

Memorandum to File

To: NDA 21-210 file

From: S. Markofsky (Acting Team Leader)

Subject: Storage Statement for Jerome Sevens Pharmaceutical's Levothyroxine Sodium (Tablets)

Date: 8-4-00

In the labeling provided in NDA 21-210 for their Levothyroxine Sodium (Tablets), Jerome Sevens Pharmaceutical's proposed the following storage statement:

"Store at controlled room temperature 15-30°C (59-86°F)"

The Chemistry Reviewer for this NDA (Elsbeth Chikhale), with the concurrence of the Chemistry Team Leader (Duu-Gong Wu) has suggested that the storage temperature should be changed to:

"20°-25°C (68°-77°F) with excursions between 15° and 30°C (59°-86°F)"

At a meeting on the status of this NDA (8-1-00), a question was raised about the appropriateness of the storage statement that was suggested by the Chemistry Reviewer, in view of possible conflicts with the Agency's Stability Guidance and ICH proposals. I believe our suggested statement is appropriate for the following reasons:

1) Stability studies were conducted at 25°C/60%RH. No data was provided from samples of the drug products stored at 30°C.

2) The CDER Chemistry, Manufacturing and Controls Coordinating Committee (CMC CC) has taken issue with the ICH proposal. The CMC CC's opinion was described in a "Preliminary Position Paper" on the subject, dated 9-13-96. The CMC CC position can be illustrated by the following statement, taken from the "Position Paper":

Stability studies done under the ICH conditions of 25°C/60% RH can not support continuous, long-term storage of a product at 30°C. Thus, statements like "store below 30°C", "store up to 30°C," or "store between 15 and 30°C", are no longer appropriate by themselves.

There is no new official Agency position on this subject. (The Stability Guidance is out for comment and has not yet been approved.)

3) Temperature related stability problems are well known for Levothyroxine Sodium ; therefore, storage at 30°C should be discouraged.

4) Our suggested storage statement has been discussed with Robert Seevers (Chairman of the Stability Committee), John Gibbs (Div. Dir. for DNDC II), and Yuan-Yuan Chiu (Office Dir. of ONDC); and they all agree that our suggested storage statement is appropriate.

Sheldon Markofsky
(Acting team Leader for Duu-Gong Wu)