CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: 75-256

ADMINISTRATIVE

Meeting Minutes

Date: February 9, 1998

Time: 0930 H

ANDA #: 75-256

Firm: Duramed

Drug: Desogestrel and Ethinyl Estradiol Tablets, 0.15 mg/0.03 mg

Participants:		
	Doug Sporn	Director, OGD
	Gordon Johnston	Dept. Director, OGD
	Jerry Phillips	Director, DLPS, OGD
	Peter Rickman	Chief, RSB, DLPS, OGD
	Gregg Davis	CSO, OGD

Objective:

To discuss the filing issues surrounding ANDA 75-256, Duramed's Desogestrel and Ethinyl Estradiol Tablets, 0.15 mg/0.03 mg and to determine a course of action for accepting this application for filing with a fasting bioequivalence study completed against the old reference listed drug (Desogen).

Background:

* OGD received ANDA 75-256 on November 20, 1997
* ANDA 75-256 was refused to file on January 16, 1998 citing the incorrect reference listed drug
* OGD received an amendment in response to the refuse to file letter on February 9, 1998
* OGD initiated a telecon on February 11, 1998 requesting additional information

Pertinent Facts:

* Duramed started generic development of their proposed drug product in October 1995

* Duramed contracted their definitive biostudy in July 1996

* 15th Edition(1995) Orange Book lists Desogen as RLD

* 16th Edition(1996) Orange Book has no RLD

* 16th Edition(1996), C.S. 8(August) lists Ortho-Cept as RLD

* R.W. Johnson completed a comparative biostudy between their product, Ortho-Cept and Organon's product, Desogen and was found to be bioequivalent

* Duramed also completed a biostudy comparing their proposed drug product with Organon's Desogen

Agenda Item 1: Discuss acceptability of biostudy on old RLD

* It was decided that since both R.W. Johnson's and Duramed's product were both tested against Desogen and were both found to be bioequivalent to Desogen, the biostudy from Duramed would be valid for an AB rating against Ortho-Cept. Basically, if a=b and a=c, then b=c.

* It was also decided that Reg. Support would answer DBE's concern about the study being done on a drug other than the current RLD.

Agenda Item 2: Discuss the regulatory requirements for filing

* It was decided that to accept this application for filing today, the firm would have to satisfy the current RLD requirements. Therefore, Duramed would have to supply new 505(j) info reflecting the correct RLD (Ortho-Cept).

* The firm should be called and asked to submit :

    * a new basis for ANDA submission

    * new patent and exclusivity info

    * a new comparison between the proposed drug product and new RLD

    * a new inactive ingredient comparison

    * a new environmental impact statement

* It was also decided that to justify the Office's position for filing this application, we would like to see a scientific tie between Duramed's product and the current RLD. Reg. Support will ask Duramed to supply a comparative *in vitro* dissolution study between their product and Ortho-Cept.

Action Item 1:

* Initiate a telecon with John Rapoza and ask him to submit the information detailed above including the comparative *in vitro* dissolution data.

TELEPHONE MEMO

To: Ken Phelps
(513) 458-7325

REF # ANDA 75-256

From: Lizzie Sanchez
Shriniwas Nerurkar
Nhan Tran
Pradeep Sathe

Date: September 1, 1998

Subject: **Desogestrel/Ethinyl Estradiol Tablets**

Requested by: Ken Phelps

Mr. Phelps requested guidance on the dissolution method for this product recommended in a deficiency letter dated August 7, 1998. The firm has difficulty conducting dissolution testing in the recommended media (water containing 0.05% SLS). The percentage of desogestrel dissolved in the media is low and variable.

There is information available to the agency that indicates that this method should work for this product. Since there is difficulty with this method, the firm was advised to submit data using 0.1% and 0.3% SLS, using the paddle at two different speeds, 50 and 75 rpm. The firm was asked to fax this information followed by a hard copy. Label Bioequivalence Telephone Amendment. A decision on the appropriate method will be made after the data is reviewed.

