive Summary Section

B. Description of How the Drug Product is Intended to be Used

Sodium Chloride Injection USP, 0.9% is indicated only for diluting or dissolving drugs for intravenous, intramuscular or subcutaneous injection, according to the instructions of the manufacturer of the drug to be administered.

Sodium Chloride Injection USP, 0.9% is supplied in 5 mL and 10 mL polypropylene ampoules in cartons containing 20 ampoules.

The volume of the preparation to be used for diluting or dissolving any drug for injection, is dependent on the vehicle concentration, dose and route of administration as recommended by the manufacturer.

This parenteral should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.

The recommended storage condition is 20° – 25°C (68° – 77°F).

C. Basis for Approvability or Not-Approval Recommendation

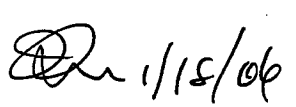
CMC is approvable – Micro and EER are Pending. Labeling is deficient 11/30/05

III. Administrative

A. Reviewer's Signature


Nashed E. Nashed, Ph.D.

B. Endorsement Block


James M. Fan

APPEARS THIS WAY
ON ORIGINAL

Withheld 17 page(s)
of trade secret and/or
confidential commercial
information from

_____ Chemistry Review #2 _____

(b) (4)

CHEMISTRY REVIEW

Chemistry Assessment Section

36. CHEMISTRY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 77-407

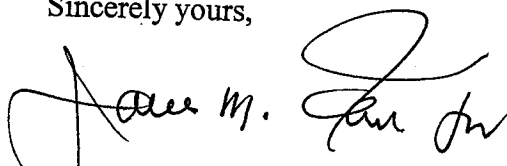
APPLICANT: Taro Pharmaceuticals Ireland Ltd.

DRUG PRODUCT: Sodium Chloride Injection USP, 9%- 5 mL and 10 mL – SDV ampules

The deficiency presented below represents a Minor deficiency:

Labeling deficiencies were communicated to you via facsimile on November 29, 2005. You should address the issues in the November 29, communication prior to or concurrent with your response to this communication.

Sincerely yours,

 1/18/06

Rashmikant M. Patel, Ph.D.
Director
Division of Chemistry I
Office of Generic Drugs
Center for Drug Evaluation and Research

**APPEARS THIS WAY
ON ORIGINAL**

CHEMISTRY REVIEW

Chemistry Assessment Section

cc: ANDA 77-407
ANDA DUP
Division File
Field Copy

Endorsements:

HFD-627/N.Nashed/12/29/05

HFD-627/J.Fan/1/2/06

HFD-617/A.Vu

F/T:ard/1/17/06

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#3



CHEMISTRY REVIEW



ANDA 77- 407

Sodium Chloride Injection USP, 0.9%, 5 mL and 10 mL ampules

Taro Pharmaceuticals Ireland Ltd.

Nashed E. Nashed, Ph.D.

Chemistry Division 1

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A. Recommendation and Conclusion on Approvability.....	7
B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable	7
II. Summary of Chemistry Assessments.....	7
A. Description of the Drug Product(s) and Drug Substance(s).....	7
B. Description of How the Drug Product is Intended to be Used	8
C. Basis for Approvability or Not-Approval Recommendation	8
Chemistry Assessment.....	9



Chemistry Review Data Sheet

1. ANDA: 77- 407 (First Generic)
2. REVIEW #: 3
3. REVIEW DATE: 3/16/06
4. REVIEWER: Nashed E. Nashed, Ph.D.
5. PREVIOUS DOCUMENTS:

Previous Documents

N/A

Document Date

N/A

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) ReviewedDocument Date

Original Submission

11/29/04

Acceptable for filing

11/30/04

New Correspondence

11/30/04

New Correspondence

1/13/05

Minor Amendment

7/28/05

Gratuitous Amendment

9/22/05

Labeling Amendment

1/23/06

Minor Amendment (Labeling)

3/3/06

Microbiology Amendment

5/30/06

7. NAME & ADDRESS OF APPLICANT:

Name: Taro Pharmaceuticals Ireland Ltd.

Address: Lourdes Road, Roscrea, Co. Tipperary, Ireland

Taro Pharmaceuticals U.S.A., Inc.

Representative: 5 Skyline Drive, Hawthorne, NY 10532

Kalpana Rao

Telephone: 914-345-9001

8. DRUG PRODUCT NAME/CODE/TYPE:

a) Proprietary Name: N/A

b) Non-Proprietary Name (USAN): Sodium Chloride Injection, USP



CHEMISTRY REVIEW



Chemistry Review Data Sheet

9. LEGAL BASIS FOR SUBMISSION:

The firm has provided a Paragraph I Certification.

Taro certifies, in its opinion and to the best of its knowledge, that there are no patents listed in the Approved Drugs Products with Therapeutic Equivalence that claim the drug referred to in this application.

Taro certifies that in its opinion and to the best of its knowledge, there are no unexpired Exclusivities for Sodium Chloride Injection USP, 0.9% in plastic container.

The Reference Listed Drug is Sodium Chloride Injection USP, 0.9% in Plastic Container, NDA 19-217, manufactured by Hospira Ltd. and labeled for Abbott Laboratories.

10. PHARMACOL CATEGORY:

Electrolyte Replenishment, LVI

11. DOSAGE FORM: Solution for Injection

12. STRENGTH/POTENCY: 0.9% w/v (9 mg/mL)

13. ROUTE OF ADMINISTRATION: Injectable; Injection

14. Rx/OTC DISPENSED: ☒ Rx ☐ OTC

15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):

☐ SPOTS product – Form Completed

☒ Not a SPOTS product

16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:

Empirical formula is NaCl and Molecular weight is 58.44.

