CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

022572Orig1s000

CLINICAL PHARMACOLOGY AND BIOPHARMACEUTICS REVIEW(S)

OFFICE OF CLINICAL PHARMACOLOGY REVIEW

NDA:	22-572
Submission Date(s):	August 8, 2011
Brand Name	Mitosol™
Generic Name	Mitomycin
Primary Reviewer	Yongheng Zhang, Ph.D.
Team Leader	Philip Colangelo, Pharm.D; Ph. D.
OCP Division	DCP4
OND Division	DTOT
Applicant	Mobius Therapeutics, LLC
Relevant IND(s)	IND 75,734
Submission Type; Code	Resubmission, Class 2
Formulation; Strength(s)	Mitosol™ (mitomycin for solution). NOT FOR INJECTION. Each vial contains 0.2 mg of mitomycin
Indication	As an adjunct to ab externo glaucoma surgery

1. EXECUTIVE SUMMARY

On December 22, 2010, the Agency issued a complete response to the NDA 22-572 submitted on June 21, 2010. In the current submission, the Applicant submitted a complete, class 2 response to the December 22, 2010, action letter.

There is no additional clinical pharmacology studies submitted in the resubmission, therefore, no substantial review is needed from a clinical pharmacology perspective for the current review cycle. Please refer to Clinical Pharmacology Review on the original submission by Dr. Kimberly Bergman on November 18, 2010, which contained the label recommendations. As the sponsor submitted a new proposed label in the resubmission, the reviewer updated the label recommendations from a clinical pharmacology perspective.

Reference ID: 3028137

Yongheng Zhang, Ph.D.

Division of Clinical Pharmacology 4

Office of Clinical Pharmacology

Concurrence: Philip Colangelo, Pharm.D.; Ph.D.

Team Leader

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Office of Clinical Pharmacology

cc:

Division File: NDA 22-572

HFD-520 (CSO/Germain)

HFD-520 (MO/Boyd)

HFD-520 (Chambers)

HFD-880 (Lazor)

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/s/

YONGHENG ZHANG
10/12/2011

PHILIP M COLANGELO
10/21/2011

OFFICE OF CLINICAL PHARMACOLOGY REVIEW

NDA:	22-572
Submission Date(s):	21JUN2010
Brand Name	Optomycin™ Kit
Generic Name	Mitomycin for ophthalmic solution 0.2 mg/vial
Primary Reviewer	Kimberly L. Bergman, Pharm.D.
Team Leader	Charles Bonapace, Pharm.D.
OCP Division	DCP4
OND Division	DAIOP
Applicant	Mobius Therapeutics, LLC
Relevant IND(s)	IND 75,734
Submission Type; Code	505(b)(2) application
Formulation; Strength(s)	Optomycin™ Kit for Ophthalmic Use, mitomycin for ophthalmic solution 0.2 mg/vial
Indication	Treatment of refractory glaucoma as an adjunct to ab externo glaucoma surgery by topical application to the exposed site of a filtering bleb during trabeculectomy surgery to prolong the closing of the surgically created fistula, thereby allowing maintenance of sub-hypertensive intraocular pressure in patients refractory to maximal medical therapy in whom trabeculectomy surgery is indicated

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1. EXECUTIVE SUMMARY

Mobius Therapeutics has developed an ophthalmic preparation of mitomycin in kit form (Optomycin™). The Optomycin™ Kit consists of a sterile single-use package of components to provide a standardized 1-mL volume of 0.2 mg/mL Mitomycin, USP. Mitomycin is an antibiotic derived from *Streptomyces caespitosis* that has anti-proliferative properties. Available for many decades as a standard of care cancer chemotherapeutic agent, mitomycin C is a potent DNA alkylating agent that inhibits DNA replication and cell proliferation. Widely recognized as a potent anti-proliferative agent, mitomycin has been extensively tested off-label for a variety of ocular indications in which inhibited cell proliferation was postulated as a useful adjunct to surgery. Optomycin™ Kit is proposed for the treatment of refractory glaucoma as an adjunct to ab externo glaucoma surgery by topical application to the exposed site of a filtering bleb during trabeculectomy surgery to prolong the closing of the surgically created fistula, thereby allowing maintenance of sub-hypertensive intraocular pressure in patients refractory to maximal medical therapy in whom trabeculectomy surgery is indicated.

