

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

21-980

ADMINISTRATIVE and CORRESPONDENCE
DOCUMENTS

Department of Health and Human Services
Food and Drug Administration

Form Approved: OMB No. 0910-0513
Expiration Date: 07/31/06
See OMB Statement on Page 3.

**PATENT INFORMATION SUBMITTED WITH THE
FILING OF AN NDA, AMENDMENT, OR SUPPLEMENT**

**For Each Patent That Claims a Drug Substance
(Active Ingredient), Drug Product (Formulation and
Composition) and/or Method of Use**

NDA NUMBER

21-980

NAME OF APPLICANT / NDA HOLDER

Alcon, Inc

The following is provided in accordance with Section 505(b) and (c) of the Federal Food, Drug, and Cosmetic Act.

TRADE NAME (OR PROPOSED TRADE NAME)

FLUORESCITE® Injection

ACTIVE INGREDIENT(S)

fluorescein sodium

STRENGTH(S)

10%

DOSAGE FORM

solution for injection

This patent declaration form is required to be submitted to the Food and Drug Administration (FDA) with an NDA application, amendment, or supplement as required by 21 CFR 314.53 at the address provided in 21 CFR 314.53(d)(4). Within thirty (30) days after approval of an NDA or supplement, or within thirty (30) days of issuance of a new patent, a new patent declaration must be submitted pursuant to 21 CFR 314.53(c)(2)(ii) with all of the required information based on the approved NDA or supplement. The information submitted in the declaration form submitted upon or after approval will be the only information relied upon by FDA for listing a patent in the Orange Book.

For hand-written or typewriter versions (only) of this report: If additional space is required for any narrative answer (i.e., one that does not require a "Yes" or "No" response), please attach an additional page referencing the question number.

will not list patent information if you file an incomplete patent declaration or the patent declaration indicates the patent is not eligible for listing.

For each patent submitted for the pending NDA, amendment, or supplement referenced above, you must submit all the information described below. If you are not submitting any patents for this pending NDA, amendment, or supplement, complete above section and sections 5 and 6.

GENERAL

a. United States Patent Number	b. Issue Date of Patent	c. Expiration Date of Patent
d. Name of Patent Owner	Address (of Patent Owner)	
	City/State	
	ZIP Code	FAX Number (if available)
	Telephone Number	E-Mail Address (if available)
e. Name of agent or representative who resides or maintains a place of business within the United States authorized to receive notice of patent certification under section 505(b)(3) and (j)(2)(B) of the Federal Food, Drug, and Cosmetic Act and 21 CFR 314.52 and 314.95 (if patent owner or NDA applicant/holder does not reside or have a place of business within the United States)	Address (of agent or representative named in 1.e.)	
	City/State	
	ZIP Code	FAX Number (if available)
	Telephone Number	E-Mail Address (if available)
f. Is the patent referenced above a patent that has been submitted previously for the approved NDA or supplement referenced above? <input type="checkbox"/> Yes <input type="checkbox"/> No		
g. If the patent referenced above has been submitted previously for listing, is the expiration date a new expiration date? <input type="checkbox"/> Yes <input type="checkbox"/> No		

For the patent referenced above, provide the following information on the drug substance, drug product and/or method of use that is the subject of the pending NDA, amendment, or supplement.

Drug Substance (Active Ingredient)

- Does the patent claim the drug substance that is the active ingredient in the drug product described in the pending NDA, amendment, or supplement? Yes No
- 2.2 Does the patent claim a drug substance that is a different polymorph of the active ingredient described in the pending NDA, amendment, or supplement? Yes No
- 2.3 If the answer to question 2.2 is "Yes," do you certify that, as of the date of this declaration, you have test data demonstrating that a drug product containing the polymorph will perform the same as the drug product described in the NDA? The type of test data required is described at 21 CFR 314.53(b). Yes No
- 2.4 Specify the polymorphic form(s) claimed by the patent for which you have the test results described in 2.3.
- 2.5 Does the patent claim only a metabolite of the active ingredient pending in the NDA or supplement? (Complete the information in section 4 below if the patent claims a pending method of using the pending drug product to administer the metabolite.) Yes No
- 2.6 Does the patent claim only an intermediate? Yes No
- If the patent referenced in 2.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.) Yes No

Drug Product (Composition/Formulation)

- 3.1 Does the patent claim the drug product, as defined in 21 CFR 314.3, in the pending NDA, amendment, or supplement? Yes No
- 3.2 Does the patent claim only an intermediate? Yes No
- 3.3 If the patent referenced in 3.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.) Yes No

4. Method of Use

Sponsors must submit the information in section 4 separately for each patent claim claiming a method of using the pending drug product for which approval is being sought. For each method of use claim referenced, provide the following information:

- 4.1 Does the patent claim one or more methods of use for which approval is being sought in the pending NDA, amendment, or supplement? Yes No
- 4.2 Patent Claim Number (as listed in the patent) Does the patent claim referenced in 4.2 claim a pending method of use for which approval is being sought in the pending NDA, amendment, or supplement? Yes No
- 4.2a If the answer to 4.2 is "Yes," identify with specificity the use with reference to the proposed labeling for the drug product. Use: (Submit indication or method of use information as identified specifically in the approved labeling.)

5. No Relevant Patents

For this pending NDA, amendment, or supplement, there are no relevant patents that claim the drug substance (active ingredient), drug product (formulation or composition) or method(s) of use, for which the applicant is seeking approval and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use, or sale of the drug product. Yes

Patent Certification

The undersigned declares that this is an accurate and complete submission of patent information for the NDA, amendment, or supplement pending under section 505 of the Federal Food, Drug, and Cosmetic Act. This time-sensitive patent information is submitted pursuant to 21 CFR 314.53. I attest that I am familiar with 21 CFR 314.53 and this submission complies with the requirements of the regulation. I verify under penalty of perjury that the foregoing is true and correct.

Warning: A willfully and knowingly false statement is a criminal offense under 18 U.S.C. 1001.

6.2 Authorized Signature of NDA Applicant/Holder or Patent Owner (Attorney, Agent, Representative or other Authorized Official) (Provide Information below)

Date Signed
9/27/2005

Gregg C. Brown

NOTE: Only an NDA applicant/holder may submit this declaration directly to the FDA. A patent owner who is not the NDA applicant/holder is authorized to sign the declaration but may not submit it directly to FDA. 21 CFR 314.53(c)(4) and (d)(4).

Check applicable box and provide information below.

<input type="checkbox"/> NDA Applicant/Holder	<input checked="" type="checkbox"/> NDA Applicant's/Holder's Attorney, Agent (Representative) or other Authorized Official
<input type="checkbox"/> Patent Owner	<input type="checkbox"/> Patent Owner's Attorney, Agent (Representative) or Other Authorized Official
Name Gregg C. Brown	
Address 6201 South Freeway	City/State Fort Worth, Texas
ZIP Code 76134-2099	Telephone Number 817-551-8663
FAX Number (if available) 817-551-4610	E-Mail Address (if available) gregg.brown@alconlabs.com

The public reporting burden for this collection of information has been estimated to average 9 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

Food and Drug Administration
CDER (HFD-007)
5600 Fishers Lane
Rockville, MD 20857

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

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EXCLUSIVITY SUMMARY

NDA # 21-980

SUPPL #

HFD # 520

Trade Name Fluorescite Injection

Generic Name

Applicant Name Alcon, Inc.

Approval Date, If Known

PART I IS AN EXCLUSIVITY DETERMINATION NEEDED?

1. An exclusivity determination will be made for all original applications, and all efficacy 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 a 505(b)(1), 505(b)(2) or efficacy supplement?

YES NO

If yes, what type? Specify 505(b)(1), 505(b)(2), SE1, SE2, SE3, SE4, SE5, SE6, SE7, SE8

505(b)(2)

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?

3 years

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

YES NO

If the answer to the above question in YES, is this approval a result of the studies submitted in response to the Pediatric Written Request?

IF YOU HAVE ANSWERED "NO" TO ALL OF THE ABOVE QUESTIONS, GO DIRECTLY TO THE SIGNATURE BLOCKS AT THE END OF THIS DOCUMENT.

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

YES NO

IF THE ANSWER TO QUESTION 2 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8 (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# 17-869

fundescein-25

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 8. (Caution: The questions in part II of the summary should only be answered "NO" for original approvals of new molecular entities.)

IF "YES," GO TO PART III.

PART III THREE-YEAR EXCLUSIVITY FOR NDAs AND SUPPLEMENTS

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 8.

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.

(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 8:

The clinical investigations conducted by Alcon, Inc., are not essential to approval of this application. 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.

(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:

Studies comparing two products with the same ingredient(s) are considered to be bioavailability studies for the purpose of this section.

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

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

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

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

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"):

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:

Name of person completing form: Alison Rodgers

Title: Project Manager, Division of Anti-Infective and Ophthalmology Products

Date: March 15, 2006

Name of Office/Division Director signing form: Wiley Chambers, M.D.