17. RELATED/SUPPORTING DOCUMENTS:



CHEMISTRY REVIEW



Chemistry Review Data Sheet

A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE ¹	STATUS ²	DATE REVIEW COMPLETED	COMMENTS
b(4)	III			4			

¹ Action codes for DMF Table:

1 – DMF Reviewed.

Other codes indicate why the DMF was not reviewed, as follows:

2 – Type 1 DMF

3 – Reviewed previously and no revision since last review

4 – Sufficient information in application

5 – Authority to reference not granted

6 – DMF not available

7 – Other (explain under "Comments")

² Adequate, Inadequate, or N/A (There is enough data in the application, therefore the DMF did not need to be reviewed)

B. Other Documents: N/a

DOCUMENT	APPLICATION NUMBER	DESCRIPTION

18. STATUS:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Microbiology	Acceptable	06/28/06	B. Pillari
EES	Acceptable	07/06/06	
Methods Validation	Not required.		
Labeling	Acceptable	02/10/06	A. Payne
Bioequivalence	Acceptable	03/28/05	B. Fabian-Fritsch
EA	Acceptable		
Radiopharmaceutical	N/A		



CHEMISTRY REVIEW



Chemistry Review Data Sheet

19. ORDER OF REVIEW

The application submission(s) covered by this review was taken in the date order of receipt. ____ Yes xx No If no, explain reason(s) below:

The application is Minor

The Chemistry Review for ANDA 77- 407

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

The application is approvable

B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable

N/A

II. Summary of Chemistry Assessments

A. Description of the Drug Product(s) and Drug Substance(s)

The drug product Sodium Chloride Injection USP, 0.9% will be packaged in 5 mL and 10 mL ampoules.

The Reference Listed Drug is Sodium Chloride Injection USP, 0.9% in Plastic Container, NDA 19-217, manufactured by Hospira Ltd. and labeled for Abbott Laboratories.

The drug substance sodium chloride is a white crystalline powder, colorless crystals or white pearls with empirical formula NaCl and molecular weight is 58.44.

b(4)

The firm has submitted blank copy of the master batch record (MBR) for the intended maximum production batch size of [] (both 5 mL and 10 mL ampoules) in Section 3.2.P.3.3.A.

b(4)

The firm has provided copies of the exhibit batch records Lot #TP44 (Batch size: [] for the 5 mL Ampoule and Lot #TP47 (Batch size: [] for the 10 mL Ampoule. See Section 3.2.R.1.

b(4)

The drug product is [] in accordance with the USP.

Executive Summary Section

B. Description of How the Drug Product is Intended to be Used

Sodium Chloride Injection USP, 0.9% is indicated only for diluting or dissolving drugs for intravenous, intramuscular or subcutaneous injection, according to the instructions of the manufacturer of the drug to be administered.

Sodium Chloride Injection USP, 0.9% is supplied in 5 mL and 10 mL polypropylene ampoules in cartons containing 20 ampoules.

The volume of the preparation to be used for diluting or dissolving any drug for injection, is dependent on the vehicle concentration, dose and route of administration as recommended by the manufacturer.

This parenteral should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.

The recommended storage condition is 20° – 25°C (68° – 77°F).

C. Basis for Approvability or Not-Approval Recommendation

The application is approvable

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of trade secret and/or
confidential commercial
information from

_____ Chemistry Review #3 _____

(b) (4)



CHEMISTRY REVIEW



Chemistry Assessment Section

30. MICROBIOLOGY

Micro is acceptable on 06/28/06 by B. Pillari

31. SAMPLES AND RESULTS/METHODS VALIDATION STATUS

Not required.

32. LABELING

Labeling is acceptable by A. Payne on 02/10/06

33. ESTABLISHMENT INSPECTION

EER is acceptable on 07/06/06

34. BIOEQUIVALENCE

Bio is Acceptable per B. Fabian-Fritsch on 3/28/05.

35. ENVIRONMENTAL IMPACT CONSIDERATIONS/CATEGORICAL EXCLUSION: Satisfactory

Taro Pharmaceuticals Ireland Ltd., requests a categorical exclusion under 21 CFR 25.30 and 25.31(a). Also, certifies that, to the best of its knowledge and belief, the firm is in compliance with all local environmental laws.

**APPEARS THIS WAY
ON ORIGINAL**



CHEMISTRY REVIEW



Chemistry Assessment Section

cc: ANDA 77-407
ANDA DUP
Division File
Field Copy

Endorsements:

HFD-627/N.Nashed
HFD-627/J.Fan
HFD-617/R.Adigun/7/20/06

NW 8/10/06
Q 8/10/06

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CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 77-407

BIOEQUIVALENCE REVIEW

MAR 28 2005

**OFFICE OF GENERIC DRUGS
DIVISION OF BIOEQUIVALENCE**

ANDA #: 77-407 SPONSOR: Taro Pharmaceuticals Ireland Ltd.

