CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

50-780

ADMINISTRATIVE DOCUMENTS

Patent Information
On Any Patent Which Claims The Drug

A patent search was performed to locate any drug substance, drug product or method of use patents regarding cefuroxime. This search revealed ten patents regarding cefuroxime, U.S. Patent No. 3,974,153, 4,267,320, 4,562,181, 4,865,851, 4,897,270, 4,602,012, 4,446,317, 4,128,715, 4,277,601, and 5,677,443. The 4,267,320, 4,562,181, 4,865,851, 4,897,270, 4,602,012, 4,446,317, 4,128,715, 4,277,601, and 5,677,443 patents are not infringed. The 3,974,153 expired on August 10, 1993.

Please refer to the November 2, 1999, letter from Christie, Parker & Hale, LLP Intellectual Property Lawyers that follows. This letter contains details of the patent search, includes a copy of the 3,974,153 cefuroxime patent referenced above, and supports this conclusion.

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JAMES B. CHRISTIE (1904-1959)
ROBERT L. PARKER (1920-1980)

November 2, 1999

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OUR REFERENCE
K163:90.2-19

By Facsimile and Confirmation by U.S. Mail
660-2200 20 pages

CONFIRMATION

Mr. John D'Angelo
V.P. Regulatory Affairs
B. BRAUN MEDICAL, INC.
2525 McGaw Avenue
Irvine, California 92614-4895

Re: Patent Information required under 21 CFR § 314.50 for Cefuroxime

Dear John:

As discussed, you will be filing a New Drug Application (NDA) for cefuroxime and will be required to identify in the application any patents that claim the cefuroxime drug product or methods of using cefuroxime. As is required by statute, for each such patent, you will be required to provide the patent number and to certify that, in your opinion, and to the best of your knowledge, one of the following circumstances:

1. That the patent information has not been submitted to the FDA; or

2. That the patent has expired; or

3. The date on which the patent will expire; or

4. The patent is invalid, or unenforceable or not infringed.

In my discussions with Rebecca Stolarick, she advised that the cefuroxime drug will be used by itself, i.e., there will be no additives or other ingredients associated therewith, except that it will be mixed with a diluent at the time of delivery. Thus, in this case the cefuroxime drug is the same as the cefuroxime drug product.

You asked that we conduct a search for patents which may cover cefuroxime to provide you with information so that you may comply with the FDA reporting requirement.

In view of the foregoing, we conducted a search for patents on cefuroxime as well as those directed to its method of use. The results of our study are set forth below.

We initially consulted the Patent and Exclusivity Data appendix contained in the U.S. Department of Health and Human Services' Approved Drug Products manual. However, no unexpired patents were listed for cefuroxime.

The original patents for cefuroxime as listed in the Merck Index are U.S. Patent Nos. 3,974,153 and 4,267,320, both assigned to Glaxo Laboratories. The '153 patent claims cefuroxime, as well as salts thereof, and so is relevant to B. Braun's cefuroxime antibiotic as will be used in the Duplex product. However, this patent expired on August 10, 1993, and so should be disclosed in the NDA certification as an expired patent. The '320 patent covers cefuroxime axetil, an ester of cefuroxime. This patent has been granted a term extension to May 12, 2000. There is no need to disclose this patent, however, as it is limited to cefuroxime esters, useful as orally administrable antibiotics, and it is our understanding that the Duplex product will not include such esters.

We performed a family patent search for the '153 patent and identified 16 additional patents, all assigned to Glaxo Laboratories. We have reviewed all of these and have determined that none of them are relevant to the B. Braun Duplex cefuroxime product.

We next consulted the Glaxo Laboratories web page. No patents are listed for the Zinacef® (cefuroxime) product, while four patents (U.S. Patent Nos. 4,267,320, 4,562,181, 4,865,851 and 4,897,270) are listed for the Ceftin® (cefuroxime axetil) product. Again, patents covering cefuroxime axetil are not relevant to the B. Braun Duplex cefuroxime product and need not be disclosed in the NDA.