Title: Deputy Director, Division of Anti-Infective and Ophthalmology Products

Form OGD-011347; Revised 05/10/2004; formatted 2/15/05

**This is a representation of an electronic record that was signed electronically and
this page is the manifestation of the electronic signature.**

/s/

Wiley Chambers
4/13/2006 11:15:24 PM

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PEDIATRIC PAGE

(Complete for all filed original applications and efficacy supplements)

VA/BLA #: 21-980 Supplement Type (e.g. SE5): _____ Supplement Number: _____

Stamp Date: 9-29-05 Action Date: _____

HFD 520 Trade and generic names/dosage form: _____

Applicant: Alcon, Inc. Therapeutic Class: Diagnostic Dye

Indication(s) previously approved:

Each approved indication must have pediatric studies: Completed, Deferred, and/or Waived.

Number of indications for this application(s): 1

Indication #1: Diagnostic fluorescein angiography or angioscopy of the retina and iris

Is there a full waiver for this indication (check one)?

Yes: Please proceed to Section A.

No: Please check all that apply: Partial Waiver Deferred Completed

NOTE: More than one may apply

Please proceed to Section B, Section C, and/or Section D and complete as necessary.

Section A: Fully Waived Studies

Reason(s) for full waiver:

- Products in this class for this indication have been studied/labeled for pediatric population
- Disease/condition does not exist in children
- Too few children with disease to study
- There are safety concerns
- Other: _____

If studies are fully waived, then pediatric information is complete for this indication. If there is another indication, please see Attachment A. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section B: Partially Waived Studies

Age/weight range being partially waived:

Min _____ kg _____ mo. _____ yr. _____ Tanner Stage _____
Max _____ kg _____ mo. _____ yr. _____ Tanner Stage _____

Reason(s) for partial waiver:

- Products in this class for this indication have been studied/labeled for pediatric population
- Disease/condition does not exist in children
- Too few children with disease to study
- There are safety concerns
- Adult studies ready for approval
- Formulation needed
- Other: _____

If studies are deferred, proceed to Section C. If studies are completed, proceed to Section D. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section C: Deferred Studies

Age/weight range being deferred:

Min _____ kg _____ mo. _____ yr. 0 Tanner Stage _____
Max _____ kg _____ mo. _____ yr. 16 Tanner Stage _____

Reason(s) for deferral:

- Products in this class for this indication have been studied/labeled for pediatric population
- Disease/condition does not exist in children
- Too few children with disease to study
- There are safety concerns
- Adult studies ready for approval
- Formulation needed

Other: _____

Date studies are due (mm/dd/yy): _____

If studies are completed, proceed to Section D. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section D: Completed Studies

Age/weight range of completed studies:

Min _____ kg _____ mo. _____ yr. _____ Tanner Stage _____
Max _____ kg _____ mo. _____ yr. _____ Tanner Stage _____

Comments:

If there are additional indications, please proceed to Attachment A. Otherwise, this Pediatric Page is complete and should be entered into DFS.

This page was completed by:

{See appended electronic signature page}

Regulatory Project Manager

cc: NDA 21-980
HFD-960/ Grace Carmouze

FOR QUESTIONS ON COMPLETING THIS FORM CONTACT THE DIVISION OF PEDIATRIC DRUG DEVELOPMENT, HFD-960, 301-594-7337.

(revised 12-22-03)

**This is a representation of an electronic record that was signed electronically and
this page is the manifestation of the electronic signature.**

/s/

Alison Rodgers
3/28/2006 04:00:37 PM

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Item 16: Debarment Certification

CTD ITEM 3.A.3.

Alcon, Inc. and its affiliated companies, Alcon Research Ltd., hereby certify 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.


Terry J. Dagnon
Associate Director Regulatory Affairs

9/22/2005

Date

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NDA/EFFICACY SUPPLEMENT ACTION PACKAGE CHECKLIST

Application Information		
NDA 21-980	Efficacy Supplement Type SE-	Supplement Number
Drug: Fluorescite® (fluorescein injection, USP) 10%		Applicant: Alcon, Inc.
RPM: Alison Rodgers	HFD-520	Phone # 301-796-0797
<p>Application Type: () 505(b)(1) (X) 505(b)(2) (This can be determined by consulting page 1 of the NDA Regulatory Filing Review for this application or Appendix A to this Action Package Checklist.)</p> <p>If this is a 505(b)(2) application, please review and confirm the information previously provided in Appendix B to the NDA Regulatory Filing Review. Please update any information (including patent certification information) that is no longer correct.</p> <p>(X) Confirmed and/or corrected</p>	Listed drug(s) referred to in 505(b)(2) application (NDA #(s), Drug name(s)):	
❖ Application Classifications:		
• Review priority	() Standard (X) Priority	
• Chem class (NDAs only)	5	
• Other (e.g., orphan, OTC)	N/A	
❖ User Fee Goal Dates		
		3-29-06
❖ Special programs (indicate all that apply)		
		(X) None Subpart H () 21 CFR 314.510 (accelerated approval) () 21 CFR 314.520 (restricted distribution) () Fast Track () Rolling Review () CMA Pilot 1 () CMA Pilot 2
❖ User Fee Information		
• User Fee	(X) Paid UF ID number	
• User Fee waiver	() Small business () Public health () Barrier-to-Innovation () Other (specify)	
• User Fee exception	() Orphan designation () No-fee 505(b)(2) (see NDA Regulatory Filing Review for instructions) () Other (specify)	
❖ Application Integrity Policy (AIP)		
• Applicant is on the AIP	() Yes (X) No	

received a written notice from the applicant (or the patent owner or its representative) stating that a legal action was filed within 45 days of receipt of its notice of certification. The applicant is required to notify the Division in writing whenever an action has been filed within this 45-day period (see 21 CFR 314.107(f)(2)).

If "No," the patent owner (or NDA holder, if it is an exclusive patent licensee) has until the expiration of the 45-day period described in question (1) to waive its right to bring a patent infringement action or to bring such an action. After the 45-day period expires, continue with question (4) below.

- (4) Did the patent owner (or NDA holder, if it is an exclusive patent licensee) submit a written waiver of its right to file a legal action for patent infringement within the 45-day period described in question (1), as provided for by 21 CFR 314.107(f)(3)?

() Yes () No

If "Yes," there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip to the next box below (Exclusivity).

If "No," continue with question (5).

- (5) Did the patent owner, its representative, or the exclusive patent licensee bring suit against the applicant for patent infringement within 45 days of the patent owner's receipt of the applicant's notice of certification?

() Yes () No

(Note: This can be determined by confirming whether the Division has received a written notice from the applicant (or the patent owner or its representative) stating that a legal action was filed within 45 days of receipt of its notice of certification. The applicant is required to notify the Division in writing whenever an action has been filed within this 45-day period (see 21 CFR 314.107(f)(2)). If no written notice appears in the NDA file, confirm with the applicant whether a lawsuit was commenced within the 45-day period).

If "No," there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip to the next box below (Exclusivity).

If "Yes," a stay of approval may be in effect. To determine if a 30-month stay is in effect, consult with the Director, Division of Regulatory Policy II, Office of Regulatory Policy (HFD-007) and attach a summary of the response.

❖ Exclusivity (approvals only)		
<ul style="list-style-type: none"> Exclusivity summary Is there remaining 3-year exclusivity that would bar effective approval of a 505(b)(2) application? (Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.) 	No	
<ul style="list-style-type: none"> Is there existing orphan drug exclusivity protection for the "same drug" for the proposed indication(s)? Refer to 21 CFR 316.3(b)(13) for the definition of "same drug" for an orphan drug (i.e., active moiety). This definition is NOT the same as that used for NDA chemical classification. 	() Yes, Application # _____ (X) No	
❖ Administrative Reviews (Project Manager, ADRA) (indicate date of each review)		2-17-06

❖ Actions	
<ul style="list-style-type: none"> Proposed action 	(X) AP () TA () AE () NA
<ul style="list-style-type: none"> Previous actions (specify type and date for each action taken) 	
<ul style="list-style-type: none"> Status of advertising (approvals only) 	(X) Materials requested in AP letter () Reviewed for Subpart H
❖ Public communications	
<ul style="list-style-type: none"> Press Office notified of action (approval only) 	(X) Yes () Not applicable
<ul style="list-style-type: none"> Indicate what types (if any) of information dissemination are anticipated 	(X) None () Press Release () Talk Paper () Dear Health Care Professional Letter
❖ Labeling (package insert, patient package insert (if applicable), MedGuide (if applicable))	
<ul style="list-style-type: none"> Division's proposed labeling (only if generated after latest applicant submission of labeling) 	
<ul style="list-style-type: none"> Most recent applicant-proposed labeling 	Submitted 3-23-06
<ul style="list-style-type: none"> Original applicant-proposed labeling 	Submitted 9-28-05
<ul style="list-style-type: none"> Labeling reviews (including DDMAC, DMETS, DSRCS) and minutes of labeling meetings (<i>indicate dates of reviews and meetings</i>) 	DDMAC -3-1-06 DMETS - 3-9-06
<ul style="list-style-type: none"> Other relevant labeling (e.g., most recent 3 in class, class labeling) 	
❖ Labels (immediate container & carton labels)	
<ul style="list-style-type: none"> Division proposed (only if generated after latest applicant submission) 	
<ul style="list-style-type: none"> Applicant proposed 	Submitted 3-16-06
<ul style="list-style-type: none"> Reviews 	See Division Director's Memorandum dated 3-24-06
❖ Post-marketing commitments	
<ul style="list-style-type: none"> Agency request for post-marketing commitments 	
<ul style="list-style-type: none"> Documentation of discussions and/or agreements relating to post-marketing commitments 	
<ul style="list-style-type: none"> Outgoing correspondence (i.e., letters, E-mails, faxes) 	2-13-06; 1-23-06; 1-11-06; 11-28-05; 10-27-05
<ul style="list-style-type: none"> Memoranda and Telecons 	N/A
❖ Minutes of Meetings	
<ul style="list-style-type: none"> EOP2 meeting (indicate date) 	
<ul style="list-style-type: none"> Pre-NDA meeting (indicate date) 	
<ul style="list-style-type: none"> Pre-Approval Safety Conference (indicate date; approvals only) 	
<ul style="list-style-type: none"> Other 	
❖ Advisory Committee Meeting	
<ul style="list-style-type: none"> Date of Meeting 	N/A
<ul style="list-style-type: none"> 48-hour alert 	
<ul style="list-style-type: none"> Federal Register Notices, DESI documents, NAS/NRC reports (if applicable) 	N/A