DRUG AND DOSAGE FORM: Sodium Chloride Injection USP

STRENGTH (S): 0.9%, 5 mL and 10 mL

STUDY SUMMARY: The test drug product is a parental solution intended solely for administration by injection and contains the same active and inactive ingredients in the same concentration as the approved reference listed product. A waiver of the in-vivo bioavailability/bioequivalence study requirements is granted [21 CFR 320.22(b)(1)]

DSI INSPECTION STATUS

Inspection needed: No	Inspection status:	Inspection results:
First Generic No _____	Inspection requested: (date)	
New facility _____	Inspection completed: (date)	
For cause _____		
Other _____		

PROJECT MANAGER: BETH FABIAN FRITSCH, R.PH., MBA BRANCH: IV

INITIAL: BFF DATE: 3/24/05

TEAM LEADER: AIDA L. SANCHEZ, PHARM.D.

INITIAL: AS DATE: 3/25/05

DIRECTOR, DIVISION OF BIOEQUIVALENCE: DALE P. CONNER, PHARM.D.

INITIAL: DP DATE: 3/28/05

BIOEQUIVALENCE COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 77-407

APPLICANT: Taro Pharmaceuticals Ireland Ltd.

DRUG PRODUCT: Sodium Chloride Injection USP, 0.9%, 5 mL and 10 mL

The Division of Bioequivalence has completed its review and has no further questions at this time.

Please note that the bioequivalence comments provided in this communication are preliminary. These comments are subject to revision after review of the entire application, upon consideration of the chemistry, manufacturing and controls, microbiology, labeling, or other scientific or regulatory issues. Please be advised that these reviews may result in the need for additional bioequivalence information and/or studies, or may result in a conclusion that the proposed formulation is not approvable.

Sincerely yours,

A handwritten signature in black ink, appearing to read "Dale P. Conner", is written over a horizontal line.

Dale P. Conner, Pharm. D.

Director,

Division of Bioequivalence

Office of Generic Drugs

Center for Drug Evaluation and Research

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 77-407

MICROBIOLOGY REVIEWS

Product Quality Microbiology Review

Review for HFD-640

15 May 2006

ANDA: 77-407

Drug Product Name

Proprietary: none

Non-proprietary: Sodium Chloride Injection USP, 0.9%

Drug Product Priority Classification: N/A

Review Number: 1

Dates of Submission(s) Covered by this Review

Letter	Stamp	Consult Sent	Assigned to Reviewer
11-29-04	11-30-04	N/A	5-12-06

Submission History (for amendments only)

Submission Date(s)	Microbiology Review #	Review Date(s)
N/A		

Applicant/Sponsor

Name: Taro Pharmaceuticals Ireland Ltd.

Address: Lourdes Road

Roscrea, Co. Tipperary Ireland

USA Agent: Taro Pharmaceuticals USA Inc.

Address: 5 Skyline Drive

Hawthorne, NY 10532

Representative: Kalpana Rao, Vice President Regulatory Affairs

Telephone: 914-345-9001 ext. 6298

Name of Reviewer: Brenda Pillari, Ph.D.

Conclusion: Not recommended for approval based on sterility assurance

Product Quality Microbiology Data Sheet

- A.
1. **TYPE OF SUBMISSION:** Original submission
 2. **SUBMISSION PROVIDES FOR:** Initial marketing of sterile drug product
 3. **MANUFACTURING SITE:** Taro Pharmaceuticals Ireland Ltd.
 Lourdes Road
 Roscrea, Co. Tipperary
 Ireland
 4. **DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:** sterile, solution, intravenous, intramuscular, or subcutaneous injection
 5. **METHOD(S) OF STERILIZATION:** b(4)
 6. **PHARMACOLOGICAL CATEGORY:** Diluent. Only for diluting or dissolving drugs according to instructions of the manufacturer of the drug to be administered
- B. **SUPPORTING/RELATED DOCUMENTS:** none
- C. **REMARKS:** none

filename: 77-407.doc

Executive Summary

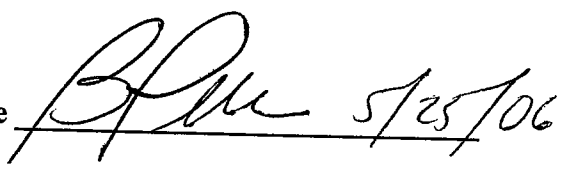
I. Recommendations

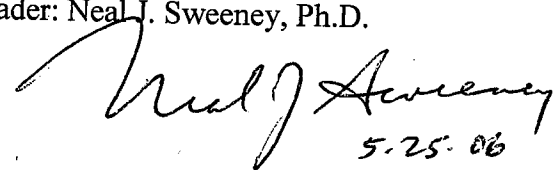
- A. **Recommendation on Approvability - Not Recommended** for approval based on sterility assurance. Specific comments regarding the manufacture of sterile drug products are provided in "H. List of Microbiology Deficiencies and Comments" sections.
- B. **Recommendations on Phase 4 Commitments and/or Agreements, if Approvable - N/A**

II. Summary of Microbiology Assessments

- A. **Brief Description of the Manufacturing Processes that relate to Product Quality Microbiology** - Filling of product into 5mL and 10mL polypropylene ampoules in an unknown room ☐
b(4)
- B. **Brief Description of Microbiology Deficiencies-Incomplete and unclear information for validation of ☐**
b(4) ☒ incomplete environmental monitoring information, and incomplete container closure integrity information.
- C. **Assessment of Risk Due to Microbiology Deficiencies** - The public health risk associated with these deficiencies is moderate.