Optomycin™ is intended for topical application to the surgical site of glaucoma filtration surgery. It is not intended for direct intraocular administration. Each vial of Optomycin™ contains 0.2 mg of mitomycin and mannitol in a 1:2 concentration ratio to be reconstituted with sterile water for injection. (b) (4)

The current submission, a 505(b)(2) application, presents existing published literature and information referenced in previously submitted NDAs for the mitomycin C oncology indications to support product approval for the proposed ophthalmic use of Optomycin™ Kit. The applicant has not conducted nor sponsored any additional nonclinical or clinical studies of mitomycin C. The applicant has submitted a request for waiver of the requirement for submission of evidence of in vivo bioavailability for the proposed mitomycin kit based on a comparison to the Reference Listed Drug (RLD) Mutamycin (Mitomycin for Injection USP; Bristol Myers Squibb; NDA 062336).

Based upon the expected systemic exposure following administration of the proposed ophthalmic preparation of mitomycin versus clinical doses of the RLD, the applicant's request to waive the requirement for in vivo bioavailability studies is acceptable.

1.1. Recommendation

The applicant's request to waive the requirement for in vivo bioavailability studies is acceptable from a clinical pharmacology perspective.

1.2. Phase IV Commitments

No phase IV commitments are recommended.

1.3. Summary of Important Clinical Pharmacology Findings

As described in this 505(b)(2) application, the pharmacokinetic characteristics of mitomycin have been previously well-described for the IV formulation with the same active and inactive ingredients. The applicant has submitted a request for waiver of the requirement for submission of evidence of in vivo bioavailability for the proposed mitomycin kit based on the rationale that the bioavailability to the RLD is self-evident because this 505(b)(2) NDA is based upon the RLD Mutamycin (Mitomycin for Injection USP; Bristol Myers Squibb; NDA 062336).

The applicant's request to waive the requirement for in vivo bioavailability studies is acceptable, as outlined in 21CFR320.22(b)(1). The bioavailability of the proposed drug product is self-evident since "the drug product (i) is a parenteral solution intended solely for administration by injection, or an ophthalmic or otic solution; and (ii) contains the same active and inactive ingredients in the same concentration as a drug product that is the subject of an approved full new drug application or abbreviated new drug application."

_____
Kimberly L. Bergman, Pharm.D.
Division of Clinical Pharmacology 4
Office of Clinical Pharmacology

Concurrence:

_____
Charles R. Bonapace, Pharm.D.
Team Leader

cc:
Division File: NDA 22-572
HFD-520 (CSO/Rodgers)
HFD-520 (MO/Boyd)
HFD-520 (Chambers)
HFD-880 (Lazor, Reynolds, Bonapace)

2. QUESTION BASED REVIEW

Since this submission is an NDA for a locally administered ophthalmic drug product, only relevant questions from the OCP question-based review (QBR) format are addressed below.

2.1. General Attributes of the Drug

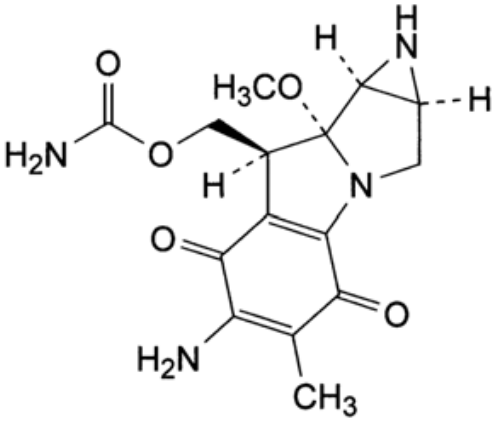
2.1.1. What are the highlights of the chemistry and physical-chemical properties of the drug substance and the formulation of the drug product?