Summary of Approval Review	
❖ Summary Reviews (e.g., Office Director, Division Director, Medical Team Leader) <i>(indicate date for each review)</i>	3-24-06; 3-17-06
Clinical Information	
❖ Clinical review(s) <i>(indicate date for each review)</i>	3-15-06
❖ Microbiology (efficacy) review(s) <i>(indicate date for each review)</i>	
❖ Safety Update review(s) <i>(indicate date or location if incorporated in another review)</i>	See page 48 Clinical Review
❖ Risk Management Plan review(s) <i>(indicate date/location if incorporated in another rev)</i>	N/A
❖ Pediatric Page (separate page for each indication addressing status of all age groups)	
❖ Demographic Worksheet <i>(NME approvals only)</i>	N/A
❖ Statistical review(s) <i>(indicate date for each review)</i>	N/A
❖ Biopharmaceutical review(s) <i>(indicate date for each review)</i>	3-22-06
❖ Controlled Substance Staff review(s) and recommendation for scheduling <i>(indicate date for each review)</i>	N/A
❖ Clinical Inspection Review Summary (DSI)	N/A
• Clinical studies	
• Bioequivalence studies	
CMC Information	
❖ CMC review(s) <i>(indicate date for each review)</i>	3-22-06; 2-16-06
❖ Environmental Assessment	N/A- See p. 59 CMC review
• Categorical Exclusion <i>(indicate review date)</i>	
• Review & FONSI <i>(indicate date of review)</i>	
• Review & Environmental Impact Statement <i>(indicate date of each review)</i>	
❖ Microbiology (validation of sterilization & product sterility) review(s) <i>(indicate date for each review)</i>	3-1-06
❖ Facilities inspection (provide EER report)	Date completed: 3-21-06 <input checked="" type="checkbox"/> Acceptable <input type="checkbox"/> Withhold recommendation
❖ Methods validation	<input checked="" type="checkbox"/> Completed <input type="checkbox"/> Requested <input type="checkbox"/> Not yet requested
Nonclinical Pharm/Tox Information	
❖ Pharm/tox review(s), including referenced IND reviews <i>(indicate date for each review)</i>	2-16-06
❖ Nonclinical inspection review summary	N/A
❖ Statistical review(s) of carcinogenicity studies <i>(indicate date for each review)</i>	N/A
❖ CAC/ECAC report	N/A

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Appendix A to NDA/Efficacy Supplement Action Package Checklist

An application is likely to be a 505(b)(2) application if:

- (1) it relies on literature to meet any of the approval requirements (unless the applicant has a written right of reference to the underlying data)
- (2) it relies on the Agency's previous approval of another sponsor's drug product (which may be evidenced by reference to publicly available FDA reviews, or labeling of another drug sponsor's drug product) to meet any of the approval requirements (unless the application includes a written right of reference to data in the other sponsor's NDA)
- (3) it relies on what is "generally known" or "scientifically accepted" about a class of products to support the safety or effectiveness of the particular drug for which the applicant is seeking approval. (Note, however, that this does not mean *any* reference to general information or knowledge (e.g., about disease etiology, support for particular endpoints, methods of analysis) causes the application to be a 505(b)(2) application.)
- (4) it seeks approval for a change from a product described in an OTC monograph and relies on the monograph to establish the safety or effectiveness of one or more aspects of the drug product for which approval is sought (see 21 CFR 330.11).

Products that may be likely to be described in a 505(b)(2) application include combination drug products (e.g., heart drug and diuretic (hydrochlorothiazide) combinations), OTC monograph deviations, new dosage forms, new indications, and new salts.

If you have questions about whether an application is a 505(b)(1) or 505(b)(2) application, please consult with the Director, Division of Regulatory Policy II, Office of Regulatory Policy (HFD-007).

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If you need assistance in determining if the applicant is claiming a new indication for a use, please contact the user fee staff.

- Is there any 5-year or 3-year exclusivity on this active moiety in an approved (b)(1) or (b)(2) application? YES NO

If yes, explain:

- Does another drug have orphan drug exclusivity for the same indication? YES NO

- If yes, is the drug considered to be the same drug according to the orphan drug definition of sameness [21 CFR 316.3(b)(13)]? YES NO

If yes, consult the Director, Division of Regulatory Policy II, Office of Regulatory Policy (HFD-007).

- Is the application affected by the Application Integrity Policy (AIP)? YES NO

If yes, explain.

- If yes, has OC/DMPQ been notified of the submission? YES NO

- Does the submission contain an accurate comprehensive index? YES NO

- Was form 356h included with an authorized signature? YES NO

If foreign applicant, both the applicant and the U.S. agent must sign.

- Submission complete as required under 21 CFR 314.50? YES NO

If no, explain:

- If an electronic NDA, does it follow the Guidance? N/A YES NO

If an electronic NDA, all certifications must be in paper and require a signature.
 Which parts of the application were submitted in electronic format?

Additional comments:

- If in Common Technical Document format, does it follow the guidance? N/A YES NO

- Is it an electronic CTD? N/A YES NO

If an electronic CTD, all certifications must be in paper and require a signature.
 Which parts of the application were submitted in electronic format?

Additional comments:

- Patent information submitted on form FDA 3542a? YES NO
- Exclusivity requested? YES, 3 years NO
NOTE: An applicant can receive exclusivity without requesting it; therefore, requesting exclusivity is not required.
- Correctly worded Debarment Certification included with authorized signature? YES NO
If foreign applicant, both the applicant and the U.S. Agent must sign the certification.

NOTE: Debarment Certification should use wording in FD&C Act section 306(k)(1) i.e., "[Name of applicant] 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." Applicant may not use wording such as "To the best of my knowledge"

- Financial Disclosure forms included with authorized signature? YES NO*
(Forms 3454 and 3455 must be used and must be signed by the APPLICANT.)
*Forms not included since clinical studies conducted in 1970's.
- Field Copy Certification (that it is a true copy of the CMC technical section)? YES NO

Refer to 21 CFR 314.101(d) for Filing Requirements

- PDUFA and Action Goal dates correct in COMIS? YES NO
If not, have the document room staff correct them immediately. These are the dates EES uses for calculating inspection dates.
- Drug name/Applicant name correct in COMIS? If not, have the Document Room make the corrections. Yes
- List referenced IND numbers: N/A
- End-of-Phase 2 Meeting(s)? Date(s) _____ NO
If yes, distribute minutes before filing meeting.
- Pre-NDA Meeting(s)? Date(s) _____ NO
If yes, distribute minutes before filing meeting.

Project Management

- All labeling (PI, PPI, MedGuide, carton and immediate container labels) consulted to DDMAC? YES NO
- Trade name (plus PI and all labels and labeling) consulted to ODS/DMETS? YES NO
- MedGuide and/or PPI (plus PI) consulted to ODS/DSRCS? N/A YES NO

- If a drug with abuse potential, was an Abuse Liability Assessment, including a proposal for scheduling, submitted? N/A YES NO

If Rx-to-OTC Switch application:

- OTC label comprehension studies, all OTC labeling, and current approved PI consulted to ODS/DSRCS? N/A YES NO
- Has DOTCDP been notified of the OTC switch application? YES NO

Clinical

- If a controlled substance, has a consult been sent to the Controlled Substance Staff? N/A
YES NO

Chemistry

- Did applicant request categorical exclusion for environmental assessment? YES NO
- If no, did applicant submit a complete environmental assessment? YES NO
- If EA submitted, consulted to Florian Zielinski (HFD-357)? YES NO
- Establishment Evaluation Request (EER) submitted to DMPQ? YES NO
- If a parenteral product, consulted to Microbiology Team (HFD-805)? YES NO

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ATTACHMENT

MEMO OF FILING MEETING

DATE: November 4, 2005

BACKGROUND: Fluorescite® (fluorescein injection, USP) 10% has been marketed in the United States for over 30 years without an approved NDA. It is used on a daily basis by ophthalmologists in diagnostic fluorescein angiography or angiography of retina and iris vasculature. Alcon was contacted by the CDER Drug Shortages Team about a possible shortage of fluorescein in the United States. Alcon is filing this NDA as fulfillment of the commitment made to the CDER Drug Shortages Team, the CDER Office of Compliance, and the CDER Ophthalmology Review Division.