III. Administrative

- A. **Reviewer's Signature**  5/25/06
- B. **Endorsement Block**
Microbiology Reviewer: Brenda Pillari, Ph.D.
Microbiology Team Leader: Neal J. Sweeney, Ph.D.
- C. **CC Block**
cc:
Original ANDA 77-407
HFD- 600
Field Copy

 5.25.06

Withheld 13 page(s)
of trade secret and/or
confidential commercial
information from

Microbiology Review #1

(b) (4)

Product Quality Microbiology Review

Review for HFD-640

19 June 2006

ANDA: 77-407

Drug Product Name

Proprietary: none

Non-proprietary: Sodium Chloride Injection USP, 0.9%

Drug Product Priority Classification: N/A

Review Number: 2

Dates of Submission(s) Covered by this Review

Letter	Stamp	Consult Sent	Assigned to Reviewer
5-30-06	5-31-06	N/A	6-12-06

Submission History (for amendments only)

Submission Date(s)	Microbiology Review #	Review Date(s)
11-29-04	1	5-15-06

Applicant/Sponsor

Name: Taro Pharmaceuticals Ireland Ltd.

Address: Lourdes Road

Roscree, Co. Tipperary Ireland

USA Agent: Taro Pharmaceuticals USA Inc.

Address: 5 Skyline Drive

Hawthorne, NY 10532

Representative: Kalpana Rao, Vice President Regulatory Affairs

Telephone: 914-345-9001 ext. 6298

Name of Reviewer: Brenda Pillari, Ph.D.

Conclusion: Recommended for approval based on sterility assurance

Product Quality Microbiology Data Sheet

- A. 1. **TYPE OF SUBMISSION:** Original submission
2. **SUBMISSION PROVIDES FOR:** Initial marketing of sterile drug product
3. **MANUFACTURING SITE:** Taro Pharmaceuticals Ireland Ltd.
 Lourdes Road
 Roscrea, Co. Tipperary
 Ireland
4. **DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:** sterile, solution, intravenous, intramuscular, or subcutaneous injection
- b(4) 5. **METHOD(S) OF STERILIZATION:** ☐
6. **PHARMACOLOGICAL CATEGORY:** Diluent. Only for diluting or dissolving drugs according to instructions of the manufacturer of the drug to be administered
- B. **SUPPORTING/RELATED DOCUMENTS:** none
- C. **REMARKS:** none

filename: 77-407a1.doc

Executive Summary

I. Recommendations

- A. Recommendation on Approvability - Not Recommended** for approval based on sterility assurance. Specific comments regarding the manufacture of sterile drug products are provided in "H. List of Microbiology Deficiencies and Comments" sections.
- B. Recommendations on Phase 4 Commitments and/or Agreements, if Approvable - N/A**

II. Summary of Microbiology Assessments

- A. Brief Description of the Manufacturing Processes that relate to Product Quality Microbiology - Filling of product into 5mL and 10mL polypropylene ampoules in an unknown room** ☐
- B. Brief Description of Microbiology Deficiencies- None identified**
- C. Assessment of Risk Due to Microbiology Deficiencies – None identified**

b(4)

III. Administrative

- A. Reviewer's Signature**

 6/19/06

- B. Endorsement Block**

Microbiology Reviewer: Brenda Pillari, Ph.D.

Microbiology Team Leader: Neal J. Sweeney, Ph.D.

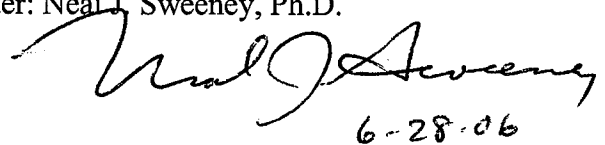
- C. CC Block**

cc:

Original ANDA 77-407

HFD- 600

Field Copy

 6-28-06

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of trade secret and/or
confidential commercial
information from

Microbiology Review #2

(b) (4)

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 77-407

ADMINISTRATIVE and CORRESPONDENCE
DOCUMENTS



Taro Pharmaceuticals U.S.A., Inc.

November 29, 2004

Office of Generic Drugs
Food and Drug Administration, CDER
Document Control Room
Metro Park North II
7500 Standish Place
Room 150
Rockville, MD 20855-2773

30516172
M. J. [Signature]
77-407
[Signature]
[Signature]

**RE: Abbreviated New Drug Application
Sodium Chloride Injection USP, 0.9%**

Dear Sir/ Madam:

Taro Pharmaceuticals Ireland Ltd. (Taro) submits, today, an original, abbreviated new drug application (ANDA) seeking approval to market Sodium Chloride Injection USP, 0.9% based on the referenced listed drug 0.9% Sodium Chloride Injection, USP manufactured by Hospira and labeled for Abbott Laboratories.

This ANDA is prepared in the ICH-CTD format, following the recommendations of the following guidance documents:

Submitting Marketing Applications According to the ICH-CTD Format – General Considerations

M4: Organization of the CTD

M4E: The CTD – Efficacy

M4Q: The CTD – Quality

M4S: The CTD – Safety

This ANDA is comprised of 5 volumes. The volumes are distributed as follows:

- Module 1 – Administrative and Prescribing Information (1 volume)
- Module 2 – Common Technical Document Summaries (1 volume)
- Module 3 – Quality (3 volumes)
- Module 4 – Non-clinical Study Reports (Not Applicable)
- Module 5 – Clinical Study Reports (Not Applicable)

RECEIVED

NOV 30 2004

OGD / CDER

Taro Pharmaceuticals U.S.A., Inc., the U. S. Agent for Taro Pharmaceuticals Ireland Ltd., is filing archival, review and field copies as follows:

Archival copy (5 volumes)	Blue Jackets: Modules 1, 2 and 3
Review Copy (5 volumes)	Red Jackets Modules 1, 2 and 3
Field Copy (5 volume)	Maroon Jacket: Module 1, 2 and 3
Pharmacokinetic Copy (1 volume)	Orange Jacket Module 1

Taro hereby certifies that the "field copy" is a true copy of the technical sections of the ANDA (copy: this letter, 356h form, "true copy certification). This "field copy" is contained in Maroon folders.

