



~~Sealed~~

IN THE UNITED STATES DISTRICT COURT  
SOUTHERN DISTRICT OF FLORIDA  
MIAMI DIVISION

FILED BY: [Signature]  
02 OCT -8 PM 12:26  
CLERK, U.S. DISTRICT COURT  
S.D. OF FL. - MIAMI

Case No. 00-7823 -CIV-HIGHSMITH/GARBER

ABBOTT LABORATORIES,  
an Illinois Corporation,  
Plaintiff,

vs.

ANDRX CORPORATION, a Florida corporation,  
ANDRX PHARMACEUTICALS, INC., a Florida  
Corporation, and ANDRX PHARMACEUTICALS,  
L.L.C., a Virginia limited liability company,  
Defendants.

Unsealed 12/04/03

**FILED UNDER SEAL.**

**JOINT STATUS REPORT AND MOTION TO EXTEND STAY**

Pursuant to the Court's January 8, 2002, Order staying the above captioned litigation, Plaintiff Abbott Laboratories ("Abbott") and Defendants Andrx Corporation, Andrx Pharmaceuticals, Inc. and Andrx Pharmaceuticals, LLC (collectively, "Andrx"), by their respective counsel, jointly submit the following status report detailing the current posture of this litigation and move this Court to extend the stay for four (4) months until May 8, 2003.

**Background**

1. In December 1999, Andrx filed an Abbreviated New Drug Application ("ANDA") with the Food and Drug Administration ("FDA") requesting permission to sell a generic version of DEPAKOTE<sup>®</sup> (divalproex sodium). The branded drug DEPAKOTE<sup>®</sup> is sold by Abbott.

2. Subsequently, Abbott filed this action pursuant to the federal Hatch-Waxman Act, alleging that the product described in Andrx's ANDA infringed United States Patent Nos. 4,988,731 and 5,212,326.

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3. On January 24, 2001, the FDA notified Andrx that it was suspending any further review of Andrx's ANDA because the product described in the ANDA did not meet the statutory requirements for an ANDA.

4. Thereafter, Andrx began a series of communications with the FDA in an attempt to have review of the ANDA reinstated.

5. On January 2, 2002, the parties jointly moved for a stay because the correspondence with the FDA was taking longer than expected. By Order dated January 8, 2002, the joint motion for a stay was granted. The Order stayed this action until January 8, 2003. *See Exhibit A.* In addition, the order extended the statutory stay on FDA approval of the ANDA until the same date.

6. On July 18, 2002, the FDA finally rejected Andrx's ANDA because the active ingredient in Andrx's proposed generic product was not identical to the active ingredient in DEPAKOTE®. *See Exhibit B.*

#### Status

7. Since the final rejection of the ANDA, Andrx has contacted the FDA requesting permission to convert the rejected ANDA into a New Drug Application ("NDA"). *See Exhibit C.*

8. Andrx has been informed that the FDA will meet with Andrx representatives on November 7, 2002 to discuss the conversion of the rejected ANDA into an NDA. Abbott and Andrx respectfully request that the Court extend the current stay until for four (4) months until May 8, 2003 and allow the parties to file a subsequent joint status report on or before March 18, 2003. The subsequent status report will advise the Court whether the ANDA will be converted into an NDA or if this entire matter can be dismissed.

9. The parties agree that neither of them would be prejudiced by the proposed stay of the litigation or extension of the stay on FDA approval of the ANDA. Abbott expressly reserves its right to claim at a later time that, based on facts and circumstances existing now or in the future,

the statutory stay of FDA approval of the ANDA should be lengthened beyond the time period agreed to by the parties in this Joint Motion.

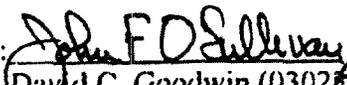
WHEREFORE, Plaintiff Abbott Laboratories and Defendants Andrx Corporation, Andrx Pharmaceuticals, Inc. and Andrx Pharmaceuticals, LLC respectfully request that this Court enter an Order:

- (a) Extending the current stay of this litigation for four (4) months until May 8, 2003;
- (b) Extending the statutory stay on FDA approval of the ANDA until the date coterminous with the stay of the litigation; and
- (c) Directing the parties to submit a joint status report not later than March 18, 2003.