ATTENDEES: Alison Rodgers, Maureen Dillon-Parker, Jeff Tworzyanski, Zhou Chen, Lin Qi, Bill Boyd, Wiley Chambers, Jennifer Harris, Lucious Lim, Rhea Lloyd, Mike Puglisi, Raphael Rodriguez

ASSIGNED REVIEWERS:

<u>Discipline</u>	<u>Reviewer</u>
Medical:	Bill Boyd
Secondary Medical:	
Statistical:	N/A
Pharmacology:	Zhou Chen
Statistical Pharmacology:	
Chemistry:	Lin Qi
Environmental Assessment (if needed):	
Biopharmaceutical:	Jeff Tworzyanski
Microbiology, sterility:	Vinayak Pawar
Microbiology, clinical (for antimicrobial products only):	
DSI:	N/A
Regulatory Project Management:	Alison Rodgers
Other Consults:	

Per reviewers, are all parts in English or English translation? YES NO
 If no, explain:

CLINICAL FILE X REFUSE TO FILE _____

- Clinical site inspection needed: YES NO
- Advisory Committee Meeting needed? YES, date if known _____ NO
- If the application is affected by the AIP, has the division made a recommendation regarding whether or not an exception to the AIP should be granted to permit review based on medical necessity or public health significance? N/A YES NO

CLINICAL MICROBIOLOGY NA X FILE _____ REFUSE TO FILE _____

Appendix A to NDA Regulatory Filing Review

An application is likely to be a 505(b)(2) application if:

- (0) it relies on literature to meet any of the approval requirements (unless the applicant has a written right of reference to the underlying data)
- (0) it relies on the Agency's previous approval of another sponsor's drug product (which may be evidenced by reference to publicly available FDA reviews, or labeling of another drug sponsor's drug product) to meet any of the approval requirements (unless the application includes a written right of reference to data in the other sponsor's NDA)
- (0) it relies on what is "generally known" or "scientifically accepted" about a class of products to support the safety or effectiveness of the particular drug for which the applicant is seeking approval. (Note, however, that this does not mean *any* reference to general information or knowledge (e.g., about disease etiology, support for particular endpoints, methods of analysis) causes the application to be a 505(b)(2) application.)
- (0) it seeks approval for a change from a product described in an OTC monograph and relies on the monograph to establish the safety or effectiveness of one or more aspects of the drug product for which approval is sought (see 21 CFR 330.11).

Products that may be likely to be described in a 505(b)(2) application include combination drug products (e.g., heart drug and diuretic (hydrochlorothiazide) combinations), OTC monograph deviations, new dosage forms, new indications, and new salts.

If you have questions about whether an application is a 505(b)(1) or 505(b)(2) application, please consult with the Director, Division of Regulatory Policy II, Office of Regulatory Policy (HFD-007).

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**Appendix B to NDA Regulatory Filing Review
Questions for 505(b)(2) Applications**

1. Does the application reference a listed drug (approved drug)? YES NO

If "No," skip to question 3.

1. Name of listed drug(s) referenced by the applicant (if any) and NDA/ANDA #(s):

1. The purpose of this and the questions below (questions 3 to 5) is to determine if there is an approved drug product that is equivalent or very similar to the product proposed for approval and that should be referenced as a listed drug in the pending application.

- (a) Is there a pharmaceutical equivalent(s) to the product proposed in the 505(b)(2) application that is already approved?

YES NO

(Pharmaceutical equivalents are drug products in identical dosage forms that: (1) contain identical amounts of the identical active drug ingredient, i.e., the same salt or ester of the same therapeutic moiety, or, in the case of modified release dosage forms that require a reservoir or overage or such forms as prefilled syringes where residual volume may vary, that deliver identical amounts of the active drug ingredient over the identical dosing period; (2) do not necessarily contain the same inactive ingredients; **and** (3) meet the identical compendial or other applicable standard of identity, strength, quality, and purity, including potency and, where applicable, content uniformity, disintegration times, and/or dissolution rates. (21 CFR 320.1(c))

If "No," skip to question 4. Otherwise, answer part (b).

- (a) Is the approved pharmaceutical equivalent(s) cited as the listed drug(s)? YES NO
(The approved pharmaceutical equivalent(s) should be cited as the listed drug(s).)

If "Yes," skip to question 6. Otherwise, answer part (c).

- (b) Have you conferred with the Director, Division of Regulatory Policy II, Office of Regulatory Policy (ORP) (HFD-007)?

YES NO

If "No," please contact the Director, Division of Regulatory Policy II, ORP. Proceed to question 6.

1. (a) Is there a pharmaceutical alternative(s) already approved? YES NO

(Pharmaceutical alternatives are drug products that contain the identical therapeutic moiety, or its precursor, but not necessarily in the same amount or dosage form or as the same salt or ester. Each such drug product individually meets either the identical or its own respective compendial or other applicable standard of identity, strength, quality, and purity, including potency and, where applicable, content uniformity, disintegration times and/or dissolution rates. (21 CFR 320.1(d)) Different dosage forms and strengths within a product line by a single manufacturer are thus pharmaceutical alternatives, as are extended-release products when compared with immediate- or standard-release formulations of the same active ingredient.)

If "No," skip to question 5. Otherwise, answer part (b).

- (b) Is the approved pharmaceutical alternative(s) cited as the listed drug(s)? YES NO
(The approved pharmaceutical alternative(s) should be cited as the listed drug(s).)

Fluorescein 25% can be considered a pharmaceutical alternative; however, it has been discontinued. Novartis discontinued this product because it was less expensive to buy Akorn's unapproved fluorescein and resell it than make it under their own NDA.

NOTE: If there is more than one pharmaceutical alternative approved, consult the Director, Division of Regulatory Policy II, Office of Regulatory Policy (ORP) (HFD-007) to determine if the appropriate pharmaceutical alternatives are referenced.

If "~~Yes~~," skip to question 6. Otherwise, answer part (c).

- (c) Have you conferred with the Director, Division of Regulatory Policy II, ORP? YES NO

If "No," please contact the Director, Division of Regulatory Policy II, ORP. Proceed to question 6.

1. (a) Is there an approved drug product that does not meet the definition of "pharmaceutical equivalent" or "pharmaceutical alternative," as provided in questions 3(a) and 4(a), above, but that is otherwise very similar to the proposed product?

YES NO

If "No," skip to question 6.

If "Yes," please describe how the approved drug product is similar to the proposed one and answer part (b) of this question. Please also contact the Director, Division of Regulatory Policy II, Office of Regulatory Policy (HFD-007), to further discuss.

- (a) Is the approved drug product cited as the listed drug? YES NO

1. Describe the change from the listed drug(s) provided for in this (b)(2) application (for example, "This application provides for a new indication, otitis media" or "This application provides for a change in dosage form, from capsules to solution").

N/A

1. Is the application for a duplicate of a listed drug and eligible for approval under section 505(j) as an ANDA? (Normally, FDA will refuse-to-file such NDAs (see 21 CFR 314.101(d)(9)).) YES NO

- | | | |
|---|-----|----|
| 1. Is the extent to which the active ingredient(s) is absorbed or otherwise made available to the site of action less than that of the reference listed drug (RLD)? (See 314.54(b)(1)). If yes, the application should be refused for filing under 21 CFR 314.101(d)(9). N/A | YES | NO |
| 1. Is the rate at which the product's active ingredient(s) is absorbed or otherwise made available to the site of action unintentionally less than that of the RLD (see 21 CFR 314.54(b)(2))? If yes, the application should be refused for filing under 21 CFR 314.101(d)(9).
N/A | YES | NO |
| 1. Are there certifications for each of the patents listed for the listed drug(s)? N/A | YES | NO |
| 1. Which of the following patent certifications does the application contain? (Check all that apply <u>and</u> identify the patents to which each type of certification was made, as appropriate.) | | |

21 CFR 314.50(i)(1)(i)(A)(1): The patent information has not been submitted to FDA. (Paragraph I certification)

21 CFR 314.50(i)(1)(i)(A)(2): The patent has expired. (Paragraph II certification)

21 CFR 314.50(i)(1)(i)(A)(3): The date on which the patent will expire. (Paragraph III certification)

21 CFR 314.50(i)(1)(i)(A)(4): The patent is invalid, unenforceable, or will not be infringed by the manufacture, use, or sale of the drug product for which the application is submitted. (Paragraph IV certification)

*IF FILED, and if the applicant made a "Paragraph IV" certification [21 CFR 314.50(i)(1)(i)(A)(4)], the applicant must **subsequently** submit a signed certification stating that the NDA holder and patent owner(s) were notified the NDA was filed [21 CFR 314.52(b)]. The applicant must also submit documentation showing that the NDA holder and patent owner(s) received the notification [21 CFR 314.52(e)].*

21 CFR 314.50(i)(1)(ii): No relevant patents.

21 CFR 314.50(i)(1)(iii): The patent on the listed drug is a method of use patent and the labeling for the drug product for which the applicant is seeking approval does not include any indications that are covered by the use patent as described in the corresponding use code in the Orange Book. Applicant must provide a statement that the method of use patent does not claim any of the proposed indications. (Section viii statement)

_____ 21 CFR 314.50(i)(3): Statement that applicant has a licensing agreement with the patent owner (must also submit certification under 21 CFR 314.50(i)(1)(i)(A)(4) above).