If you have any questions regarding this application, please contact the undersigned (the U. S. Agent) at 914-345-9001, ext. 6298.

Sincerely,



11/29/04

Kalpana Rao (U.S. Agent)
Vice President, Regulatory Affairs (Global, CMC)

77-407



Taro Pharmaceuticals U.S.A., Inc.

November 30, 2004

Office of Generic Drugs
Food and Drug Administration, CDER
Document Control Room
Metro Park North II
7500 Standish Place
Room 150
Rockville, MD 20855-2773

NEW CORRESP
MC

**RE: Abbreviated New Drug Application
Sodium Chloride Injection USP, 0.9%**

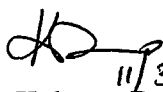
Dear Sir/ Madam:

Taro Pharmaceuticals Ireland Ltd. (Taro) submits, today, electronic labeling (inadvertently omitted from the original submission made on November 29, 2004) for Sodium Chloride Injection USP, 0.9%. FDA Form 356h is also attached.

Taro Pharmaceuticals U.S.A., Inc., is the U. S. Agent for Taro Pharmaceuticals Ireland Ltd.

If you have any questions regarding this application, please contact the undersigned (the U. S. Agent) at 914-345-9001, ext. 6298.

Sincerely,


11/30/04

Kalpana Rao (U.S. Agent)
Vice President, Regulatory Affairs (Global, CMC)

RECEIVED

DEC 01 2004

OGD / CDER

RECORD OF TELEPHONE CONVERSATION

ANDA #: 77-407

DATE: January 10, 2005

TIME: 11:00 am

DRUG: Sodium Chloride Injection USP, 0.9%

FIRM: Ms. Barbara Canter for Taro Pharmaceuticals

FDA PARTICIPANTS: Emily Thakur

PHONE NUMBER: 914-345-9001

TOPIC: Missing items

I asked Ms. Canter to provide contact information and COA for the API. I needed a reprocessing statement. Also need a list of addresses for inactives and container/closures.



Taro Pharmaceuticals U.S.A., Inc.

January 13, 2005

Office of Generic Drugs Food and Drug Administration, CDER
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773
Attn: Emily Thakur

NEW CORRESP

NC

**RE: Abbreviated New Drug Application 77-407
Sodium Chloride Injection USP, 0.9%
Correspondence**

Dear Ms. Thakur:

Thank you for your telephone call of January 10, 2005 and continued clarification of January 13, 2005. Taro Pharmaceuticals hereby submits the following, as requested:

- b(6)** • **Contact name and address of API supplier:**
☐ ☒ Head of Regulatory Affairs, Tel. ☐ ☒
- b(4)** • **Certificate of Analysis for sodium chloride** (from ☐ ☒ manufacturer of sodium chloride): ☐ ☒ has supplied their Certificate of Analysis (Module 3, section 3.2.S.4 [Control of Drug Substance], page 48). ☐ ☒ has stated that the material is traceable back to the original manufacturer and may release the C/A directly to a government agency.
- **Reprocessing Statement:** see attachment A
- **List of addresses for inactive and container closure system:** see Attachment B

FDA Form 356h is also attached.

If you have any questions regarding this application, please contact Ms. Kalpana Rao (the U. S. Agent) at 914-345-9001, ext. 6298.

Sincerely,

Barbara Lynn Cantor
Director, Regulatory Affairs (International)

RECEIVED

JAN 14 2005

OGD / CDER

JAN 14 2005

ANDA 77-407

Taro Pharmaceuticals U.S.A., Inc.
U.S. Agent for Taro Pharmaceuticals Ireland Ltd.
Attention: Kalpana Rao
5 Skyline Drive
Hawthorne, NY 10532
|||||

Dear Madam:

We acknowledge the receipt of your abbreviated new drug application submitted pursuant to Section 505(j) of the Federal Food, Drug and Cosmetic Act.

Reference is made to the telephone conversation dated January 10, 2005 and your correspondence dated January 13, 2005.

NAME OF DRUG: Sodium Chloride Injection USP, 0.9%, 5 mL ampoules

DATE OF APPLICATION: November 29, 2004

DATE (RECEIVED) ACCEPTABLE FOR FILING: November 30, 2004

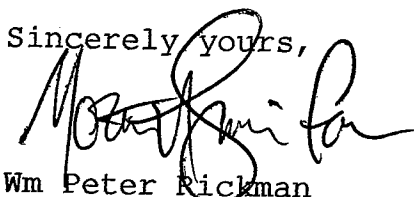
We will correspond with you further after we have had the opportunity to review the application.

Please identify any communications concerning this application with the ANDA number shown above.

Should you have questions concerning this application, contact:

Peter Chen
Project Manager
(301) 827-5848

Sincerely yours,



Wm Peter Rickman
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

ANDA 77-407

cc: DUP/Jackets

HFD-600/Division File

Field Copy

HFD-610

HFD-92

Endorsement:

HFD-615/MShimer, Chief, RSB

HFD-615/ETHakur, CSO

Word File V:\Firmsnz\taro\ltrs&rev\77407.ack

F/T ETT01/13/05

ANDA Acknowledgment Letter!

date

date

15 Jan 2005

MAY 12 2005

36. CHEMISTRY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 77-407

APPLICANT: Taro Pharmaceuticals Ireland Ltd.