The applicant has developed an ophthalmic preparation of mitomycin in kit form (Optomycin™). The Optomycin™ Kit contains Mitomycin, USP ophthalmic solution, 0.2 mg/vial in a sterile single-use package.

The chemical structure and physical-chemical properties of the active ingredient mitomycin are as follows:

Structural Formula: $C_{15}H_{18}N_4O_5$

Chemical Structure:



Chemical Name: 7-amino-9α-methoxymitosane

Compendial Name: Mitomycin (USP, Ph Eur)

Chemical Abstract Service (CAS) Registry Number: 50-07-7

Molecular Weight: 334.3

Physical Description: blue-violet crystals or crystalline powder

Solubility: slightly soluble in water, freely soluble in dimethylacetamide, sparingly soluble in methanol, slightly soluble in acetone

The qualitative and quantitative composition of the proposed Optomycin™ kit drug product is shown in Table 2.2-1.

Table 2.2-1 Composition of Optomycin™ Drug Product

Ingredient	Quality Standard	Function	Composition of lyophilized product (mg/vial)	Composition of reconstituted product (mg/mL)
Mitomycin	USP/Ph. Eur.	Active ingredient	0.2	0.2
Mannitol	USNF/Ph. Eur.	(b) (4)	0.4	0.4

(b) (4)

USP, United States Pharmacopoeia
USNF, United States National Formulary
Ph. Eur., European Pharmacopoeia
Source: Section 2.3.P.1

The drug product consists of lyophilized blue violet powder/cake which must be reconstituted with sterile water for injection before administration. Each mL of reconstituted solution contains 0.2 mg of Mitomycin.

2.1.2. What is the proposed mechanism of drug action and therapeutic indication?

Mitomycin is an antibiotic derived from *Streptomyces caespitosis* that has anti-proliferative properties. Available for many decades as a standard of care cancer chemotherapeutic agent, mitomycin C is a potent DNA alkylating agent that inhibits DNA replication and cell proliferation. Widely recognized as a potent anti-proliferative agent, mitomycin has been extensively tested off-label for a variety of ocular indications in which inhibited cell proliferation was postulated as a useful adjunct to surgery. Optomycin™ Kit is proposed for the treatment of refractory glaucoma as an adjunct to ab externo glaucoma surgery by topical application to the exposed site of a filtering bleb during trabeculectomy surgery to prolong the closing of the surgically created fistula, thereby allowing maintenance of sub-hypertensive intraocular pressure in patients refractory to maximal medical therapy in whom trabeculectomy surgery is indicated.

2.1.3. What is the proposed dosage and route of administration?

Optomycin™ is intended for topical application to the surgical site of glaucoma filtration surgery. It is not intended for direct intraocular administration. Each vial of Optomycin™ contains 0.2 mg of mitomycin and mannitol in a 1:2 concentration ratio to be reconstituted with sterile water for injection. (b) (4)

2.2. General Clinical Pharmacology

2.2.1. What are the design features of the clinical pharmacology and clinical studies used to support dosing claims?

Subsequent to agreement with the FDA, the current submission, a 505(b)(2) application, presents existing published literature and information referenced in previously submitted NDAs for the mitomycin C oncology indications to support product approval for the proposed ophthalmic use of Optomycin™ Kit. The applicant has not conducted nor sponsored any additional nonclinical or clinical studies with mitomycin C, or more specifically Optomycin™ Kit. The submission

includes data gathered from 22 published papers describing prospective clinical studies with mitomycin as adjuvant therapy to glaucoma filtration surgery. In addition, efficacy findings from 20 published papers describing retrospective studies with mitomycin and two review articles supporting the efficacy of mitomycin in filtration surgery are described. The drug product used in these published reports is the previously approved and marketed 5 to 40 mg/vial formulations of mitomycin for intravenous use.