Finally, we conducted a search of both the U.S. Patent and Trademark Office database and the Lexis database using the search terms "carbamoyloxymethyl w/10 methoxyiminoacetamido" and identified 74 potentially relevant patents. These have all been reviewed. Of particular interest are U.S. Patent Nos. 4,602,012, 4,446,317, 4,128,715, and 4,277,601, all assigned to Glaxo Laboratories. The '012 and '317 patents both claim cefuroxime esters, while the '715 patent claims a lysine salt of cefuroxime. As these do not apply to the B. Braun Duplex cefuroxime product, they need not be disclosed in the NDA. The '601 patent discloses a process for the preparation of the sodium salt of cefuroxime. Process patents, however, need not be disclosed in the NDA. We also identified an additional patent claiming cefuroxime axetil, U.S. Pat. No. 5,677,443, assigned to ACS Dobfar. Again, this cefuroxime ester is not relevant to the B. Braun Duplex product.

Given that the cefuroxime drug that will be used by B. Braun is an antibiotic and that the original '153 patent discloses the use of cefuroxime as a broad-spectrum antibiotic, in our opinion it would not be possible that any U.S. patents claiming the use of cefuroxime as an antibiotic would still be in force.

In summary, the only patent developed by our search which is relevant to the NDA is the '153 patent, which expired long ago. (A copy of the '153 patent is enclosed).

Please contact me if you have any questions regarding this analysis.

Sincerely,

William P. Christie

WPC/CAB/bl
Enclosure: Copy of U.S. Patent No. 3,974,153

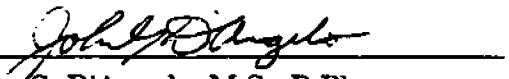
cc: Charles A. Dinardo, Esq.
Hugh M. Morrison, Esq.
Shari Sandberg

BL IRV1030941.1-*-11/2/99 2:50 PM

Patent Certification
With Respect to Any Patent Which Claims the Drug

Reference is made to the Approved Prescription Drug Products with Therapeutic Equivalence Evaluations, 18th Edition and Cumulative Supplements. Cefuroxime for Injection USP and Dextrose Injection USP is not listed in the patent and exclusivity tables. The appropriate patent certification follows:

B. Braun Medical Inc. hereby certifies that in our opinion and to the best of our knowledge and of our patent counsel, there are no patents, active or valid, that claim the drug in this application, Cefuroxime for Injection USP and Dextrose Injection USP or that claim use of Cefuroxime for Injection USP and Dextrose Injection USP have been filed or that such patents have expired.



4/17/00

John G. D'Angelo, M.S., R.Ph.
Corporate Vice President
Regulatory and Medical Affairs

Date

EXCLUSIVITY SUMMARY for NDA # 50-780 **SUPPL #** _____

Trade Name none **Generic Name** Cefuroxime for Injection and Dextrose Injection in the DUPLEX

Applicant Name B Braun Medical Inc. **HFD-** 520 Contain

Approval Date 2/21/01

PART I: IS AN EXCLUSIVITY DETERMINATION NEEDED?

1. An exclusivity determination will be made for all original applications, but only for certain supplements. Complete Parts II and III of this Exclusivity Summary only if you answer "YES" to one or more of the following questions about the submission.

   a) Is it an original NDA? YES/ ✓ / NO /___/

   b) Is it an effectiveness supplement? YES /___/ NO / ✓ /

      If yes, what type(SE1, SE2, etc.)? _____

   c) Did it require the review of clinical data other than to support a safety claim or change in labeling related to safety? (If it required review only of bioavailability or bioequivalence data, answer "NO.")

      YES /___/ NO / ✓ /

      If your answer is "no" because you believe the study is a bioavailability study and, therefore, not eligible for exclusivity, EXPLAIN why it is a bioavailability study, including your reasons for disagreeing with any arguments made by the applicant that the study was not simply a bioavailability study.

      _____

      _____

      If it is a supplement requiring the review of clinical data but it is not an effectiveness supplement, describe the change or claim that is supported by the clinical data:

      _____

      _____

d) Did the applicant request exclusivity?

YES /___/ NO /✓/

If the answer to (d) is "yes," how many years of exclusivity did the applicant request?

_____

_____

e) Has pediatric exclusivity been granted for this Active Moiety?

YES /___/ NO /✓/

IF YOU HAVE ANSWERED "NO" TO ALL OF THE ABOVE QUESTIONS, GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9.

2. Has a product with the same active ingredient(s), dosage form, strength, route of administration, and dosing schedule previously been approved by FDA for the same use? (Rx to OTC) Switches should be answered No - Please indicate as such).

YES /✓/ NO /___/

If yes, NDA # 50-558 Drug Name Ziracef

IF THE ANSWER TO QUESTION 2 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9.