DRUG PRODUCT: Sodium Chloride Injection USP, 0.9%, 5 mL

The deficiencies presented below represent MINOR deficiencies.

A. Deficiencies:

1. ☐

2.

3.

b(4)

4.

5.

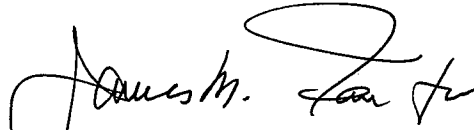
6. ☐

B. In addition to responding to the deficiencies presented above, please note and acknowledge the following comments in your response:

1. The firms referenced in your application should be in compliance with cGMP at the time of approval.
2. Please provide all available drug product room temperature stability data.

3. Labeling and microbiology information you have provided is pending review. After the reviews are completed, any deficiencies found will be communicated to you under a separate cover.

Sincerely yours,

A handwritten signature in black ink, appearing to read "Rashmikant M. Patel". The signature is fluid and cursive, with a large loop at the end.

Rashmikant M. Patel, Ph.D.
Director
Division of Chemistry I
Office of Generic Drugs
Center for Drug Evaluation and Research

**APPEARS THIS WAY
ON ORIGINAL**

July 28, 2005



Taro Pharmaceuticals U.S.A., Inc.

Thuyanh (Ann) Vu, Project Manager
Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room, Metro Park North II
7500 Standish Place, Room 150
Rockville MD 20855

ORIG AMENDMENT

N / AMI

MINOR AMENDMENT

Re: ANDA 77-407
Sodium Chloride Injection USP, 0.9%

Dear Sir/Madam:

Reference is made to Taro Pharmaceutical Ireland Ltd.'s Abbreviated New Drug Application (ANDA) submitted, on November 29, 2004, under section 505(j) of the Federal Food, Drug and Cosmetic Act, for Sodium Chloride Injection USP, 0.9%. Reference is also made to the Agency letter dated May 12, 2005, in which the following deficiencies were communicated:

A. Deficiencies

b(4)

OGD/CDER

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of trade secret and/or

confidential commercial

information from

TARO amendment letter dated 7/28/05

Comment 2

Please provide all available drug product room temperature stability data.

Response

The comment is noted and acknowledged by Taro. Drug product stability data, to nine months, at room temperature ($25^{\circ}\text{C} \pm 2^{\circ}\text{C}/40\% \pm 5\% \text{RH}$), for TP 44 (5 mL ampoule) and TP 47 (10 mL ampoule), are provided in Module 3, section 3.2.P.8.3.

Comment 3

Labeling and microbiology information you have provided is pending review. After the reviews are completed, any deficiencies found will be communicated to you under separate cover.

Response

The comment is noted and acknowledged by Taro.

Should you have any questions, please contact the undersigned at 914-345-9001, ext. 6298.
Sincerely,


7/28/01

Kalpana Rao (US Agent)
Vice-President, Regulatory Affairs (Global)

ORIG AMENDMENT

N/A



Taro Pharmaceuticals U.S.A., Inc.

September 22, 2005

Ms. Thuyanh (Ann) Vu
Project Manager
Office of Generic Drugs, Food and Drug Administration, CDER
Document Control Room, Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

GRATUITOUS AMENDMENT

RE: ANDA 77-407
Sodium Chloride Injection USP, 0.9%

Dear Ms. Vu:

Reference is made to Taro Pharmaceutical Ireland Ltd.'s Abbreviated New Drug application (ANDA) 77-407, submitted on November 29, 2004 under section 505(j) of the Federal Food, Drug and Cosmetic Act, for Sodium Chloride Injection USP, 0.9% in 5 mL and 10 mL plastic containers.

Enclosed, please find a gratuitous amendment to the ANDA. This amendment is to include Taro Pharmaceutical Industries Ltd., 14 Hakitor Street, Haifa Bay, 26110, Israel as an alternative site for USP particulate testing of the finished product and stability samples, inadvertently omitted from our previous submissions. The revised Module 3, section 3.2.P.3.1 is provided.

In addition, drug product stability data for TP44 (5 mL ampoule) and TP47 (10 mL ampoule) to 12 months, at room temperature ($25^{\circ}\text{C} \pm 2^{\circ}\text{C}/40\% \pm 5\% \text{RH}$) are provided in revised Module 3, section 3.2.P.8.

If you have any questions regarding this application, please contact Ms. Kalpana Rao at 914-345-9001, ext. 6298.

Sincerely,

A handwritten signature in black ink, appearing to read "Kalpana Rao", with the date "9/22/05" written below it.

Kalpana Rao
GVP, Regulatory Affairs (Global)

RECEIVED

SEP 23 2005

OGD/CDER

January 23, 2006



Taro Pharmaceuticals U.S.A., Inc.

Attention: Angela Payne
Office of Generic Drugs
CDER, FDA
Document Control Room, Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855

ORIG AMENDMENT

N/AF

**Re: ANDA #77-407
Sodium Chloride Injection USP, 0.9%
Labeling Amendment**

Dear Ms. Payne:

Reference is made to our Abbreviated New Drug Application (ANDA) for Sodium Chloride Injection USP, 0.9% submitted November 29, 2004, and to the labeling deficiency letters received on November 29, 2005 and January 20, 2006 in which the following was requested:

Labeling Deficiencies:

1. We believe you have used an incorrect NDA to model your product labeling after. You used NDA 19-217 (0.9% Sodium Chloride Injection USP- in life shield Fliptop Glass vials - Thermoject System). We believe your insert should model NDA 18-803 (0.9% Sodium Chloride Injection USP in fliptop Plastic vials). Please comment on why you chose 19-217 as the reference listed drug. The inserts are very similar and there are not many changes required below.