_____ Written statement from patent owner that it consents to an immediate effective date upon approval of the application.

1. Did the applicant:

- Identify which parts of the application rely on information (e.g. literature, prior approval of another sponsor's application) that the applicant does not own or to which the applicant does not have a right of reference? YES NO
- Submit a statement as to whether the listed drug(s) identified has received a period of marketing exclusivity? N/A YES NO
- Submit a bioavailability/bioequivalence (BA/BE) study comparing the proposed product to the listed drug? N/A YES NO
- Certify that it is seeking approval only for a new indication and not for the indications approved for the listed drug if the listed drug has patent protection for the approved indications and the applicant is requesting only the new indication (21 CFR 314.54(a)(1)(iv)).? N/A YES NO

13. If the (b)(2) applicant is requesting 3-year exclusivity, did the applicant submit the following information required by 21 CFR 314.50(j)(4):

- Certification that at least one of the investigations included meets the definition of "new clinical investigation" as set forth at 314.108(a). YES NO
- A list of all published studies or publicly available reports that are relevant to the conditions for which the applicant is seeking approval. YES NO
- EITHER
The number of the applicant's IND under which the studies essential to approval were conducted. IND # _____ NO
OR
A certification that the NDA sponsor provided substantial support for the clinical investigation(s) essential to approval if it was not the sponsor of the IND under which those clinical studies were conducted? YES NO

13. Has the Associate Director for Regulatory Affairs, OND, been notified of the existence of the (b)(2) application?

YES ~~NO~~

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**This is a representation of an electronic record that was signed electronically and
this page is the manifestation of the electronic signature.**

/s/

Alison Rodgers
3/21/2006 02:33:06 PM
CSO

Alison Rodgers
3/21/2006 02:36:37 PM
CSO

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CONSULTATION RESPONSE

**DIVISION OF MEDICATION ERRORS AND TECHNICAL SUPPORT
OFFICE OF DRUG SAFETY
(DMETS; HFD-420)**

DATE RECEIVED: November 7, 2005	DESIRED COMPLETION DATE: February 1, 2006	ODS CONSULT #: 05-0255
DATE OF DOCUMENT: September 28, 2005	PDUFA DATE: March 29, 2006	

TO: Janice Soreth, MD
Director, Division of Anti-Infective and Ophthalmology Products
HFD-520

THROUGH: Todd Bridges, RPh, Acting Team Leader
Denise Toyer, PharmD, Deputy Director
Carol Holquist, RPh, Director
Division of Medication Errors and Technical Support

FROM: Kristina C. Arnwine, PharmD, Safety Evaluator
Division of Medication Errors and Technical Support

PRODUCT NAME: **Fluorescite**
(Fluorescein Injection, USP) 10%

NDA#: 21-980

NDA SPONSOR: Alcon, Inc.

- RECOMMENDATIONS:**
1. DMETS has no objections to the use of the proprietary name, Fluorescite. DMETS considers this a final decision. However, if the approval of the NDA is delayed beyond 90 days from the signature date of this document, the firm should be notified that this name with its associated labels and labeling must be re-evaluated. A re-review of the name prior to NDA approval will rule out any objections based upon approvals of other proprietary and established names from this date forward.
 2. DMETS recommends implementation of the label and labeling revisions outlined in section III of this review to minimize potential errors with the use of this product.
 3. DDMAC finds the proprietary name, Fluorescite, acceptable from a promotional perspective.

DMETS would appreciate feedback of the final outcome of this consult. We would be willing to meet with the Division for further discussion, if needed. If you have further questions or need clarifications, please contact Diane Smith, project manager, at 301-796-0538.

**Division of Medication Errors and Technical Support (DMETS)
Office of Drug Safety
HFD-420; WO22; Mail Stop 4447
Center for Drug Evaluation and Research**

PROPRIETARY NAME REVIEW

DATE OF REVIEW: November 29, 2005
NDA# 21-980
NAME OF DRUG: Fluorescite (Fluorescein Injection, USP) 10%
NDA HOLDER: Alcon, Inc.

I. INTRODUCTION:

This consult was written in response to a request from the Division of Anti-Infective and Ophthalmology Products (HFD-520), for assessment of the proprietary name, Fluorescite, regarding potential name confusion with other proprietary or established drug names. Container labels, carton and insert labeling were provided for review and comment.

The sponsor, Alcon, has submitted a 505(b)(2) application for Fluorescite 10%, which has been marketed in the United States for over 30 years, but was never approved by the FDA. Alcon currently markets Fluorescite 10% and Fluorescite 25%. The current application is for the 10% injection only. According to Alison Rodgers, project manager in the Division of Anti-Infective and Ophthalmology Products, Alcon markets Fluorescite 25% internationally, and currently does not plan to market the 25% strength in the United States.

PRODUCT INFORMATION

Fluorescite is a sterile solution for use intravenously as a diagnostic aid in fluorescein angiography or angioscopy of the retina and iris vasculature. The usual dose of Fluorescite is 500 mg via intravenous administration. Fluorescite is supplied as a 500 mg injection in a single-use 5 mL (100 mg/mL) glass vial.

II. RISK ASSESSMENT:

The medication error staff of DMETS conducted a search of several standard published drug product reference texts^{1,2} as well as several FDA databases³ for existing drug names which sound-alike or look-alike to Fluorescite to a degree where potential confusion between drug names could occur under the usual clinical practice settings. A search of the electronic online version of the U.S. Patent and Trademark Office's Text and Image Database was also conducted⁴. The Saegis⁵ Pharma-In-Use

¹ MICROMEDEX Integrated Index, 2006, MICROMEDEX, Inc., 6200 South Syracuse Way, Suite 300, Englewood, Colorado 80111-4740, which includes all products/databases within ChemKnowledge, DrugKnowledge, and RegsKnowledge Systems.

² Facts and Comparisons, online version, Facts and Comparisons, St. Louis, MO.

³ AMF Decision Support System [DSS], the Division of Medication Errors and Technical Support [DMETS] database of Proprietary name consultation requests, New Drug Approvals 98-06, and the electronic online version of the FDA Orange Book.

⁴ WWW location <http://www.uspto.gov/tmdb/index.html>.

database was searched for drug names with potential for confusion. An expert panel discussion was conducted to review all findings from the searches. In addition, DMETS conducted three prescription analysis studies consisting of two written prescription studies (inpatient and outpatient) and one verbal prescription study, involving health care practitioners within FDA. This exercise was conducted to simulate the prescription ordering process in order to evaluate potential errors in handwriting and verbal communication of the name.

A. EXPERT PANEL DISCUSSION (EPD)

An Expert Panel discussion was held by DMETS to gather professional opinions on the safety of the proprietary name, Fluorescite. Potential concerns regarding drug marketing and promotion related to the proposed name were also discussed. This group is composed of DMETS Medication Errors Prevention Staff and representation from the Division of Drug Marketing, Advertising, and Communications (DDMAC). The group relies on their clinical and other professional experiences and a number of standard references when making a decision on the acceptability of a proprietary name.

1. DDMAC has no objections to the name, Fluorescite, from a promotional perspective.
2. The Expert Panel identified one proprietary name that was thought to have the potential for confusion with Fluorescite. This product is listed in table 1 (see below), along with the dosage form available and usual dosage.

Table 1: Potential Sound-Alike Names Identified by DMETS Expert Panel

Product Name	Dosage form(s), Established name	Usual adult dose*	Other**
Fluorescite	Fluorescein Injection 10 %	Adults: 500 mg via intravenous infusion Children: 7.7 mg/kg ³	
Floxuridine	Floxuridine Powder for Injection 500 mg	0.1—0.6 mg/kg/day as a continuous intra-arterial infusion into the hepatic artery	SA

*Frequently used, not all-inclusive.
**S/A (sound-alike)

B. PHONETIC and ORTHOGRAPHIC COMPUTER ANALYSIS (POCA)

As part of the name similarity assessment, proposed names are evaluated via a phonetic/orthographic algorithm. The proposed proprietary name is converted into its phonemic representation before it runs through the phonetic algorithm. The phonetic search module returns a numeric score to the search engine based on the phonetic similarity to the input text. Likewise, an orthographic algorithm exists which operates in a similar fashion. All names considered to have significant phonetic or orthographic similarities to Fluorescite were discussed by the Expert Panel (EPD).