3. Is this drug product or indication a DESI upgrade?

YES /___/ NO /___/

IF THE ANSWER TO QUESTION 3 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9 (even if a study was required for the upgrade).

PART II: FIVE-YEAR EXCLUSIVITY FOR NEW CHEMICAL ENTITIES
(Answer either #1 or #2, as appropriate)

1. Single active ingredient product.

Has FDA previously approved under section 505 of the Act any drug product containing the same active moiety as the drug under consideration? Answer "yes" if the active moiety (including other esterified forms, salts, complexes, chelates or clathrates) has been previously approved, but this particular form of the active moiety, e.g., this particular ester or salt (including salts with hydrogen or coordination bonding) or other non-covalent derivative (such as a complex, chelate, or clathrate) has not been approved. Answer "no" if the compound requires metabolic conversion (other than deesterification of an esterified form of the drug) to produce an already approved active moiety.

YES /___/ NO /___/

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA # _____ _____

NDA # _____ _____

NDA # _____ _____

2. Combination product.

If the product contains more than one active moiety (as defined in Part II, #1), has FDA previously approved an application under section 505 containing any one of the active moieties in the drug product? If, for example, the combination contains one never-before-approved active moiety and one previously approved active moiety, answer "yes." (An active moiety that is marketed under an OTC monograph, but that was never approved under an NDA, is considered not previously approved.)

YES /___/ NO /___/

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA # _____ _____

NDA # _____ _____

NDA # _____ _____

IF THE ANSWER TO QUESTION 1 OR 2 UNDER PART II IS "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9. IF "YES," GO TO PART III.

PART III: <u>THREE-YEAR EXCLUSIVITY FOR NDA'S AND SUPPLEMENTS</u>

To qualify for three years of exclusivity, an application or supplement must contain "reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant." This section should be completed only if the answer to PART II, Question 1 or 2, was "yes."

1. Does the application contain reports of clinical investigations? (The Agency interprets "clinical investigations" to mean investigations conducted on humans other than bioavailability studies.) If the application contains clinical investigations only by virtue of a right of reference to clinical investigations in another application, answer "yes," then skip to question 3(a). If the answer to 3(a) is "yes" for any investigation referred to in another application, do not complete remainder of summary for that investigation.

YES /___/ NO /___/

IF "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9.

2. A clinical investigation is "essential to the approval" if the Agency could not have approved the application or supplement without relying on that investigation. Thus, the investigation is not essential to the approval if 1) no clinical investigation is necessary to support the supplement or application in light of previously approved applications (i.e., information other than clinical trials, such as bioavailability data, would be sufficient to provide a basis

for approval as an ANDA or 505(b)(2) application because of what is already known about a previously approved product), or 2) there are published reports of studies (other than those conducted or sponsored by the applicant) or other publicly available data that independently would have been sufficient to support approval of the application, without reference to the clinical investigation submitted in the application.

For the purposes of this section, studies comparing two products with the same ingredient(s) are considered to be bioavailability studies.

(a) In light of previously approved applications, is a clinical investigation (either conducted by the applicant or available from some other source, including the published literature) necessary to support approval of the application or supplement?

YES /___/ NO /___/

If "no," state the basis for your conclusion that a clinical trial is not necessary for approval **AND GO DIRECTLY TO SIGNATURE BLOCK ON Page 9:**

_____

_____

(b) Did the applicant submit a list of published studies relevant to the safety and effectiveness of this drug product and a statement that the publicly available data would not independently support approval of the application?

YES /___/ NO /___/

(1) If the answer to 2(b) is "yes," do you personally know of any reason to disagree with the applicant's conclusion? If not applicable, answer NO.

YES /___/ NO /___/

If yes, explain: _____

_____

(2) If the answer to 2(b) is "no," are you aware of published studies not conducted or sponsored by the applicant or other publicly available data that could independently demonstrate the safety and effectiveness of this drug product?

YES /___/ NO /___/

If yes, explain: _____

_____

(c) If the answers to (b)(1) and (b)(2) were both "no," identify the clinical investigations submitted in the application that are essential to the approval:

Investigation #1, Study # _____

Investigation #2, Study # _____

Investigation #3, Study # _____

3. In addition to being essential, investigations must be "new" to support exclusivity. The agency interprets "new clinical investigation" to mean an investigation that 1) has not been relied on by the agency to demonstrate the effectiveness of a previously approved drug for any indication and 2) does not duplicate the results of another investigation that was relied on by the agency to demonstrate the effectiveness of a previously approved drug product, i.e., does not redemonstrate something the agency considers to have been demonstrated in an already approved application.