Response

Taro chose NDA 19-217 initially because that is the reference listed drug (RLD) in the Orange Book. The description in the Orange Book does not give the type of container and there was no labeling associated with the website. When the RLD was received we used the accompanying insert and neglected to make the necessary changes to reflect our packaging. Taro has noted the changes requested and thanks the Agency for the sending us the labeling that we should have used and has made the necessary changes.

2. CONTAINER (5 Ml and 10 mL)

Comment 1

Include the drug use "FOR DRUG DILUENT USE"

Response

Taro has revised the container label as requested.

Comment 2

Please provide a drawing of your ampules and comment on how one would gain access to the product inside the ampules. The reference listed drug uses glass ampules that must be popped at the designated line.

RECEIVED

JAN 24 2006

OGD / CDER

Response

A drawing of the 5 mL and 10 mL ampule is attached (attachment 1). This drawing was included in our original submission, under Module 3, section 3.2.P.7 Drug Product Container Closure System.

The ampule has a tab at the top that is twisted to gain access to the product.

Comment 3

Please indicate "single dose".

Response

Taro has revised the container label as requested.

Comment 4

What id the color of your cap?

Response

This product is contained in a twist-off top polypropylene ampule. There is no color cap to id the product.

3. CARTON (20s x 5 mL)

Comment 1

Place the following in bold print and all caps "FOR DRUG DILUENT USE"

Response

Taro has revised the carton as requested.

Comment 2

Revise "ampoules" to read "ampules"

Response

Taro has revised the carton as requested.

Comment 3

See comments under CONTAINER

Response

Taro notes the comments and has revised the carton as requested.

Comment 4

Include the pH range.

Response

Taro has revised the carton label as requested.

4. INSERT

Comment 1

Include the "Rx only" statement so that it follows the title and type of ampule.

Response

Taro has revised the insert as requested.

Comment 2

Please include a statement about your ampule composition.

Response

Taro has revised the insert as requested.

Comment 3

CLINICAL PHARMACOLOGY - Combine the last two sentences so that they become the last paragraph.

Response

Taro has revised the insert as requested.

Comment 4

DOSAGE AND ADMINISTRATION - Add "Use aseptic technique for entry and withdrawal from container".

Response

Taro has revised the insert as requested.

Comment 5

HOW SUPPLIED - Describe your containers as single-dose containers. Change the spelling of ampoules.

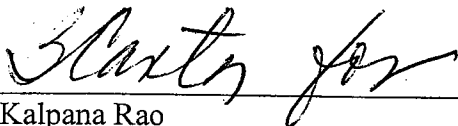
Response

Taro has revised the insert as requested.

Taro is including a CD with the PDF files of the labels and labeling as well as a Word document for the Package Insert. In addition, and in accordance with 21 CFR 314.94(a)(8)(iv) we have also provided a side-by-side comparison of our proposed labeling with our previously submitted package insert.

This completes our response to the deficiency letter of November 29, 2005. If there are any questions regarding this amendment, or if additional information is required, please contact the undersigned.

Sincerely,



Kalpana Rao
Group Vice President, Regulatory Affairs (Global)
Taro Pharmaceuticals U.S.A., Inc.

RECEIVED

MAR 06 2006

OGD / CDER



Taro Pharmaceuticals U.S.A., Inc.

March 3, 2006

Attention: Thuyanh (Ann) Vu
OGD, CDER, FDA
Document Control Room, Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855 - 2773

ORIG AMENDMENT

Re: **ANDA #77-407**
Sodium Chloride Injection USP, 0.9%
MINOR AMENDMENT

Am

Dear Ms. Vu:

Reference is made to our Abbreviated New Drug Application (ANDA) for Sodium Chloride Injection USP, 0.9% submitted November 29, 2004, and to "Chemistry Comments" dated January 20, 2006 in which the following was requested:

The deficiency presented below represents a Minor deficiency:

Labeling deficiencies were communicated to you via facsimile on November 29, 2005. You should address the issues in the November 29, communication prior to or concurrent with your response to this communication.

Response

Taro submitted a Labeling Amendment, to address the November 29, 2005 deficiency letter, on January 23, 2006. Taro, unintentionally, did not address the Chemistry Comments at that time.

Please accept this letter as the Minor Amendment, in answer to the Agency's January 20, 2006 letter.

This completes our response to the deficiency letter of January 20, 2006. If there are any questions regarding this amendment, or if additional information is required, please contact the undersigned.

Sincerely,

A handwritten signature in dark ink, appearing to be "KR" with a flourish, followed by the date "3/3/06" written below it.

Kalpana Rao (US Agent)
Group Vice President, Regulatory Affairs (Global)



Taro Pharmaceuticals U.S.A., Inc.

ORIG AMENDMENT

N/HAS

May 30, 2006

Office of Generic Drugs
CDER, FDA
Document Control Room, Metro Park North II
7500 Standish Place, Room 150
Rockville MD 20857

Attention: Office of International Program

**Re: ANDA 77-407
Sodium Chloride Injection USP, 0.9%
MINOR AMENDMENT - RESPONSE TO MICROBIOLOGY
DEFICIENCIES**

Dear Sir/Madam:

The attached document is being submitted as the field copy for the above reference amendment. Taro Pharmaceuticals U.S.A., Inc hereby certifies that the field copy is a true copy of the technical information provided in this amendment.