Dated: October 8, 2002

ABBOTT LABORATORIES

By:

  
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John F. O'Sullivan (143154)  
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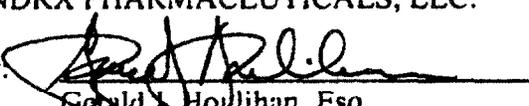
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ANDRX CORPORATION  
ANDRX PHARMACEUTICALS, INC.  
ANDRX PHARMACEUTICALS, LLC.

By:

  
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UNITED STATES DISTRICT COURT  
SOUTHERN DISTRICT OF FLORIDA

Case No. 00-6520-CIV-HIGHSMITH

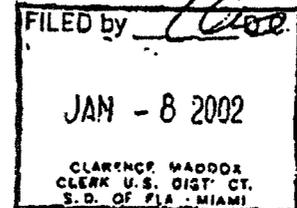
ABBOTT LABORATORIES,

Plaintiff,

v.

ANDRX CORPORATION, a Florida  
corporation, ANDRX PHARMACEUTICALS,  
INC., a Florida corporation, and  
ANDRX PHARMACEUTICALS, L.L.C., a  
Virginia limited liability company,

Defendants.



ORDER

THIS CAUSE is before the Court upon (1) the parties' Joint Motion for Stay and (2) Plaintiff's Motion to Seal Joint Motion to Stay. The Joint Motion to Stay was filed under seal. THE COURT has considered the motions and the pertinent portions of the records, and being otherwise fully advised in the premises, it is ORDERED AND ADJUDGED that:

(1) Plaintiff's motion to seal joint motion to stay is GRANTED. The parties' joint motion for stay and its accompanying exhibits shall remain under seal;

(2) The parties' joint motion for stay is GRANTED. This litigation shall be stayed for a period of twelve (12) months from the date of this order;

UNITED STATES DISTRICT COURT  
SOUTHERN DISTRICT OF FLORIDA

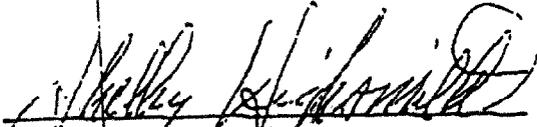
(3) The statutory stay on FDA approval of the ANDA shall be extended to a date coterminous with the stay of the litigation;

(4) This case is hereby REMOVED from the trial calendar;

(5) The parties shall submit a joint status report detailing the posture of this litigation within nine (9) months of the date of this order; and

(6) To the extent that either of the motions seek a status conference, such request is DENIED.

DONE AND ORDERED in Chambers at Miami, Florida, this 8<sup>th</sup>  
day of January, 2002.

  
SHELBY HIGHSMITH  
UNITED STATES DISTRICT JUDGE

cc: John F. O'Sullivan, Esq.  
Eric D. Isicoff, Esq.  
James V. Costigan, Esq.  
Gerald J. Houlihan

EXHIBIT B

EXHIBIT B



ANDA 75-770

Food and Drug Administration  
Rockville MD 20857

Andrx Pharmaceuticals, Inc.  
Attention: Diane Servello  
4955 Orange Drive  
Fort Lauderdale, FL 33314

JUL 18 2002

Reference Number: OGD # 01-375

Dear Ms. Servello:

This letter is in reference to your abbreviated new drug application (ANDA) dated December 28, 1999, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act (Act) for Divalproex Sodium Delayed-release Tablets, 125 mg, 250 mg, and 500 mg. This letter also references the deficiency letter dated January 24, 2001, in which you were informed that your application cannot be approved under the Act because the active ingredient in your finished dosage form is not the same as the active ingredient in the reference listed drug (RLD) in NDA 18-723 Depakote® (Divalproex Sodium) Delayed-release Tablets held by Abbott Laboratories Inc. In addition, we also reference your correspondence and meeting requests dated March 8, 2001, May 2, 2001, and June 20, 2001.

In response to your correspondence, a teleconference was held between representatives of OGD and Andrx on July 26, 2001. During this teleconference, Andrx was informed that its meeting request was denied. OGD also informed Andrx during the teleconference that the ANDA cannot be approved under Section 505(j) of the Act because the active ingredient in the proposed product, i.e., valproate sodium, as determined by OGD during the ANDA review is not the same as the active ingredient in the RLD, i.e., divalproex sodium. This written response serves to reiterate that conclusion.