(a) For each investigation identified as "essential to the approval," has the investigation been relied on by the agency to demonstrate the effectiveness of a previously approved drug product? (If the investigation was relied on only to support the safety of a previously approved drug, answer "no.")

Investigation #1 YES /___/ NO /___/

Investigation #2 YES /___/ NO /___/

Investigation #3 YES /___/ NO /___/

If you have answered "yes" for one or more investigations, identify each such investigation and the NDA in which each was relied upon:

NDA # _____ Study # _____
NDA # _____ Study # _____
NDA # _____ Study # _____

(b) For each investigation identified as "essential to the approval," does the investigation duplicate the results of another investigation that was relied on by the agency to support the effectiveness of a previously approved drug product?

Investigation #1 YES /___/ NO /___/

Investigation #2 YES /___/ NO /___/

Investigation #3 YES /___/ NO /___/

If you have answered "yes" for one or more investigations, identify the NDA in which a similar investigation was relied on:

NDA # _____ Study # _____

NDA # _____ Study # _____

NDA # _____ Study # _____

(c) If the answers to 3(a) and 3(b) are no, identify each "new" investigation in the application or supplement that is essential to the approval (i.e., the investigations listed in #2(c), less any that are not "new"):

Investigation #__, Study # _____

Investigation #__, Study # _____

Investigation #__, Study # _____

4. To be eligible for exclusivity, a new investigation that is essential to approval must also have been conducted or sponsored by the applicant. An investigation was "conducted or sponsored by" the applicant if, before or during the conduct of the investigation, 1) the applicant was the sponsor of the IND named in the form FDA 1571 filed with the Agency, or 2) the applicant (or its predecessor in interest) provided substantial support for the study. Ordinarily, substantial support will mean providing 50 percent or more of the cost of the study.

(a) For each investigation identified in response to question 3(c): if the investigation was carried out under an IND, was the applicant identified on the FDA 1571 as the sponsor?

Investigation #1	
IND # _____ YES /___/	NO /___/ Explain: _____
	_____
	_____
Investigation #2	
IND # _____ YES /___/	NO /___/ Explain: _____
	_____
	_____

(b) For each investigation not carried out under an IND or for which the applicant was not identified as the sponsor, did the applicant certify that it or the applicant's predecessor in interest provided substantial support for the study?

Investigation #1	
YES /___/ Explain _____	NO /___/ Explain _____
_____	_____
_____	_____
Investigation #2	
YES /___/ Explain _____	NO /___/ Explain _____
_____	_____
_____	_____

(c) Notwithstanding an answer of "yes" to (a) or (b), are there other reasons to believe that the applicant should not be credited with having "conducted or sponsored" the study? (Purchased studies may not be used as the basis for exclusivity. However, if all rights to the drug are purchased (not just studies on the drug), the applicant may be considered to have sponsored or conducted the studies sponsored or conducted by its predecessor in interest.)

YES /___/ NO /___/

If yes, explain: _____

_____

_____

/S/
Signature of Preparer
Title: Regulatory Health Project Manager

2/21/01
Date

/S/
Signature of Office of Division Director

7/31/01
Date

cc:
Archival NDA
HFD-520/Division File
HFD-520/RPM/B. Duvall-Miller
HFD-093/Mary Ann Holovac
HFD-104/PEDS/T.Crescenzi

Form OGD-011347
Revised 8/7/95; edited 8/8/95; revised 8/25/98, edited 3/6/00

PEDIATRIC PAGE

(Complete for all original application and all efficacy supplements)

NDA Number: N 050780
Trade Name: DUPLEX CONTAINER(CEFUROXIME/DEXTROSE)1.5
Generic Name: CEFUROXIME/DEXTROSE
Supplement Number: 000 **Supplement Type**: N
Dosage Form:
Regulatory Action: OP **Action Date**: 4/21/00
COMIS Indication: TREATMENT OF SERIOUS INFECTIONS DUE TO SUSCEPTIBLE ORGANISMS

Indication #1: Lower Respiratory Tract Infections
Label Adequacy: Adequate for all pediatric age groups
Formulation Needed: Other
Comments (if any) This product is designed to deliver a 750 mg or 1.5 gram dose of cefuroxime in 50mL of dextrose. Use of this product poses a risk of overdose in pediatric patients who require less than the full adult dose of cefuroxime. Cefuroxime is available in preparations from other sponsors that are appropriate for pediatric use. This product's Pediatric Use Subsection of the label states that it should not be used in pediatric patients who require less than the full adult dose.