Should you have any questions, please contact the undersigned at 914-345-9001, ext. 6298.

Sincerely,

5/30/06

Kalpana Rao (US Agent)
GVP, Regulatory Affairs (Global)

RECEIVED

MAY 31 2006

OGD / CDER

OGD APPROVAL ROUTING SUMMARY

ANDA # 77-407 Applicant Taro Pharmaceuticals U.S.A., Inc.
 Drug Sodium Chloride Injection USP Strength(s) 0.9%

PROVAL

TENTATIVE APPROVAL

SUPPLEMENTAL APPROVAL (NEW STRENGTH)

OTHER

VIEWER:

DRAFT Package

FINAL Package

1. Martin Shimer
 Chief, Reg. Support Branch

Date 18 July 06
 Initials MS

Date 8/1/06
 Initials MS

Contains GDEA certification:
 (required if sub after 6/1/92)

Yes No

Determ. of Involvement? Yes No

Pediatric Exclusivity System
 RLD = N/A NDA# 19-217

Patent/Exclusivity Certification: Yes No

If Para. IV Certification- did applicant

Notify patent holder/NDA holder Yes No

Was applicant sued w/in 45 days: Yes No

Has case been settled: Yes No

Is applicant eligible for 180 day

Generic Drugs Exclusivity for each strength: Yes No

Date of latest Labeling Review/Approval Summary

Any filing status changes requiring addition Labeling Review Yes No

Type of Letter:

Comments:

no patents/exclusivity ∴ eligible for Full Ap

2. Project Manager, Rosalyn A. Team 3
 Review Support Branch

Date RA
 Initials 07/17/06

Date _____
 Initials _____

Original Rec'd date 11/29/04

Date Acceptable for Filing 11/30/04

Patent Certification (type) I

Date Patent/Exclus. expires N/A

Citizens' Petition/Legal Case Yes No

(If YES, attach email from PM to CP coord)

First Generic Yes No

EER Status Pending Acceptable OAI

Date of EER Status 7/16/06

Date of Office Bio Review 03/28/05

Date of Labeling Approv. Sum 02/10/06

Labeling Acceptable Email Rec'd Yes No

Labeling Acceptable Email filed Yes No

Date of Sterility Assur. App. 06/28/06

Methods Val. Samples Pending Yes No

MV Commitment Rcd. from Firm Yes No

Acceptable Bio reviews tabbed Yes No

Suitability Petition/Pediatric Waiver

Pediatric Waiver Request Accepted Rejected Pending

Previously reviewed and tentatively approved

Previously reviewed and CGMP def. /NA Minor issued

Comments:

Modified-release dosage form: Yes No

Interim Dissol. Specs in AP Ltr: Yes

Date N/A

Date N/A

3. David Read (PP IVs Only) Pre-MMA Language included
 OGD Regulatory Counsel, Post-MMA Language Included
 Comments:

Date _____
 Initials _____

Div. Dir./Deputy Dir.
 Chemistry Div. I II OR, III
 Comments:

Date 8/1/06
 Initials RL

The cmc section is satisfactory.

REVIEWER:**FINAL ACTION**

5. Frank Holcombe First Generics Only
Assoc. Dir. For Chemistry
Comments: (First generic drug review)

Date _____
Initials _____

N/A. American Pharmaceutical Partners (APP)'s ANDA
88-912 for this drug product was approved on 1/10/85.

6. Vacant RD: Sodium Chloride Injection 0.9% (in plastic container)
Deputy Dir., DLPS

Date _____
Initials _____

NDA 19-217
Vasipira Inc.

7. Peter Rickman
Director, DLPS

Date 8/11/06
Initials [Signature]

Para. IV Patent Cert: Yes No ; Pending Legal Action: Yes No ; Petition: Yes No

Comments: Acceptable EES dated 7/6/06. Verified 8/11/06. No O.A.T. affects
inter. Bioequivalence waiver granted under 21 CFR 320.32(b)(1).
Drug product is "Q+Q" to the RLD office and is endorsed 3/28/05.
OR
Microbiology/sterility assurance found acceptable 6/28/06. PPL
found acceptable for approval 2/10/06 (as endorsed 7/20/06). CMC found
acceptable for approval 8/10/06.

Robert L. West
Deputy Director, OGD

Date 8/11/2006
Initials [Signature]

Para. IV Patent Cert: Yes ☒ No; Pending Legal Action: Yes ☒ No; Petition: Yes ☒ No

Comments: There are no unexpired patents or exclusivity
listed in the current "Orange Book" for this drug product.
This ANDA is recommended for approval.

9. Gary Buehler
Director, OGD
Comments:

Date 8/11/06
Initials [Signature]

First Generic Approval

PD or Clinical for BE

Special Scientific or Reg. Issue

10. Project Manager, Team [Signature]
Review Support Branch

Date 8/11/06
Initials [Signature]

Date PETS checked for first generic drug (just prior to notification to firm)

Applicant notification:

13. Time notified of approval by phone 14. Time approval letter faxed

FDA Notification:

8/11/06 Date e-mail message sent to "CDER-OGDAPPROVALS" distribution list.

8/11/06 Date Approval letter copied to \\CDS014\DRUGAPP\ directory.