RECORD OF TELEPHONE CONVERSATION

DATE: 6-29-99

PRODUCT NAME: Desogestrel/Ethinyl Estradiol Tablets

ANDA NUMBER: 75-256

FIRM NAME: Duramed Pharmaceutical

NAME AND TITLE OF PERSON WITH WHOM CONVERSATION WAS HELD: Bill Stoltman/Annette Arlinhaus

PARTICIPANT(S) TELEPHONE: 513-731-9900

MINUTES OF CONVERSATION:

Telecon:
Denise Huie and M. Shaikh called John Rapoza in order to discuss the stability protocol cited on page 17 of April 17, 1999 amendment. Instead of talking to John Rapoza, telecon was held to Bill Stoltman/Annette Arlinhaus. Shaikh told them that they cannot establish stability protocol based on the draft stability Guidance dated June 1998 to have a reduced stability testing. They need to establish their stability protocol based on the current CDER Stability Guidelines at this stage of the ANDA. They can file a supplement for reduced stability testing when have additional stability data for production lot. They can file a telephone amendment to my attention.

Shaikh gave them the fax number.

End of Conversation.

NAME OF OGD REPRESENTATIVE: Denise Huie/M. Shaikh 6/29/99.

SIGNATURE OF OGD REPRESENTATIVE:

6/29/99

DIVISION/BRANCH: I/II

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RECORD OF TELEPHONE CONVERSATION

DATE: 7-6-99

PRODUCT NAME: Desogestrel/Ethinyl Estradiol Tablets

ANDA NUMBER: 75-256

FIRM NAME: Duramed Pharmaceutical

NAME AND TITLE OF PERSON WITH WHOM CONVERSATION WAS HELD: Bill Stoltman

PARTICIPANT(S) TELEPHONE: 513-731-9900

MINUTES OF CONVERSATION:

Telecon:
M. Shaikh called John Rapoza or Annette Arlinghaus or Bill Stoltman in order to receive revised release and stability specifications reflecting dissolution specification based on the bio letter issued to the firm in May 1999. M. Shaikh talked to Bill Stoltman. Shaikh told him to submit revised release and stability specifications as a telephone amendment. They can file a telephone amendment to my attention. He agreed to do so.

End of Conversation.

NAME OF OGD REPRESENTATIVE: M. Shaikh

SIGNATURE OF OGD REPRESENTATIVE: /S/ 7/6/99

DIVISION/BRANCH: I/II

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APPROVAL SUMMARY PACKAGE

ANDA NUMBER: 75-256

FIRM: Duramed Pharmaceuticals, Inc.

DOSAGE FORM: Tablet

STRENGTHS: 0.15 mg/0.03 mg

DRUG: Desogestrel and Ethinyl Estradiol Tablets; and placebo

CGMP STATEMENT/EIR UPDATED STATUS:
EER status for all facilities listed in Section # 33 of CR # 3 of this ANDA is Acceptable as of 3-17-99 by J.D. Ambrogia.

BIO STUDY:
Acceptable as of sign off done on 5-17-99.

METHODS VALIDATION - (DESCRIPTION OF DOSAGE FORM SAME AS FIRM'S):
MV is required for the drug product. MV is being submitted concurrent to this review.

STABILITY - ARE CONTAINERS USED IN STUDY IDENTICAL TO THOSE IN CONTAINER SECTION?
Containers used in the stability studies are identical to those listed in container section.

LABELING:
FPL: Acceptable per review completed by T. Watkins on 5-24-99.

STERILIZATION VALIDATION (IF APPLICABLE):
N/A

SIZE OF BIO BATCH - (FIRM'S SOURCE OF NDS O.K.?):
Desogestrel and Ethinyl Estradiol Tablets (used for in-vivo bio studies and in-vitro dissolution studies): Lot # C-0024 (Size: Tablets).

Present status of Referenced DMFs:

is adequate per last review conducted by this reviewer on 6-28-99.

is adequate per last review conducted by this reviewer on 3-2-99.

SIZE OF STABILITY BATCHES - (IF DIFFERENT FROM BIO BATCH WERE THEY MANUFACTURED VIA SAME PROCESS?)

Bio/stability Batches:

Desogestrel and Ethinyl Estradiol Tablets: Lot # C-0027 (Size: Tablets).

Duramed also manufactured second stability batch (lot # S-0041).

Duramed manufactured a batch of placebo tablets (lot # S-0027).

PROPOSED PRODUCTION BATCH - MANUFACTURING PROCESS THE SAME AS BIO/STABILITY?

Production batch sizes post-approval to this ANDA are: Tablets for active tablets and ablets for placebo tablets.

Manufacturing process for intended production size batch is same as used for the bio/stability batches.

Mujahid L. Shaikh
Review Chemist
Division of Chemistry I
OGD/CDER
6-30-99
Mike Smela\TM\

/S/ 7/12/99

/S/ 7/12/99

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