⁵ Data provided by Thomson & Thomson's SAEGIS™ Online Service, available at www.thomson-thomson.com

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C. PRESCRIPTION ANALYSIS STUDIES

1. Methodology:

Three separate studies were conducted within the Centers of the FDA for the proposed proprietary name to determine the degree of confusion of Fluorescite with marketed U.S. drug names (proprietary and established) due to similarity in visual appearance with handwritten prescriptions or verbal pronunciation of the drug name. These studies employed a total of 124 health care professionals (pharmacists, physicians, and nurses). This exercise was conducted in an attempt to simulate the prescription ordering process. Two inpatient orders were written, each consisting of a combination of marketed and unapproved drug products and an order for Fluorescite (see below). These prescriptions were optically scanned and one prescription was delivered to a random sample of the participating health professionals via e-mail. In addition, one inpatient order was recorded on voice mail. The voice mail messages were then sent to a random sample of the participating health professionals for their interpretations and review. After receiving either the written or verbal prescription orders, the participants sent their interpretations of the orders via e-mail to the medication error staff.

HANDWRITTEN PRESCRIPTION	VERBAL PRESCRIPTION			
Inpatient Requisition #1: <table border="1"><tr><td>1</td><td>7895</td><td>Fluorescite 5ml vial</td></tr></table>	1	7895	Fluorescite 5ml vial	"Fluorescite, #1, 5 mL vial."
1	7895	Fluorescite 5ml vial		
Inpatient Requisition #2: <table border="1"><tr><td>7895</td><td>Fluorescite #1</td><td>5ml</td></tr></table>	7895	Fluorescite #1	5ml	
7895	Fluorescite #1	5ml		

2. Results:

None of the interpretations of the proposed name overlap, sound similar, or look similar to any currently marketed U.S. product. See appendix A for the complete listing of interpretations from the verbal and written studies.

D. ADVERSE EVENT REPORTING SYSTEM (AERS) and DRUG QUALITY REPORTING SYSTEM (DQRS)

DMETS conducted a search of the Adverse Event Reporting System (AERS) for medication errors associated with Fluorescite. The Meddra preferred terms, "Medication Errors," "Accidental Overdose," "Pharmaceutical Product Complaint," "Circumstance or Information Capable of Leading to a Medication Error," and "Overdose," were used. The search did not identify any cases of name confusion between Fluorescite and any other marketed products.

Additionally, DMETS conducted a search of the Drug Quality Reporting System (DQRS) for medication errors associated with Fluorescite. The search did not identify any such medication errors.

E. SAFETY EVALUATOR RISK ASSESSMENT

In reviewing the proprietary name, Fluorescite, the primary concerns related to look-alike and sound-alike confusion with Floxuridine. Additionally, DMETS conducted prescription studies to

simulate the prescription ordering process. In this case, there was no confirmation that the proposed name could be confused with the aforementioned name. However, negative findings are not predicative as to what may occur once the drug is widely prescribed, as these studies have limitations primarily due to a small sample size. The majority of misinterpretations were misspelled/phonetic variations of the proposed name, Fluorescite.

Fluorescite was a name identified as having a similar appearance to Floxuridine when scripted. Floxuridine is a pyrimidine analog antineoplastic agent indicated for gastrointestinal adenocarcinoma metastatic to the liver in selected patients considered incurable by surgery. The beginnings of Fluorescite and Floxuridine are similar (Flu- vs. Flo-) which is the principal contribution to the look-alike characteristics of each name. In the remaining portions of each name, only the letters 'i' and 'e' are presented in the same position in each name. In addition, the upstrokes of the letter 't' in Fluorescite and the letter 'd' in Floxuridine help to distinguish the two names from each other since they appear in different positions in each name (see below). Fluorescite and Floxuridine overlap with regard to dosage form (**injection** vs. powder for **injection**) and product strength (500 mg). Additionally, after reconstitution of Floxuridine, the total drug content and resultant concentration overlap with the concentration of Fluorescite (500 mg/5 mL and 100 mg/mL, respectively). However, they do not overlap with regard to product characteristics such as route of administration (intravenous vs. intra-arterial) and dosing frequency (once vs. daily) which will likely be included on a prescription order, thereby helping to decrease the potential for confusion between the two products. Although Floxuridine has a range of doses (0.1 mg/kg/day-0.6 mg/kg/day), it is unlikely that the dose of Floxuridine will overlap with the usual dose of Fluorescite (500 mg). The two products also have very specific prescriber populations as well (ophthalmologist vs. oncologist) which also helps to decrease the potential for confusion. Additionally, although both medications may be used on an inpatient basis, Fluorescite will most likely be supplied directly to the ophthalmology department and not be dispensed to the patient's room, thereby helping to decrease the potential for confusion. Overall, the orthographic differences along with the differing usual doses, dosing frequencies, and prescribers decrease the potential for name confusion between the two products.

F L U O R E S C I T E
F L O X U R I D I N E

fluorescite floxuridine

III. LABELING, PACKAGING, AND SAFETY RELATED ISSUES:

In the review of the container labels, carton and insert labeling of Fluorescite. DMETS has identified the following areas of possible improvement, which might minimize potential user error.

A. GENERAL COMMENTS

3. Include the statement, " _____ , " on the principal display panel.

B. CONTAINER LABEL

1. See General Comments A-1 and A-2.

2. Increase the prominence of the route of administration statement.

3. If space permits, include the statement, " _____ "

C. CARTON LABELING

See General Comments A-1 and A-2 and comments B-2 and B-3.

D. PACKAGE INSERT, Dosage and Administration Section

1. The usual dose of Fluorescite is stated in terms of milligrams (i.e. 500 mg and 7.7 mg/kg) as well as milliliters (i.e. 5 mL and 2 mL). Since the usual dose for both adults and pediatrics is stated in _____

2. In order to allow healthcare practitioners to follow the directions in a stepwise manner and to provide for accurate dosing and administration, DMETS recommends revising the third paragraph of the Dosage and Administration to read as follows:

3. Relocate the statement, " _____ , " to the end of the Dosage and Administration section.

Appendix A

Inpatient Written	Outpatient Written	Verbal
Flourescite	Fluorescite	florocite
Fluorecite	Fluorescite	Florosite
Fluorescite	Fluorescite	Fluocescete
Fluorescite	Fluorescite	Fluorescetis
Fluorescite	Fluorescite	Fluorescite
Fluorescite	Fluorescite	Fluoresite
Fluorescite	Fluorescite	Fluorocite
Fluorescite	Fluorescite	Fluorocite
Fluorescite	Fluorescite	Fluorocyte
Fluorescite	Fluorescite	Fluorocyte
Fluorescite	Fluorescite	Fluoroscite
Fluorescite	Fluorescite	
Fluorescite	Fluoroscite	
Fluorescite	Forescite	
Fluorescite		
Fluorocite		

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/s/

Kristina Arnwine
3/8/2006 04:25:28 PM
DRUG SAFETY OFFICE REVIEWER

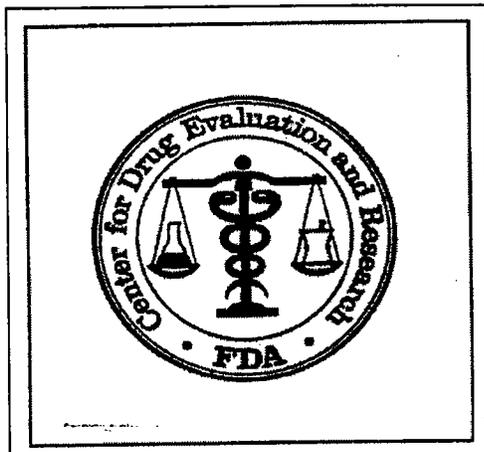
Todd Bridges
3/8/2006 05:19:43 PM
DRUG SAFETY OFFICE REVIEWER

Denise Toyer
3/9/2006 10:35:06 AM
DRUG SAFETY OFFICE REVIEWER

Carol Holquist
3/9/2006 12:22:24 PM
DRUG SAFETY OFFICE REVIEWER

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FACSIMILE TRANSMISSION
RECORD



From: Lin Qi, Ph.D.

Office of New Drug Quality Assessment

Phone 301-796-1438

Fax 301-796-9850

Date: 2/13/06

To: Name Mr. Terry J. Dagnon
Company Alcon, Inc.
City Fort Worth State TX
Phone # 817-551-4325
FAX # 817-551-4630

Number of Pages (INCLUDING COVER PAGE) 2

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Terry,

Thank you for your prompt responses to previous comments. Please respond to the following comment as soon as possible and send me a copy of the response. My email address is lin.qi@fda.hhs.gov.

Thanks!
Lin

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NDA 21-980
FLUORESCITE Injection, 10%

The following comments are being provided to you prior to completion of our review of the application to give you preliminary notice of issues that have been identified. Per the user fee reauthorization agreements, these comments do not reflect a final decision on the information reviewed and should not be construed to do so. These comments are preliminary and are subject to change as the review of your application is finalized. In addition, we may identify other information that must be provided prior to approval of this application. Depending on the timing of your response, as per user fee reauthorization agreements, we may or may not be able to consider your response prior to taking an action on your application during this review cycle.

If your response can be found in the contents of your submission, just cite those sections of the submission that are relevant to the issue under consideration. Otherwise, provide the appropriate information. Your response should be submitted as an amendment to the submission and a copy via facsimile to the reviewer.

CMC COMMENTS

1. In the section of postapproval stability protocol and stability commitment, please also commit to not releasing any drug product lots found to fall outside of the specification.