One of the basic requirements under Section 505(j) of the Act is that the ANDA contain information to show that the active ingredient of the proposed drug product is the same as the active ingredient in the RLD. See Section 505(j)(2)(A)(ii)(I) of the Act. In addition, pursuant to Section 505(j)(4)(C)(i) of the Act, FDA cannot approve the Andrx ANDA because the information submitted in the application is insufficient to show that the active ingredient in the proposed product is the same as that of the RLD. In the preamble to *Abbreviated New Drug Application Regulations: Proposed Rule*, the FDA discussed the requirement that information in the ANDA demonstrate that the active ingredient in the proposed product is the same as that in the RLD:

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ANDA 75-770  
Divalproex Sodium Delayed-release Tablets  
Andrx Pharmaceuticals, Inc.

"The agency interprets the requirement that the active ingredients in the proposed product be the same as those of the listed drug to mean that the active ingredients must be identical. For example, if the proposed drug product contained a different salt or ester of the active ingredient in the listed drug, the active ingredient would not be identical to the active ingredient in the listed drug, and could not, therefore be approved in an ANDA. Active ingredient in this context means the active ingredient in the finished drug product prior to its administration."

54 FR 28872, 28881 ( July 10, 1988)(emphasis added).

You cite the definition of active ingredient in 21 CFR Section 210.3(7) and emphasize the portion of the definition that the term active ingredient "includes those components that may undergo chemical change in the manufacture of the drug product and are present in the drug product in a modified form intended to furnish the specified activity or effect." This is a correct definition of active ingredient; however, in the context of ANDA approvals, there is the requirement that the active ingredient in the finished dosage form of the proposed drug product submitted in an ANDA must be the same as the active ingredient in the RLD. So, for example, if your manufacturing process started out with the active ingredient valproate sodium and through the manufacturing process this active ingredient was converted to divalproex sodium, this would be acceptable, because the active ingredient in the finished dosage form would be the same as the RLD. However, the converse is not true for an ANDA.

Andrx's ANDA 75-770 was found to be deficient and not approvable under 505(j) of the Act because the information submitted in the application was insufficient to show that the active ingredient is the same as the RLD pursuant to 21 CFR 314.127(a)(3)(i) and Section 505(j)(4)(C)(i) of the Act. This conclusion was based on our determination that the active ingredient of the drug product described in the Andrx ANDA exists in the finished drug product as valproate sodium. Andrx admits in its June 20, 2001, letter that its drug product does not contain divalproex sodium and that it contains valproate sodium. Depakote® contains divalproex sodium. Therefore, your product does not contain the same active ingredient as Depakote®

The information provided in your ANDA has failed to demonstrate that your product is the "same as" the RLD according to the Act and the regulations governing the approval of ANDAs. As you were previously informed during our telephone conversation, we do not believe that a meeting is warranted to discuss this matter further. During the teleconference, it was also suggested that if Andrx wishes to pursue approval of this product, it should contact the Division of Neuropharmacological Drug Products at (301) 594-2850 to discuss the possibility of submitting this application under Section 505(b) of the Act. Please note that a drug product containing valproate sodium will not be rated therapeutically equivalent to a drug product containing divalproex sodium, since they will not contain the same active ingredient. See *Approved Drug Products with Therapeutic Equivalence Evaluations (Orange Book)*, Section 1.2.

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ANDA 75-770  
Divalproex Sodium Delayed-release Tablets  
Andrx Pharmaceuticals, Inc.

If you have any questions regarding this issue, please call Ms. Cecelia Parise, R.Ph., Regulatory Policy Advisor to the Director, at (301) 827-5845. In future correspondence regarding this issue, please refer to the above OGD control number and include a copy of this letter.