2.2.2. What is the basis for selecting the response endpoints (i.e. clinical or surrogate endpoints) or biomarkers (collectively called pharmacodynamics (PD)) and how are they measured in clinical pharmacology and clinical studies?

Control of intraocular pressure (IOP), differences in postoperative visual acuity, the need for postoperative medication use, and the need for additional surgery served as the primary efficacy endpoints in the publications supporting efficacy of mitomycin for the proposed ophthalmic indication. For further discussion of the suitability of efficacy endpoints in the published studies submitted for review, refer to the Medical Officer's review of NDA 22-572.

2.2.3. Are the active moieties in the biological fluid appropriately identified and measured to assess pharmacokinetic parameters?

Not applicable (a request for waiver of in vivo bioavailability studies pursuant to 21 CFR 320.22(b)(1)(i) was submitted in the current application). See section 2.2.5.

2.2.4. Exposure-Response

2.2.4.1. What are the characteristics of the exposure-response relationships (dose-response, concentration-response) for efficacy?

The 22 prospective studies (9 randomized, controlled, masked and 13 of uncertain design) employed various doses and durations of mitomycin therapy. The most commonly used dose was 0.2 mg/mL (doses ranged between 0.1 to 0.5 mg/mL) and the most common period of exposure between 2 and 3 minutes (range: from 2 to 4 minutes). Two of the reported studies included a dose-comparison in their study design (Robin, 1997 and Sanders, 1998).

The first dose comparison study (Robin, 1997) was a prospective, double-masked, placebo-controlled study designed to evaluate the long-term dose-response relationship between mitomycin concentration/duration of exposure and the change in IOP and incidence of complications in patients undergoing trabeculectomy. Three hundred (300) eyes were randomized into four treatment groups in a prospective, double-masked fashion: Group 1: placebo; Group 2: mitomycin 0.2mg/mL/2min; Group 3: mitomycin 0.2mg/mL/4min, and Group 4: mitomycin 0.4mg/mL/2 min. Although a decrease in IOP was observed in all three mitomycin-treated groups, the differences in IOP among the three groups was not statistically significant, as summarized in Table 2.2.4.1-1. The clinical significance of differences observed between the three mitomycin-treated groups is questionable.

Table 2.2.4.1-1 Estimated Difference Between Mitomycin C Treated Groups (Robin, 1997)

Group (# of patients/# of eyes)	Estimated Difference vs. Placebo (mmHg)	95% CI	p-value
Group 2 (0.2 mg/mL/2 min)	2.0	0.8, 3.3	0.001
Group 3 (0.2 mg/mL/4 min)	3.0	1.8, 4.3	< 0.001
Group 4 (0.4 mg/mL/2 min)	2.9	1.6, 4.2	< 0.001

Reference: Robin AL, Ramakrishnan R, Krishnadas R, Smith SD, Katz JD, Selvaraj S, Skuta GL, Bhatnagar R. A long-term dose-response study of mitomycin in glaucoma filtration surgery. Arch Ophthalmol. 1997 Aug;115(8):969-74.

The second dose comparison study (Sanders, 1998) was a prospective, randomized, masked study that compared the effectiveness of 0.2mg/mL and 0.4mg/mL of mitomycin during filtering surgery in eyes that were at higher risk from previous conjunctival incisional surgery. The eyes of 50 patients with primary open-angle, pseudoexfoliation, or pigmentary glaucoma who had previously undergone either limbal cataract surgery or trabeculectomy were enrolled. Patients were randomized to receive either 0.2 mg/mL/2 min or 0.4 mg/mL/2 min of mitomycin during surgery. Overall, there were no statistically significant differences between treatment groups in mean IOP at any time point up to 12 months ($p \geq 0.25$) as summarized in Table 2.2.4.1-2.

