CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-604

APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-604

Taro Pharmaceuticals Inc.
Attention: Kalpana Rao
Vice President, Regulatory Affairs
Five Skyline Drive
Hawthorne, NY 10532

Dear Ms. Rao:

Please refer to your new drug application (NDA) dated December 30, 2002, received December 31, 2002, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Children's ElixSure™ IB (ibuprofen) Oral Suspension, 100 mg/5 mL.

We acknowledge receipt of your submissions dated November 18, December 18 and 19, 2003, and January 6, 2004.

The November 18, 2003 submission constituted a complete response to our October 31, 2003 action letter.

This new drug application provides for the use of Children's ElixSure™ IB (ibuprofen) Oral Suspension, 100 mg/5 mL for the relief of minor aches and pains due to the common cold, flu, sore throat, headache, toothache and reduction of fever in children.

We completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text.

The final printed labeling (FPL) must be identical to submitted labeling (immediate container and carton labels submitted December 18 and 19, 2003), and must be in the "Drug Facts" format (21 CFR 201.66). Marketing the product with FPL that is not identical to the approved labeling text and in the required format may render the product misbranded and an unapproved new drug.

Please submit an electronic version of the FPL according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA*. Alternatively, you may submit 20 paper copies of the FPL as soon as it is available but no more than 30 days after it is printed. Individually mount 15 of the copies on heavy-weight paper or similar material. For administrative purposes, designate this submission "**FPL for approved NDA 21-604.**" Approval of this submission by FDA is not required before the labeling is used.

All applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred. We note that you have fulfilled the pediatric study requirement for this application.

In addition, we request that you submit two copies of the introductory promotional materials you propose to use for this product. Submit all proposed materials in draft or mock-up form, not final print. Please send one copy, along with labeling, to each of the Divisions signing below.

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

Oversight of this application is being transferred to the Division of Over-the-Counter Drug Products.

If you have any questions, please call Walter Ellenberg, PhD, Regulatory Health Project Manager at (301) 827-2222.

Sincerely,

{See appended electronic signature page}

Charles Ganley, MD
Director
Division of Over-the-Counter Drug Products, HFD-560
Office of Drug Evaluation V
Center for Drug Evaluation and Research

Brian E. Harvey, MD, PhD
Acting Director
Division of Anti-Inflammatory, Analgesic and Ophthalmic Drug Products, HFD-550
Office of Drug Evaluation V
Center for Drug Evaluation and Research

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

/s/

Charles Ganley
1/7/04 03:13:42 PM

Brian Harvey
1/7/04 03:47:13 PM

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-604

APPROVABLE LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-604

Taro Pharmaceuticals USA, Inc.
Attention: Kalpana Rao
Vice President, Regulatory Affairs
Five Skyline Drive
Hawthorne, NY 10532

Dear Ms. Rao:

Please refer to your new drug application (NDA) dated December 30, 2002, received December 31, 2002, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Children's ElixSure™ IB (ibuprofen) Oral Suspension, 100 mg/5 ml.

We acknowledge receipt of your submissions dated January 24 and 31, 2003, March 7, 2003, May 28, 2003, June 20, 25 and 27, 2003, July 22, 23 and 25, 2003, August 1, 2003, September 23 and 29, 2003, and October 1, 6, 8, 16, 23 and 24, 2003.

We completed our review of this application, as amended, and it is approvable. Before the application may be approved, however, it will be necessary for you to:

1. Submit results of a randomized study of sufficient size to provide data regarding the accuracy and reproducibility of a consumer's ability to measure doses accurately. The study you submitted with the application is not adequate to assess this. In your study, all of the participants were employees of your company and most had some college education. They are not representative of the population who will use this product. We have the following comments on the study that needs to be conducted.
   a) The study should be done by (an) independent investigator(s), not related to the sponsor.
   b) The population used in the study should not be employees of the sponsor, should be randomly selected and represent an age range and educational level of the population that would be using the measuring spoon.
2. Consider ways to improve the contrast of the "½ tsp to line" marking on the spoon.
3. Upon review of your study entitled "To evaluate the feasibility of administering a 30-50 ml bolus of Taro's Children's ElixSure ™ IB (ibuprofen) Oral Suspension, 100 mg/5 ml, undiluted and in a 1:1 dilution with water, from a syringe through several different feeding tubes", we noted problems associated with the administration of this product via a feeding tube. Provide labeling indicating that this product should not be used in association with gastro-intestinal tubes or provide justification why this type of warning is not necessary.