Sincerely yours,



Gary J. Buehler  
Director  
Office of Generic Drugs  
Center for Drug Evaluation and Research

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**EXHIBIT C**

EXHIBIT C



August 29, 2002

Russell G. Katz, M.D., Director  
Food and Drug Administration  
Division of Neuropharmacological  
Drug Products, HFD-120  
5600 Fishers Lane, WOCII/Rm. 4037.  
Rockville, Maryland 20857

Subject: Proposed 505b2 Application

Dear Dr. Katz,

We are writing this letter to the Division of Neuropharmacological Drug Products at the suggestion of the Office of Generic Drugs. The OGD rejected our ANDA for Depakote because the active ingredient, sodium valproate, is different from the active ingredient of Depakote (divalproex sodium). In divalproex sodium, the ratio of sodium to valproate to valproic acid is 1:1:1; in sodium valproate, the ratio is 1:1:0. In a recent letter to us (Attachment 1), the OGD suggested that our product might be suitable for review as a 505b2 application. For your convenience we attach a brief summary of information regarding our proposed application.

The starting material for our product is divalproex sodium. In the course of manufacture of the drug product this starting material is converted to sodium valproate via neutralization with sodium hydroxide. Please see Attachment 2 for a summary of the drug product manufacturing procedure which is the same for all doses. The resulting drug product is bioequivalent to Depakote under both fed and fasted conditions. Please see Attachment 3 for a summary of bioavailability results.

We have the following questions for the Division based on the assumption that FDA will find the above summaries accurate:

1. We assume you agree with the OGD that the active ingredient in this product is sodium valproate not divalproex sodium. Is this correct?
2. If we were to file an application based on the data summarized above, would it be approvable under Section 505b2?
3. If approved would the product be AB rated to Depakote?

Andrx Labs, Inc.

401 Hackensack Avenue, Hackensack, NJ 07601 • Phone: 201-888-1883 • Fax: 201-888-1893

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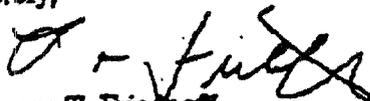
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4. If not AB rated, would the label contain the statement that the product is bioequivalent to Depakots?
5. It is our intention to submit the bioavailability data referred to above along with a Chemistry and Manufacturing data package containing stability data on 2 lots of 500-mg tablets and 1 lot each of 250-mg and 125-mg tablets for a minimum of 24 months. Is this an adequate package or are additional data (such as summaries of published data and data from SBOAs) required for approval?
6. It is our understanding that this product would not qualify for new chemical entity exclusivity. Is this understanding correct? If so, would the product qualify for new dosage form exclusivity?
7. Are there any other issues we should be aware of?

If convenient for the Division, Andrx would be pleased to discuss the Division's responses to these questions either by teleconference or in a meeting in Rockville. To make arrangements for a meeting, or to request additional information, please contact Nicholas J. Farina, Ph.D., Vice-President, Regulatory Affairs, Andrx Labs, at 610-428-2417.

Please be advised that material and data contained in this submission are confidential. The protection of such confidential material is hereby claimed under applicable provisions of 18 U.S.C., Section 1905 or 21 U.S.C., Section 331 (j).

Sincerely,



Lawrence T. Friedhoff  
Executive Vice President of Research and Development

Enclosures

AN  
A  
ANDRX COMPANY

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Attachment 1



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

ANDA 73-770

Food and Drug Administration  
Rockville, MD 20857

Andrx Pharmaceuticals, Inc.  
Attention: Diane Serralle  
4935 Orange Drive  
Fort Lauderdale, FL 33314

JUL 18 2002

Reference Number: OGD # 01-375

Dear Ms. Serralle:

This letter is in reference to your abbreviated new drug application (ANDA) dated December 28, 1999, submitted pursuant to Section 305(d) of the Federal Food, Drug, and Cosmetic Act (Act) for Divalproex Sodium Delayed-release Tablets 125 mg, 250 mg, and 500 mg. This letter also references the advisory letter dated January 14, 2001, in which you were informed that your application cannot be approved under the Act because the active ingredient in your finished dosage form is not the same as the active ingredient in the reference listed drug (RLD) in NDA 18-723 Depacon® (Divalproex Sodium) Delayed-release Tablets held by Abbott Laboratories Inc. In addition, we also reference your correspondence and meeting requests dated March 1, 2001, May 2, 2001, and June 28, 2001.

