Investigator Initiated Trial
Investigator Brochure

Alcon

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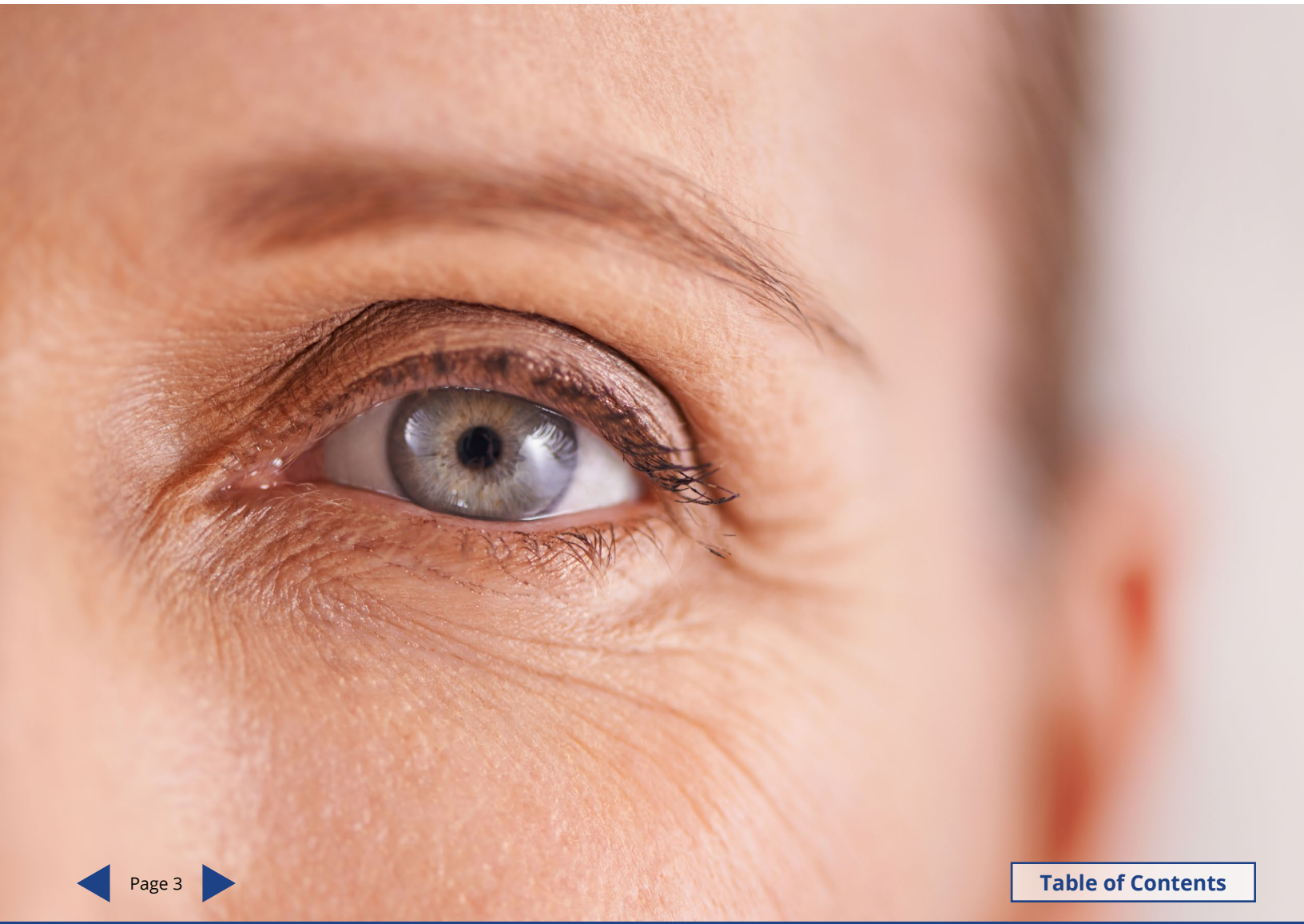
Introduction

As part of the commitment by Alcon to deliver innovative products to patients worldwide, Alcon believes in the need to support ethical independent clinical research conducted by qualified third party sponsors and investigators. The value of this scientific research, together with Alcon sponsored research, is fundamental to the understanding of the benefit/risk profile of Alcon products and the exploration of new opportunities to address unmet medical needs. This is why Alcon provides support to Investigator Initiated Trials (IITs) every year.