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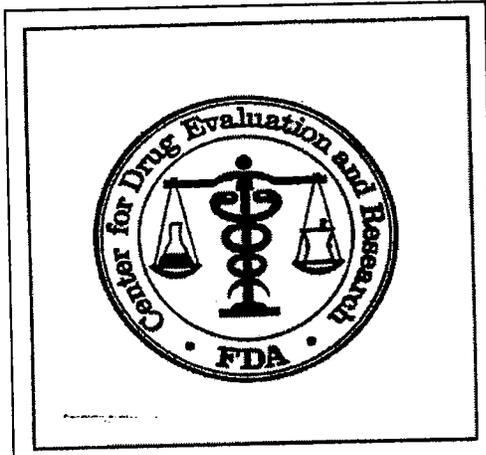
/s/

Lin Qi
2/27/2006 12:42:50 PM
CHEMIST

Elaine Morefield
2/28/2006 08:39:14 AM
CHEMIST

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From: Lin Qi, Ph.D.

Office of New Drug Quality Assessment

Phone 301-796-1438

Fax 301-796-9850

Date: 1/23/06

To: Name Mr. Terry J. Dagnon
Company Alcon, Inc.
City Fort Worth State TX
Phone # 817-551-4325

FAX # 817-551-4630

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Terry,

Thank you for your prompt response to the fax dated January 11, 2006. Please respond to the following comments as soon as possible and send me a copy of the response. My email address is lin.qi@fda.hhs.gov.

Thanks!
Lin

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NDA 21-980

FLUORESCITE Injection, 10%

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If your response can be found in the contents of your submission, just cite those sections of the submission that are relevant to the issue under consideration. Otherwise, provide the appropriate information. Your response should be submitted as an amendment to the submission and a copy via facsimile to the reviewer.

CMC COMMENTS

1. Please confirm that all tests listed in Table 3.2.P.8.1-5 will be performed for the post-approval stability study, because the stability tests mentioned under item c of Section 3.2.P.8.2 are not complete.
2. Establish a limit for the weight change % in the drug product stability testing according to the drug product stability data.

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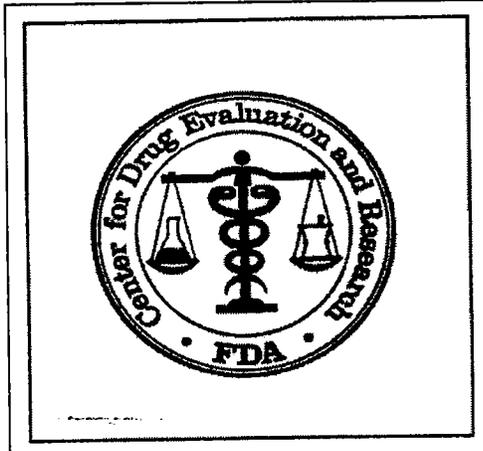
/s/

Lin Qi
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CHEMIST

Elaine Morefield
2/28/2006 08:43:24 AM
CHEMIST

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From: Lin Qi, Ph.D.

Office of New Drug Quality Assessment

Phone 301-796-1438

Fax 301-796-9850

Date: 1/11/06

To: Name Mr. Terry J. Dagnon
Company Alcon, Inc.
City Fort Worth State TX
Phone # 817-551-4325
FAX # 817-551-4630

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NDA 21-980
FLUORESCITE Injection, 10%

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If your response can be found in the contents of your submission, just cite those sections of the submission that are relevant to the issue under consideration. Otherwise, provide the appropriate information. Your response should be submitted as an amendment to the submission and a copy via facsimile to the reviewer.

CMC COMMENTS

Please submit updated stability data on the drug substance and drug product as soon as possible.

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/s/

Lin Qi
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2/28/2006 08:47:27 AM
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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

FILING COMMUNICATION

NDA 21-980

Alcon Research, Ltd.
Attention: Terry J. Dagnon
Associate Director, Regulatory Affairs
6201 South Freeway, R7-18
Fort Worth, TX 76134-2099

Dear Mr. Dagnon:

Please refer to your September 28, 2005 new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Fluorescite® (fluorescein injection, USP) 10%.

We have completed our filing review and have determined that your application is sufficiently complete to permit a substantive review. Therefore, this application will be filed under section 505(b) of the Act on November 28, 2005, in accordance with 21 CFR 314.101(a). The user fee goal date will be March 29, 2006.

At this time, we have not identified any potential filing review issues. Our filing review is only a preliminary evaluation of the application and is not indicative of deficiencies that may be identified during our review.

If you have any questions, call Alison Rodgers, Regulatory Project Manager, at (301) 796-0797.

Sincerely,

(See appended electronic signature page)

Janice M. Soreth, M.D.
Director
Division of Anti-Infective and
Ophthalmology Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

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Janice Soreth
11/28/2005 10:20:48 AM

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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-980

NDA ACKNOWLEDGMENT

Alcon Research, Ltd.
Attention: Terry J. Dagnon
Associate Director, Regulatory Affairs
6201 South Freeway, R7-18
Fort Worth, Texas 76134-2099

Dear Mr. Dagnon:

We have received your new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for the following:

Name of Drug Product:	Fluorescite® (fluorescein injection, USP), 10%
Review Priority Classification:	Pending
Date of Application:	September 28, 2005
Date of Receipt:	September 29, 2005
Our Reference Number:	NDA 21-980

Unless we notify you within 60 days of the receipt date that the application is not sufficiently complete to permit a substantive review, we will file the application on November 28, 2005, in accordance with 21 CFR 314.101(a).

All applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred. We note that you have not fulfilled the requirements. We acknowledge receipt of your request for a waiver of pediatric studies for this application. Once the application has been filed we will notify you whether we have waived the pediatric study requirement for this application.

Please cite the NDA number listed above at the top of the first page of all submissions to this application. Send all submissions, electronic or paper, including those sent by overnight mail or courier, to the following address:

NDA 21-980

Page 2

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Anti-Infective and Ophthalmology Products
5901-B Ammendale Road
Beltsville, MD 20705-1266

If you have any questions, call Alison Rodgers, Regulatory Project Manager, at (301) 796-0797.

Sincerely,

{See appended electronic signature page}

Maureen P. Dillon-Parker
Chief, Project Management Staff
Division of Anti-Infective and
Ophthalmology Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

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/s/

Maureen Dillon-Parker
10/27/2005 09:22:28 AM
NDA 21-980 - New NDA Ack Ltr

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Labeling Revision REVIEW

Application Type	NDA
Submission Number	21-980
Submission Code	Original
Letter Date	March 23, 2006
PDUFA Goal Date	March 29, 2006
Reviewer Name	Wiley A. Chambers, M.D.
Review Completion Date	March 24, 2006
Established Name	fluorescein injection
(Proposed) Trade Name	Fluorescite
Therapeutic Class	4042210 diagnostic dye
Applicant	Alcon, Inc.
Priority Designation	P
Formulation	Active ingredient: fluorescein sodium
Dosing Regimen	500 mg (100 mg/mL) via intravenous administration
Indication	diagnostic fluorescein angiography or angioscopy of the retina and iris vasculature
Intended Population	patients undergoing diagnostic fluorescein angiography or angioscopy of the retina and iris vasculature

Recommendation on Regulatory Action

It is recommended that NDA 21-980 be approved with the labeling listed in this review.

The application supports the safety and effectiveness of Fluorescite (fluorescein injection, USP) 10% for diagnostic fluorescein angiography or angiography of the retina and iris vasculature.

Labeling

Re-review of the data supporting the statement _____ was conducted after questions were raised in the Biopharm Review concerning this statement.

Reviewer's Comments:

✓

7

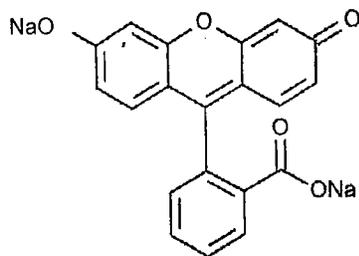
_____ . The revised labeling listed below has been reviewed and is considered acceptable.

FLUORESCITE® (fluorescein injection, USP) 10%

Sterile

DESCRIPTION

FLUORESCITE® (fluorescein injection, USP) 10% contains fluorescein sodium (equivalent to fluorescein 10% w/v). It is a sterile solution for use intravenously as a diagnostic aid. Its chemical name is spiro[isobenzofuran-1(3H),9'-[9H]xanthene]-3-one, 3',6'-dihydroxy, disodium salt. The active ingredient is represented by the chemical structure:



376.27 MW

FLUORESCITE® (fluorescein injection, USP) 10% is supplied as a sterile, unpreserved, unit dose aqueous solution, that has a pH of 8.0 - 9.8 and an osmolality of 572-858 mOsm/kg.

Active ingredient: fluorescein sodium

Inactive Ingredients

Sodium hydroxide and/or hydrochloric acid (to adjust pH), and water for injection.