Table 2.2.4.1-2 Dose Comparison of IOP Before and After Trabeculectomy for Mitomycin C Treated Groups (Sanders, 1998)

	Mitomycin C Dose Groups		
Mean (±SD) IOP in mmHg	**0.2mg/ml/2min**	**0.4mg/ml/2min**	**P-value[a]**
Before surgery	28.8 (±13.7)	25.0 ± 8.6	0.25
After surgery			
1 Day	2.8 (±2.8)	3.6 (±3.7)	0.44
1 Week	4.9 (±2.9)	5.16 (±3.9)	0.31
1 Month	13.6 (±7.6)	14.2 (±8.8)	0.81
3 Months	14.4 (±7)	12.7 (±5.7)	0.37
6 Months	13.3 (±4.7)	14.3 (±8.5)	0.65
1 Year	14.2 (±6.3)	13.7 (±6.2)	0.78

IOP = Intraocular pressure; MMC = Mitomycin; mmHg = Millimeters of mercury.
[a] Student *t* test.

Reference: Sanders SP, Cantor LB, Dobler AA, Hoop JS. Mitomycin C in higher risk trabeculectomy: a prospective comparison of 0.2- to 0.4-mg/cc doses. J Glaucoma. 1999 Jun;8(3):193-8.

In summary, a higher dose (0.4 mg/mL/2 min) of mitomycin was generally not significantly more effective than the proposed dose of 2 mg/mL/2 min. For further discussion of the efficacy of the proposed ophthalmic dose of mitomycin, refer to the Medical Officer's review of NDA 22-572.

2.2.4.2. What are the characteristics of the exposure-response relationships (dose-response, concentration-response) for safety?

The safety profile of mitomycin as an ocular topical drug has been derived from analysis of publications presenting the results of prospective controlled trials in glaucoma, supplemented by literature of retrospective studies, and from analysis of FDA's Adverse Event Reporting System

(AERS Database). Mirza and colleagues (1999) conducted a retrospective chart review of the records of all patients with advanced primary open-angle glaucoma (POAG) who had trabeculectomy with mitomycin 0.5 mg/mL applied for 5 minutes (N=17) and 0.25 mg/mL applied for 3 minutes (N=13) from January 1995 to February 1995. Results indicated that hypotony occurred in 11 patients (65%) in the 0.5 mg/mL group compared to 1 patient (8%) in the 0.25 mg/mL group; lens opacities occurred in 8 patients (47%) in the 0.5 mg/mL group compared to 7 patients (54%) in the 0.25 mg/mL group; choroidal detachment occurred in 6 patients (35%) in the 0.5 mg/mL group compared to 3 patients (23%) in the 0.25 mg/mL group; and rises in pressure (> 20 mmHg) occurred in 2 patients (11.8%) in the 0.5 mg/mL group compared to none of the patients in the 0.25 mg/mL group. In addition, disc swelling, bleb ulcer, wound leakage, and cystic bleb each occurred in 1 patient (6%) in the 0.5 mg/mL group. In the 0.25 mg/mL group, there were no cases of disc swelling, bleb ulcer, or wound leakage. However, cystic bleb occurred in 4 patients (31%) in the 0.25 mg/mL group. Based on this retrospective comparison, a dose-response for safety of mitomycin for some ocular adverse events is suggested. For further discussion of the safety of the proposed ophthalmic dose of mitomycin, refer to the Medical Officer's review of NDA 22-572.

Reference: Mirza GE, Karakucuk S, Dogan H, Erkilic K. Comparison of two different concentrations of mitomycin-C in the surgical treatment of primary open angle glaucoma. Erciyes Tip Dergisi. 1999;21(3):132-141.