Lower Range	Upper Range	Status	Date
45 kg	18 years	Completed	2/21/01

Comments: Usual adult dose range is 750 mg to 1.5 gram every 8 hours and pediatric dose is 50 to 100 mg/kg/day in equally divided doses every 6 to 8 hours. The higher dosage of 100 mg/kg/day (not to exceed maximum adult dosage) should be used for more severe or serious infections.

Indication #2: Urinary Tract Infections
Label Adequacy: Adequate for all pediatric age groups
Formulation Needed: Other
Comments (if any) This product is designed to deliver a 750 mg or 1.5 gram dose of cefuroxime in 50mL of dextrose. Use of this product poses a risk of overdose in pediatric patients who require less than the full adult dose of cefuroxime. Cefuroxime is available in preparations from other sponsors that are appropriate for pediatric use. This product's Pediatric Use Subsection of the label states that it should not be used in pediatric patients who require less than the full adult dose.

Lower Range	Upper Range	Status	Date
45 kg	18 years	Completed	2/21/01

Comments: Usual adult dose range is 750 mg to 1.5 gram every 8 hours and pediatric dose is 50 to 100 mg/kg/day in equally divided doses every 6 to 8 hours. The higher dosage of 100 mg/kg/day (not to exceed maximum adult dosage) should be used for more severe or serious infections.

Indication #3: Skin and Skin Structure Infections
Label Adequacy: Adequate for all pediatric age groups
Formulation Needed: Other

Comments (if any) This product is designed to deliver a 750 mg or 1.5 gram dose of cefuroxime in 50mL of dextrose. Use of this product poses a risk of overdose in pediatric patients who require less than the full adult dose of cefuroxime. Cefuroxime is available in preparations from other sponsors that are appropriate for pediatric use. This product's Pediatric Use Subsection of the label states that it should not be used in pediatric patients who require less than the full adult dose.

Lower Range	Upper Range	Status	Date
45 kg	18 years	Completed	2/21/01

Comments: Usual adult dose range is 750 mg to 1.5 gram every 8 hours and pediatric dose is 50 to 100 mg/kg/day in equally divided doses every 6 to 8 hours. The higher dosage of 100 mg/kg/day (not to exceed maximum adult dosage) should be used for more severe or serious infections.

Indication #4: Septicemia
Label Adequacy: Adequate for all pediatric age groups
Formulation Needed: Other
Comments (if any) This product is designed to deliver a 750 mg or 1.5 gram dose of cefuroxime in 50mL of dextrose. Use of this product poses a risk of overdose in pediatric patients who require less than the full adult dose of cefuroxime. Cefuroxime is available in preparations from other sponsors that are appropriate for pediatric use. This product's Pediatric Use Subsection of the label states that it should not be used in pediatric patients who require less than the full adult dose.

Lower Range	Upper Range	Status	Date
45 kg	18 years	Completed	2/21/01

Comments: Usual adult dose range is 750 mg to 1.5 gram every 8 hours and pediatric dose is 50 to 100 mg/kg/day in equally divided doses every 6 to 8 hours. The higher dosage of 100 mg/kg/day (not to exceed maximum adult dosage) should be used for more severe or serious infections.

Indication #5: Meningitis
Label Adequacy: Adequate for all pediatric age groups
Formulation Needed: Other
Comments (if any) This product is designed to deliver a 750 mg or 1.5 gram dose of cefuroxime in 50mL of dextrose. Use of this product poses a risk of overdose in pediatric patients who require less than the full adult dose of cefuroxime. Cefuroxime is available in preparations from other sponsors that are appropriate for pediatric use. This product's Pediatric Use Subsection of the label states that it should not be used in pediatric patients who require less than the full adult dose.

Lower Range	Upper Range	Status	Date
25 kg	18 years	Completed	2/21/01

Comments: In cases of bacterial meningitis, a larger dose of cefuroxime is recommended. The recommended pediatric dose is 200 to 240 mg/kg/day (not to exceed a total daily dose of 6 grams) in equally divided doses every 8 hours.