In response to your correspondence, a teleconference was held between representatives of OGD and Andrx on July 24, 2001. During this teleconference, Andrx was informed that its meeting request was denied. OGD also informed Andrx during the teleconference that the ANDA cannot be approved under Section 305(d) of the Act because the active ingredient in the proposed product, i.e., valproic acid, is determined by OGD during the ANDA review to not be the same as the active ingredient in the RLD, i.e., divalproex sodium. This written response serves to minimize that conclusion.

One of the basic requirements under Section 305(d) of the Act is that the ANDA contain information to show that the active ingredient of the proposed drug product is the same as the active ingredient in the RLD. See Section 305(d)(1)(A)(i)(II) of the Act. In addition, pursuant to Section 305(d)(1)(C)(i) of the Act, FDA cannot approve the Andrx ANDA because the information submitted in the application is insufficient to show that the active ingredient in the proposed product is the same as that of the RLD. In the preamble to Abbreviated New Drug Application Regulations: Proposed Rule, the FDA discussed the requirement that information in the ANDA demonstrate that the active ingredient in the proposed product is the same as that in the RLD:

ANDA 75-770  
Divalproex Sodium Delayed-Release Tablets  
Astra Pharmaceutical, Inc.

"The agency interprets the requirement that the active ingredients in the proposed product be the same as those of the listed drug to mean that the active ingredients must be identical. For example, if the proposed drug product contained a different salt or ester of the active ingredient in the listed drug, the active ingredient would not be identical to the active ingredient in the listed drug, and could not, therefore, be approved in an ANDA. Active ingredients in this context means the active ingredients in the finished drug product prior to its administration."

34 FR 23872, 23881 (July 10, 1969) (emphasis added).

You cite the definition of active ingredient in 21 CFR Section 210.3(f) and emphasize the portion of the definition that the term active ingredient "includes those components that may undergo chemical change in the manufacture of the drug product and are present in the drug product in a modified form intended to furnish the specified activity or effect." This is a correct definition of active ingredient; however, in the context of ANDA approval, there is the requirement that the active ingredient in the finished dosage form of the proposed drug product submitted in an ANDA must be the same as the active ingredient in the RLD. So, for example, if your manufacturing process started out with the active ingredient valproic sodium and through the manufacturing process this active ingredient was converted to divalproex sodium, this would be acceptable, because the active ingredient in the finished dosage form would be the same as the RLD. However, the converse is not true for an ANDA.

Astra's ANDA 75-770 was found to be deficient and not approvable under 505(b) of the Act because the information submitted in the application was insufficient to show that the active ingredient is the same as the RLD pursuant to 21 CFR 214.127(a)(3)(5) and Section 505(b)(4)(C)(i) of the Act. This conclusion was based on our determination that the active ingredient of the drug product described in the Astra ANDA differs in the finished drug product as valproate sodium. Astra admits in its June 20, 2001, letter that its drug product does not contain divalproex sodium and that it contains valproic sodium. Divalproex contains divalproex sodium. Therefore, your product does not contain the same active ingredient as Depakote®.

The information provided in your ANDA has failed to demonstrate that your product is the "same as" the RLD according to the Act and the regulations governing the approval of ANDAs. As you were previously informed during our telephone conversation, we do not believe that a meeting is warranted to discuss this matter further. During the teleconference, it was also suggested that if Astra wishes to pursue approval of this product, it should contact the Division of Neuropharmacological Drug Products at (202) 594-2858 to discuss the possibility of submitting this application under Section 505(f) of the Act. Please note that a drug product containing valproic sodium will not be considered therapeutically equivalent to a drug product containing divalproex sodium, since they will not contain the same active ingredient. See *Approved Drug Products with Therapeutic Equivalents Evaluations* (Orange Book), Section 1.2.

ANDA 72-772  
EVALPAR 500mg Delayed-release Tablets  
Astra Pharmaceutical, Inc.

If you have any questions regarding this issue, please call Ms. Cecelia Parris, J.P.H., Regulatory Policy Advisor to the Director, at (301) 827-5846. In future correspondence regarding this issue, please refer to the above OGD control number and include a copy of this letter.

Sincerely yours,



Gary I. Durbler  
Director  
Office of Generic Drugs  
Center for Drug Evaluation and Research

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Attachment 2

Manufacturing Process for  
Divalproex Sodium Delayed-release Tablets,  
500 mg Valproic Acid Activity