CLINICAL PHARMACOLOGY

Mechanism of Action

Fluorescein sodium responds to electromagnetic radiation and light between the wavelengths of 465-490 nm and fluoresces, i.e., emits light at wavelengths of 520-530 nm. Thus, the hydrocarbon is excited by blue light and emits light that appears yellowish-green. Following intravenous injection of fluorescein sodium in an aqueous solution, the unbound fraction of the fluorescein can be excited with a blue light flash from a fundus camera as it circulates through the ocular vasculature, and the yellowish green fluorescence of the dye is captured by the camera. In the fundus, the fluorescence of the dye demarcates the retinal and/or choroidal vasculature under observation, distinguishing it from adjacent areas/structures.

Pharmacokinetics

Distribution:

Within 7 to 14 seconds after IV administration into antecubital vein, fluorescein usually appears in the central artery of the eye. Within a few minutes of IV administration of fluorescein sodium, a yellowish discoloration of the skin occurs, which begins to fade after 6 to 12 hours of dosing. Various estimates of volume of distribution indicate that fluorescein distributes well into interstitial space (0.5 L/kg).

Metabolism:

Fluorescein undergoes rapid metabolism to fluorescein monoglucuronide. After IV administration of fluorescein sodium (14 mg/kg) to 7 healthy subjects, approximately 80% of fluorescein in plasma was converted to glucuronide conjugate after a period of 1 hour post dose, indicating relatively rapid conjugation.

Excretion:

Fluorescein and its metabolites are mainly eliminated via renal excretion. After IV administration, the urine remains slightly fluorescent for 24 to 36 hours. A renal clearance of 1.75 mL/min/kg and a hepatic clearance (due to conjugation) of 1.50 mL/min/kg have been estimated. The systemic clearance of fluorescein was essentially complete by 48 to 72 hours after administration of 500 mg fluorescein.

INDICATIONS AND USAGE:

FLUORESCITE® Injection 10% is indicated in diagnostic fluorescein angiography or angioscopy of the retina and iris vasculature.

CONTRAINDICATIONS

FLUORESCITE® Injection 10% is contraindicated in patients with known hypersensitivity to fluorescein sodium or any other ingredients in this product.

WARNINGS

FOR INTRAVENOUS USE

Care must be taken to avoid extravasation during injection as the high pH of fluorescein solution can result in severe local tissue damage. The following complications resulting from extravasation of fluorescein have been noted to occur: Sloughing of the skin, superficial phlebitis, subcutaneous granuloma, and toxic neuritis along the median curve in the antecubital area. Complications resulting from extravasation can cause severe pain in the arm for up to several hours. When significant extravasation occurs, the injection should be discontinued and conservative measures to treat damaged tissue and to relieve pain should be implemented. Rare cases of death due to anaphylaxis have been reported (See PRECAUTIONS).

PRECAUTIONS

General

Caution is to be exercised in patients with a history of allergy or bronchial asthma. An emergency tray should be available in the event of possible reaction to FLUORESCITE® Injection 10%. Use only if the container is undamaged.

Information for Patients

Skin will attain a temporary yellowish discoloration. Urine attains a bright yellow color. Discoloration of the skin usually fades in 6 to 12 hours and usually fades in urine in 24 to 36 hours.

Laboratory Information

If a potential allergy is suspected, an intradermal skin test may be performed prior to intravenous administration, i.e., 0.05 mL injected intradermally to be evaluated 30 to 60 minutes following injection. Given the sensitivity and specificity of skin testing, a negative skin test is not proof that a patient is not allergic to fluorescein.

Carcinogenesis, Mutagenesis, Impairment of Fertility

There have been no long-term studies done using fluorescein in animals to evaluate carcinogenic potential.

Pregnancy

Teratogenic Effects: Pregnancy Category C

Adequate animal reproduction studies have not been conducted with fluorescein sodium. It is also not known whether fluorescein sodium can cause fetal harm when administered to a pregnant woman. Fluorescein sodium should be given to a pregnant woman only if clearly needed.

Nursing Mothers

Fluorescein sodium has been demonstrated to be excreted in human milk. Caution should be exercised when fluorescein sodium is administered to a nursing woman.

Pediatric Use

Safety and effectiveness in pediatric patients have been established.

Geriatric Use

No overall differences in safety or effectiveness have been observed between elderly and other adult patients.

ADVERSE REACTIONS (see WARNINGS and PRECAUTIONS)

Nausea, vomiting, gastrointestinal distress, headache, syncope, hypotension, and symptoms and signs of hypersensitivity have occurred. Cardiac arrest, basilar artery ischemia, severe shock, convulsions, thrombophlebitis at the injection site, and rare cases of death have been reported. Extravasation of the solution at the injection site causes intense pain at the site and a dull aching pain in the injected arm (see WARNINGS). Generalized hives and itching, bronchospasm and anaphylaxis have been reported. A strong taste may develop after injection.

DOSAGE AND ADMINISTRATION

The normal adult dose of FLUORESCITE® Injection 10% is 500 mg (100 mg/mL) via intravenous administration.

For children, the dose should be calculated on the basis of 35 mg for each ten pounds of body weight (7.7 mg/kg body weight).

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration. Do not mix or dilute with other solutions or drugs. Flush intravenous cannulas before and after drugs are injected to avoid physical incompatibility reactions.

Inject the dose rapidly (1 mL per second is normally recommended) into the antecubital vein, after taking precautions to avoid extravasation. A syringe, filled with FLUORESCITE®, may be attached to transparent tubing and a 23 gauge butterfly needle for injection. Insert the needle and draw the patient's blood to the hub of the syringe so that a small air bubble separates the patient's blood in the tubing from the fluorescein. With the room lights on, slowly inject the blood back into the vein while watching the skin over the needle tip. If the needle has extravasated, the patient's blood will be seen to bulge the skin and the injection should be stopped before any fluorescein is injected. When assured that extravasation has not occurred, the room light may be turned off and the fluorescein injection completed. Luminescence usually appears in the retina and choroidal vessels in 7 to 14 seconds and can be observed by standard viewing equipment.

Reduction in dose from 5 ml to 2 ml of FLUORESCITE Injection 10% may be appropriate in cases when a highly sensitive imaging system e.g., scanning laser ophthalmoscope is used.

HOW SUPPLIED

FLUORESCITE® (fluorescein injection, USP) 10% is supplied in a single use 5 mL glass vial with a gray FluroTec coated chlorobutyl (latex free) stopper and purple flip-off aluminum seal. It contains a sterile, red-orange solution of fluorescein sodium.

NDC 0065-0092-05

Deputy Division Director Labeling Revision Review
Wiley A. Chambers, M.D.
NDA 21-980
Fluorescite (fluorescein injection, USP) 10%

Storage

Store at 2°- 25°C (36°- 77°F). Do Not Freeze
RX Only

Mfd. for:

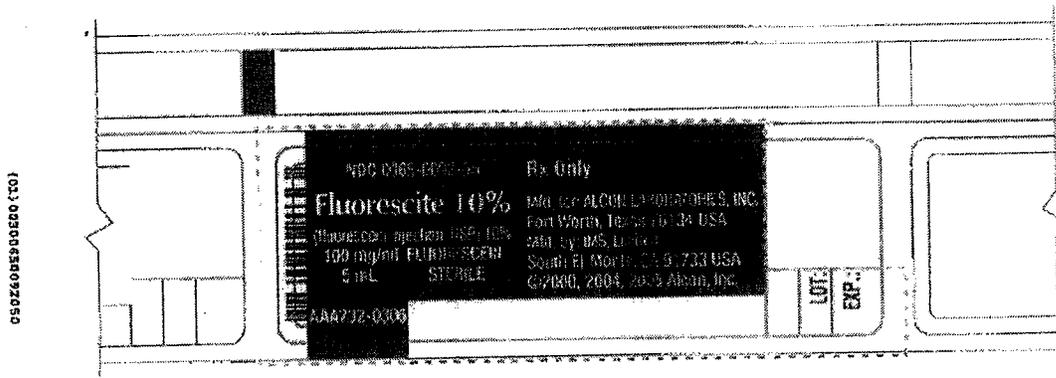
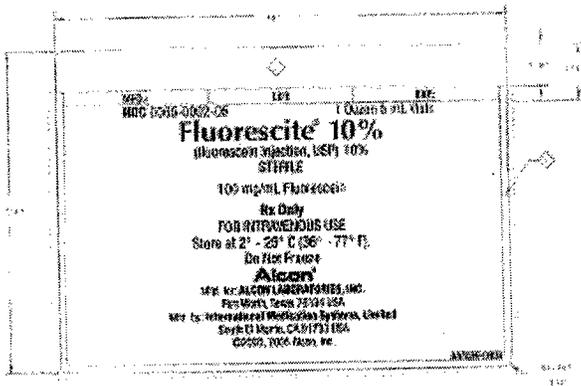
ALCON LOGO®
ALCON, INC.
Fort Worth, Texas 76134 USA

Mfd. by:

International Medication Systems, Limited
South El Monte, CA 91733 USA
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Proposed Carton and Container Labeling



Reviewer's Comments: *Acceptable.*

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/s/

Wiley Chambers
3/24/2006 10:30:12 AM
MEDICAL OFFICER

William Boyd
3/27/2006 10:09:34 AM
MEDICAL OFFICER

Janice Soreth
3/28/2006 03:42:26 PM
MEDICAL OFFICER

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