

Clinical Investigator Financial Disclosure NDA 206276
Review Template

Application Number: 206276

Submission Date(s): July 30, 2014

Applicant: Alcon Laboratories

Product: Olopatadine hydrochloride 0.7%

Reviewer: Wiley A. Chambers, MD

Date of Review: December 14, 2014

Covered Clinical Study (Name and/or Number): C-10-126

Was a list of clinical investigators provided:	Yes <input checked="" type="checkbox"/>	No <input type="checkbox"/> (Request list from applicant)
Total number of investigators identified: <u>3</u>		
Number of investigators who are sponsor employees (including both full-time and part-time employees): <u>0</u>		
Number of investigators with disclosable financial interests/arrangements (Form FDA 3455): <u>0</u>		
<p>If there are investigators with disclosable financial interests/arrangements, identify the number of investigators with interests/arrangements in each category (as defined in 21 CFR 54.2(a), (b), (c) and (f)):</p> <p style="padding-left: 40px;">Compensation to the investigator for conducting the study where the value could be influenced by the outcome of the study: _____</p> <p style="padding-left: 40px;">Significant payments of other sorts: _____</p> <p style="padding-left: 40px;">Proprietary interest in the product tested held by investigator: _____</p> <p style="padding-left: 40px;">Significant equity interest held by investigator in sponsor of covered study: _____</p>		
Is an attachment provided with details of the disclosable financial interests/arrangements:	Yes <input checked="" type="checkbox"/>	No <input type="checkbox"/> (Request details from applicant)
Is a description of the steps taken to minimize potential bias provided:	Yes <input checked="" type="checkbox"/>	No <input type="checkbox"/> (Request information from applicant)
Number of investigators with certification of due diligence (Form FDA 3454, box 3) <u>0</u>		
Is an attachment provided with the reason:	Yes <input type="checkbox"/>	No <input type="checkbox"/> (Request explanation from applicant)

Covered Clinical Study (Name and/or Number): C-12-053

Was a list of clinical investigators provided:	Yes <input checked="" type="checkbox"/>	No <input type="checkbox"/> (Request list from applicant)
Total number of investigators identified: <u>6</u>		
Number of investigators who are sponsor employees (including both full-time and part-time employees): <u>0</u>		
Number of investigators with disclosable financial interests/arrangements (Form FDA 3455): <u>0</u>		
<p>If there are investigators with disclosable financial interests/arrangements, identify the number of investigators with interests/arrangements in each category (as defined in 21 CFR 54.2(a), (b), (c) and (f)):</p> <p>Compensation to the investigator for conducting the study where the value could be influenced by the outcome of the study: _____</p> <p>Significant payments of other sorts: _____</p> <p>Proprietary interest in the product tested held by investigator: _____</p> <p>Significant equity interest held by investigator in sponsor of covered study: _____</p>		
Is an attachment provided with details of the disclosable financial interests/arrangements:	Yes <input checked="" type="checkbox"/>	No <input type="checkbox"/> (Request details from applicant)
Is a description of the steps taken to minimize potential bias provided:	Yes <input checked="" type="checkbox"/>	No <input type="checkbox"/> (Request information from applicant)
Number of investigators with certification of due diligence (Form FDA 3454, box 3) <u>0</u>		
Is an attachment provided with the reason:	Yes <input type="checkbox"/>	No <input type="checkbox"/> (Request explanation from applicant)

Covered Clinical Study (Name and/or Number): C-12-028

Was a list of clinical investigators provided:	Yes <input checked="" type="checkbox"/>	No <input type="checkbox"/> (Request list from applicant)
Total number of investigators identified: <u>15</u>		
Number of investigators who are sponsor employees (including both full-time and part-time employees): <u>0</u>		
Number of investigators with disclosable financial interests/arrangements (Form FDA 3455): <u>1</u>		
<p>If there are investigators with disclosable financial interests/arrangements, identify the number of investigators with interests/arrangements in each category (as defined in 21 CFR 54.2(a), (b), (c) and (f)):</p> <p>Compensation to the investigator for conducting the study where the value could be influenced by the outcome of the study: <u>0</u></p> <p>Significant payments of other sorts: <u>1</u></p> <p>Proprietary interest in the product tested held by investigator: <u>0</u></p> <p>Significant equity interest held by investigator in sponsor of covered study: <u>0</u></p>		
Is an attachment provided with details of the disclosable financial interests/arrangements:	Yes <input checked="" type="checkbox"/>	No <input type="checkbox"/> (Request details from applicant)
Is a description of the steps taken to minimize potential bias provided:	Yes <input checked="" type="checkbox"/>	No <input type="checkbox"/> (Request information from applicant)
Number of investigators with certification of due diligence (Form FDA 3454, box 3) <u>0</u>		
Is an attachment provided with the reason:	Yes <input type="checkbox"/>	No <input type="checkbox"/> (Request explanation from applicant)

The applicant has adequately disclosed financial interests/arrangements with clinical investigators. The one reported interest is not likely to raise questions about the integrity of the data because the studies were multicenter, masked trials and the one investigator with a potential interest was responsible for a small percentage of the overall application. The applicant reports that they took the following steps to minimize potential bias:

- The studies were double-masked in which patients were randomized sequentially at each investigational center to receive 1 of 2 (in C-12-028), 3 (in C-10-126) or 4 (in C-12-053) masked study drugs.
- For each study, a list of sequential subject numbers was generated by a member of the Alcon SAS programming group not involved in the conduct of the study or had any contact with study subjects or investigators. Each subject number was associated with a treatment according to a random process. Only once all study data was verified, validated and the database locked, individual subject data were unmasked.
- As a double-masked study, the patients, the Investigators, the investigational center staff, the Sponsor, and the clinical monitors were not aware of the treatment assigned to the individual study patients.
- All study drugs were identical in appearance and supplied in masked bottles with identical packaging and labeling.
- To minimize any potential Investigator bias, designated study site staff personnel administered the first dose of study medication in the subject's eyes during Visit 1 in C-12-028 and at all dosing visits for studies C-10-126 (Visits 3A, 4A and 5) and C-12-053 (Visits 3A and 4).
- All efficacy and safety variables were assessed by masked observers.
- The treatment code was not broken at any time during any of the studies by either the investigator or the Sponsor.
- Frequent on-site monitoring was performed during the conduct of the studies to ensure compliance with protocol guidelines.

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/s/

WILEY A CHAMBERS
12/14/2014