Indication #6: Gonorrhea
Label Adequacy: Adequate for all pediatric age groups
Formulation Needed: Other
Comments (if any) This product is designed to deliver a 750 mg or 1.5 gram dose of cefuroxime in 50mL of dextrose. Use of this product poses a risk of overdose in pediatric patients who require less than the full adult dose of cefuroxime. Cefuroxime is available in preparations from other sponsors that are appropriate for pediatric use. This product's Pediatric Use

Subsection of the label states that it should not be used in pediatric patients who require less than the full adult dose.

Lower Range	Upper Range	Status	Date
45 kg	18 years	Completed	2/21/01

Comments: Usual adult dose range is 750 mg to 1.5 gram every 8 hours and pediatric dose is 50 to 100 mg/kg/day in equally divided doses every 6 to 8 hours. The higher dosage of 100 mg/kg/day (not to exceed maximum adult dosage) should be used for more severe or serious infections.

Indication #7: Bone and Joint Infections
Label Adequacy: Adequate for all pediatric age groups
Formulation Needed: Other
Comments (if any) This product is designed to deliver a 750 mg or 1.5 gram dose of cefuroxime in 50mL of dextrose. Use of this product poses a risk of overdose in pediatric patients who require less than the full adult dose of cefuroxime. Cefuroxime is available in preparations from other sponsors that are appropriate for pediatric use. This product's Pediatric Use Subsection of the label states that it should not be used in pediatric patients who require less than the full adult dose.

Lower Range	Upper Range	Status	Date
30 kg	18 years	Completed	2/21/01

Comments: The pediatric dose for bone and joint infections is 150 mg/kg/day (not to exceed the maximum adult dosage) in 3 equally divided doses every 8 hours.

This page was last edited on 2/23/01

/S/ 2/23/01

Signature Date

Debarment Certification

B. Braun Medical Inc. hereby certifies that it did not and will not use in any capacity the services of any person debarred under Section 306 of the Federal Food, Drug, and Cosmetic Act in connection with this application.

John G. D'Angelo, M.S., R.Ph.
Corporate Vice President
Regulatory and Medical Affairs

4/17/00
Date

B|BRAUN

Fax

To	From
Shrikant Pagay	B. Braun Medical Inc. John Spoden
	Fax 949.660.3292
To Fax Number 301.827.2326	Tel 949.660.2379
Pages (Including cover) 2	Date February 16, 2001

Dr. Pagay,

Attached is the correspondence regarding the regulatory specifications for NDA 50-780. I intend on sending this via FedEx to FDA today. If you have any other suggestions for the document, please call me. Otherwise, if it is acceptable, I will send it out at 4:30 pm PST.

Thank you,

John Spoden

MEMORANDUM OF A TELEPHONE CONVERSATION

Date 16-Feb-2001

Between: John Spoden
(949)-660-2379

And: Shrikant Pagay, Ph. D.
Review Chemist, HFD-520

Subject: NDA 50-780 Concurrence on Regulatory Specifications

Please examine the Draft Regulatory Specifications referred as Attachment 2 which will be included in my Review 3 of this NDA. These specifications will be used as regulatory specifications for the commercialized product.

Thank you.

Note: Attachment 2 was faxed to the applicant.

cc: use same distribution as review

4 page(s) have been removed because it contains trade secret and/or confidential information that is not disclosable.

MEMORANDUM

DATE: March 17, 2001

TO: File, NDA 50-780

FROM: Francis R. Pelsor, Pharm.D.
Team Leader
Division of Pharmaceutical Evaluation III
Office of Clinical Pharmacology and Biopharmaceutics

SUBJECT: Clinical Pharmacology/Biopharmaceutics Review
Of Submission Dated 4/21/2000.

The applicant submitted a new drug application for alternative packaging (DUPLEX dual chamber container) of sterile cefuroxime sodium. Sterile cefuroxime sodium products for parenteral administration (ZINACEF, Glaxo) are approved, however, the applicant Braun proposes to market a product containing drug (Cefuroxime For Injection USP) and diluent (Dextrose Injection USP) in separate chambers within the product. At the time of administration the seal between the two chambers is broken and the contents of the chambers are mixed.

The applicant provided no new Clinical Pharmacology/Biopharmaceutics information in the NDA submission. Instead, the applicant requested a waiver for submission of evidence demonstrating in vivo bioavailability or bioequivalence under 21 CFR § 320.22 (b)(1). Since the proposed drug product is 1) a parenteral solution intended solely for administration by injection, and 2) the product contains the same active ingredient in the same concentration as a drug product that is the subject of an approved full NDA, the waiver should be granted.