2.2.5. What are the PK characteristics of the drug and its major metabolite?

As described in this 505(b)(2) application, the pharmacokinetic characteristics of mitomycin have been previously well-described for the IV formulation with the same active and inactive ingredients. The applicant has submitted a request for waiver of the requirement for submission of evidence of in vivo bioavailability for the proposed mitomycin kit based on the rationale that the bioavailability is self-evident as outlined in 21CFR320.22(b)(1), as this 505(b)(2) NDA is based upon the RLD Mutamycin (Mitomycin for Injection USP; Bristol Myers Squibb; NDA 062336).

The applicant's request to waive the requirement for in vivo bioavailability studies is acceptable. The proposed ophthalmic preparation of mitomycin in kit form (Optomycin™) contains the same active and inactive ingredients in the same dosage form, differing only in the route of administration (ophthalmic versus IV) and drug product strength (0.2 mg/vial for single use versus 5, 20, or 40 mg/vial for the RLD). Based on a comparison of the proposed dose of up to 0.2 mg in the current 505(b)(2) application to IV doses used clinically for treatment of oncologic indications (up to 20 mg/m^2), systemic concentrations in humans upon ocular administration are expected to be multiple orders of magnitude lower than those achieved by IV administration. In addition, the safety of mitomycin at doses of up to 20 mg/m^2 is well-established based on years of clinical experience.

2.3. Intrinsic Factors
Not applicable.

2.4. Extrinsic Factors
Not applicable.

2.5. General Biopharmaceutics
Not applicable.

2.6. Analytical Section

Not applicable.

3. LABELING RECOMMENDATIONS

The following changes reflect Clinical Pharmacology Reviewer recommendations to the proposed labeling (recommendations appear in bold, italicized, underlined, and/or strikethrough type).

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

(b) (4) inhibits the synthesis of deoxyribonucleic acid (DNA). The guanine and cytosine content correlates with the degree of mitomycin-induced cross-linking. (b) (4) cellular RNA and protein synthesis (b) (4) suppressed.

12.(b) (4)3 (b) (4) Pharmacokinetics

(b) (4)

Absorption

The systemic exposure of mitomycin following ocular administration of (b) (4) in humans is unknown. Based on a comparison of the proposed dose of up to 0.2 mg to intravenous (IV) doses of mitomycin used clinically for treatment of oncologic indications (up to 20 mg/m^2), systemic concentrations in humans upon ocular administration are expected to be multiple orders of magnitude lower than those achieved by IV administration.

Metabolism

~~*In humans, mitomycin is* (b) (4) *cleared from ophthalmic tissue after intraoperative topical application and irrigation, as metabolism occurs in other affected tissues.*~~ Systemic clearance is affected primarily by metabolism in the liver, (b) (4) The rate of clearance is inversely proportional to the maximal serum concentration because (b) (4) of saturation of the degradative pathways.

(b) (4)

Excretion

Approximately 10% of an injectable dose of mitomycin is excreted unchanged in the urine. Since metabolic pathways are saturated at relatively low doses, the percent of a dose excreted in urine increases (b) (4)

(b) (4)

4. APPENDICES

4.1. Applicant Request for Waiver of In Vivo Bioavailability Studies

Applicant's Justification:
Pursuant to 21 CFR 320.22(b), "the in vivo bioavailability/bioequivalence of the drug product may be self-evident. FDA shall waive the requirement for the submission of evidence obtained in vivo measuring the bioavailability or demonstrating the bioequivalence of these drug products. A drug product's in vivo bioavailability or bioequivalence may be considered self-evident based on other data in the application if the product meets one of the following criteria: (1) The drug product (i) Is a parenteral solution intended solely for administration by injection, or an ophthalmic or otic solution." Thus, the bioavailability to the RLD is self-evident as outlined in 21CFR320.22(b)(1), as this 505(b)(2) NDA is based upon the RLD Mutamycin (Mitomycin for Injection USP; Bristol Myers Squibb; NDA 062336).