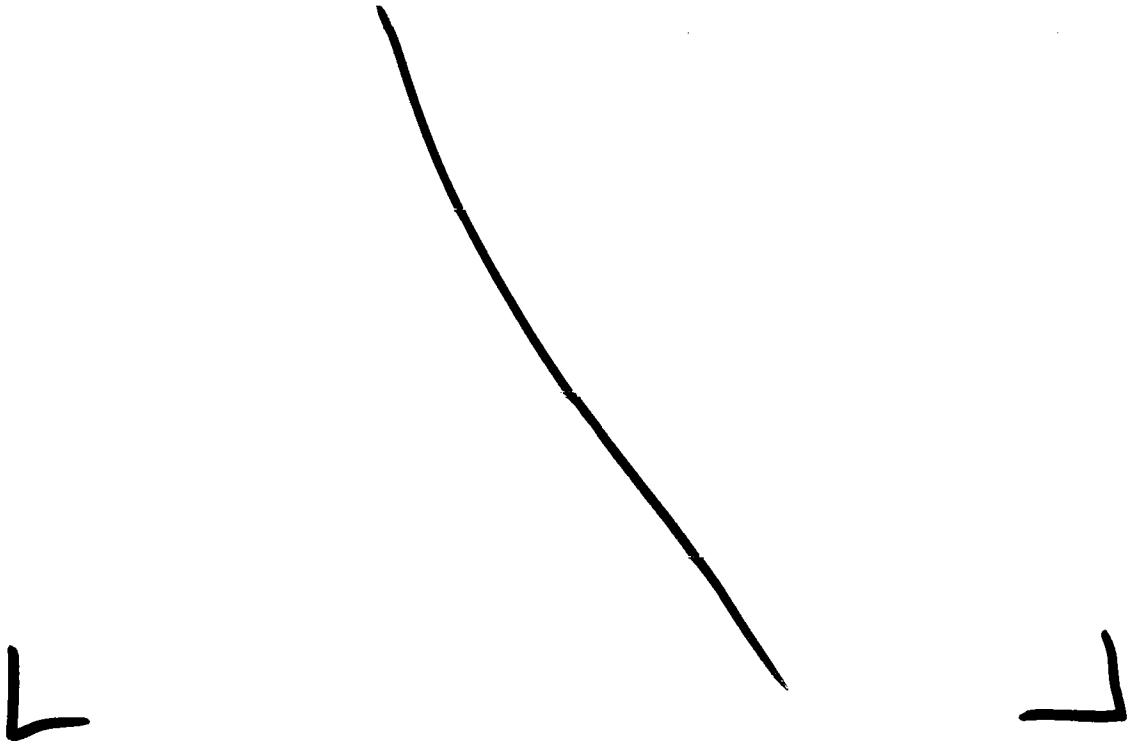
1 Page(s) Withheld

_____ § 552(b)(4) Trade Secret / Confidential

✓ § 552(b)(4) Draft Labeling

_____ § 552(b)(5) Deliberative Process

Withheld Track Number: Approvable Letter- 1 of 1



Biopharmaceutical Comments:

3. In the future, include subjects with both genders and representative ethnic groups in the study.
4. In the future, study PK in targeted pediatric patient population, e.g., febrile children.
5. In the future, when evaluating food effects using 90% confidence intervals, use data from fasting conditions as the reference and data from fed conditions as the test.

Within 10 days after the date of this letter, you are required to amend this application, notify us of your intent to file an amendment, or follow one of your other options under 21 CFR 314.110. If you do not follow one of these options, we will consider your lack of response a request to withdraw the application under 21 CFR 314.65. Any amendment should respond to all the deficiencies listed. We will not process a partial reply as a major amendment nor will the review clock be reactivated until all deficiencies have been addressed.

Under 21 CFR 314.102(d), you may request an informal meeting or telephone conference with the Division of Anti-Inflammatory, Analgesic and Ophthalmic Drug Products, HFD-550 and the Division of Over-the-Counter Drug Porducts, HFD-560to discuss what steps need to be taken before the application may be approved.

The drug product may not be legally marketed until you have been notified in writing that the application is approved.

If you have any questions, please call Ms. Jane A. Dean, RN, MSN, Regulatory Health Project Manager, at (301) 827-2090.

Sincerely,

{See appended electronic signature page}

Curtis Rosebraugh, MD
Deputy Director
Division of Over-the-Counter Drug Products
ODE V
Center for Drug Evaluation and Research

Lee S. Simon, MD
Director
Division of Anti-Inflammatory, Analgesic and
Ophthalmic Drug Products, HFD-550 ODE V
Center for Drug Evaluation and Research

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

/s/

Lee Simon
10/30/03 05:54:47 PM

Curtis Rosebraugh
10/31/03 01:22:53 PM