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APPLICATION NUMBER:

22-121

**CLINICAL PHARMACOLOGY AND
BIOPHARMACEUTICS REVIEW(S)**

CLINICAL PHARMACOLOGY REVIEW

NDA:	21-924 and 22-121
Submission Date(s):	May 31, 2007; July 25, 2007
Brand Name:	Tirosint™
Generic Name:	Levothyroxine Sodium
Reviewer:	Sang M. Chung, Ph.D.
Team Leader:	Sally Choe, Ph.D. (Acting)
OCP Division:	Clinical Pharmacology 2
ORM Division:	Metabolism and Endocrinology Products
Sponsor:	Institut Biochimique SA (IBSA)
Submission Type:	Response to AE
Formulation (strength):	Soft Capsule (NDA 22-121 for 13 µg and NDA 21-924 for 25, 50, 75, 100, 125 & 150 µg)
Indication:	Hypothyroidism / Pituitary TSH Suppression

1 Executive Summary

1.1 Recommendation

The Office of Clinical Pharmacology / Division of Clinical Pharmacology 2 (OCP/DCP2) has reviewed the response to the Agency's request for the validity of bioanalytical analyses in the pivotal Study AA05227. The response is complete and acceptable.

Background:

The sponsor submitted NDA 21-924 for Tirosint™ (levothyroxine sodium soft capsule for 12.5, 25, 50, 75, 100, 125 & 150 µg) as a 505(b)(2) referencing Synthroid® (NDA 21-402). The NDA was approved except for the lowest strength because of its clinical utility. Therefore, the NDA was administratively unbundled for the lowest strength as NDA 22-121 with the Agency's recommendation replacing 12.5 µg with 13 µg as a chemistry amendment.

One of the pivotal pharmacokinetic studies (Study AA05227) for NDA 21-924 was conducted by _____ facility. However, because this analytical study site was inspected by Division of Scientific Investigations (DSI) for

another application relating levothyroxine in 2003-2004, DSI inspection was not requested.

To ensure quality of the Study AA05227 results, the Agency requested submission of the validity of bioanalytical analyses and the sponsor submitted the response with the scientific audit conducted by an independent expert (see Attachment).

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/s/

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4/18/2007 08:48:08 AM
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