Reviewer Assessment:
The applicant's request to waive the requirement for in vivo bioavailability studies is acceptable, as outlined in 21CFR320.22(b)(1). The bioavailability is self-evident since "the drug product (i) is a parenteral solution intended solely for administration by injection, or an ophthalmic or otic solution; and (ii) contains the same active and inactive ingredients in the same concentration as a drug product that is the subject of an approved full new drug application or abbreviated new drug application." The proposed ophthalmic preparation of mitomycin in kit form (Optomycin™) contains the same active and inactive ingredients in the same dosage form, differing only in the route of administration (ophthalmic versus IV) and drug product strength (0.2 mg/vial for single use versus 5, 20, or 40 mg/vial for the RLD). Based on a comparison of the proposed dose of up to 0.2 mg in the current 505(b)(2) application to IV doses used clinically for treatment of oncologic indications (up to 20 mg/m^2), systemic concentrations in humans upon ocular administration are expected to be multiple orders of magnitude lower than those achieved by IV administration. In addition, the safety of mitomycin at doses of up to 20 mg/m^2 is well-established based on years of clinical experience.

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/s/

KIMBERLY L BERGMAN
11/18/2010

CHARLES R BONAPACE
11/18/2010

CLINICAL PHARMACOLOGY NDA FILEABILITY CHECKLIST

NDA:	22-572
Drug Name:	Optomycin™ (mitomycin) Kit for Ophthalmic Use
Applicant:	Mobius therapeutics, LLC
Submission Date:	21JUN2010
Filing Date:	21AUG2010
PDUFA Date:	22DEC2010
OCP Primary Reviewer:	Kimberly L. Bergman, PharmD
OCP Team Leader:	Charles Bonapace, PharmD

QUESTION	***YES***	***NO***	***NA***	***COMMENTS***
Fileability: ***Is the Clinical Pharmacology section of the application fileable?*** ***(if 'NO', please comment as to why it is not fileable)***	***X***			
Fileability Review Components				
1. Is the clinical pharmacology section of the NDA organized in a manner to allow substantive review to begin (including a table of contents, proper pagination, reference links, etc.)?	☒	☐	☐	
2. Are the clinical pharmacology studies of appropriate design and breadth of investigation to meet the basic requirements for approvability of this product?	☐	☐	☒	No clinical pharmacology studies were submitted in this application. The Applicant has requested a waiver of the requirement for in vivo bioavailability studies.
3. If multiple formulations were used in the clinical development of the product, does the NDA contain appropriate biopharmaceutics information to allow comparison between the clinical development and to-be-marketed product(s) (i.e. pivotal BE)?	☐	☐	☒	See additional comments below.
4. If unapproved products or altered approved products were used as active controls, was bioequivalence to the approved product demonstrated?	☐	☐	☒	
5. Are complete and relevant bioanalytical reports included in the NDA submission?	☐	☐	☒	
6. If applicable, was the sponsor's request for a waiver of the requirement for submission of in vivo bioavailability data included in the NDA submission?	☒	☐	☐	
7. Are complete datasets supporting the clinical pharmacology studies included in the NDA submission?	☐	☐	☒	
Additional Comments: The current 505(b)(2) application is for a single-use ophthalmic preparation of mitomycin in kit form (Optomycin™). The support for efficacy and safety of this drug product is based on existing published literature describing off-label use of the already approved and marketed IV mitomycin drug product for the proposed indication. In the proposed lyophilized drug product, the proportion of API (mitomycin) to the excipient (mannitol) is kept similar to that in the lyophilized approved injectable product.				

OCP Primary Reviewer	Date
OCP Team Leader	Date

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22572	ORIG-1	MOBIUS THERAPEUTICS	Optomycin Kit for Ophthalmic Use

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/s/

KIMBERLY L BERGMAN
07/16/2010

CHARLES R BONAPACE
07/16/2010