An IIT is defined as a study with scientific and medical merit developed and sponsored by an independent investigator or academic sponsor. An IIT may be a clinical or non-clinical study, for which the IIT sponsor requests Alcon to provide either funding, product or both. If your IIT proposal is accepted, you will retain full responsibility and control of the design, initiation, management, data analysis, monitoring, and reporting, as the sponsor of the study.

The purpose of this brochure is to provide a clear description of each of the essential requirements that must be fulfilled before support will be considered by Alcon, and to highlight your obligations as the study sponsor when your IIT is being supported by Alcon.



Requirements to Conduct an IIT

Below are the key requirements that will need to be fulfilled in order for Alcon to evaluate and consider supporting your study. Should you have any questions on these requirements, please speak to your local Medical contact.

Investigator qualifications

The Investigator's curriculum vitae would be obtained to ensure that the Investigator is suitably qualified and able to conduct the evaluation and analyses. All of the following must be met:

- Current valid license to practice medicine or optometry for clinical studies
- Good clinical practice (GCP) training within the previous 2 years to conduct a clinical study

Study criteria – the proposed study should be:

- For a legitimate research purpose – scientific merit, which complements Alcon generated research
  - To better understand the risk/benefit profile of the product
  - Address an unmet medical need
- Aligned with the Alcon product scientific/development strategy – strategic fit

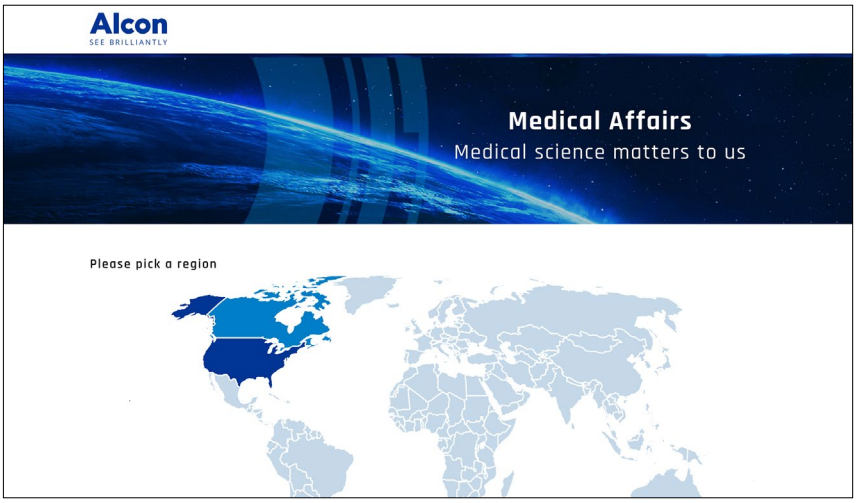
Resources – the Investigator must have the right infrastructure in place and capability to conduct the study proposed.

IIT Application Process

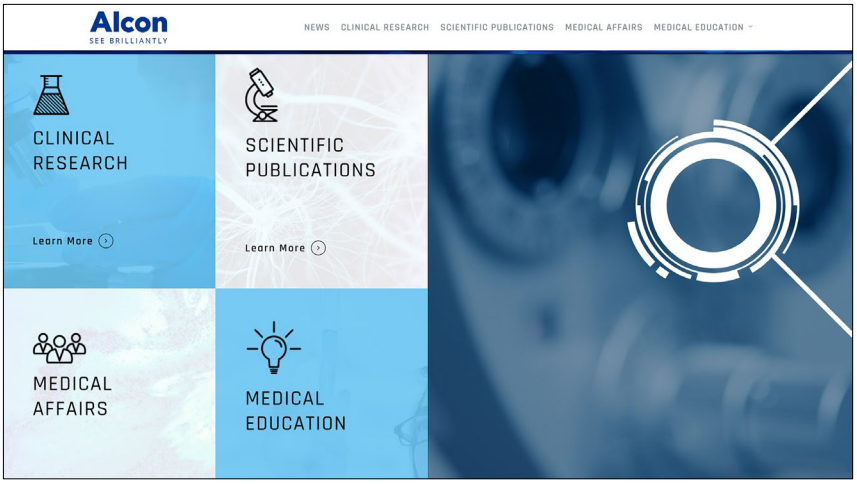
All requests for support must be submitted by the Investigator into the IIT web portal system:

Go to alconscience.com to locate IIT application portal.

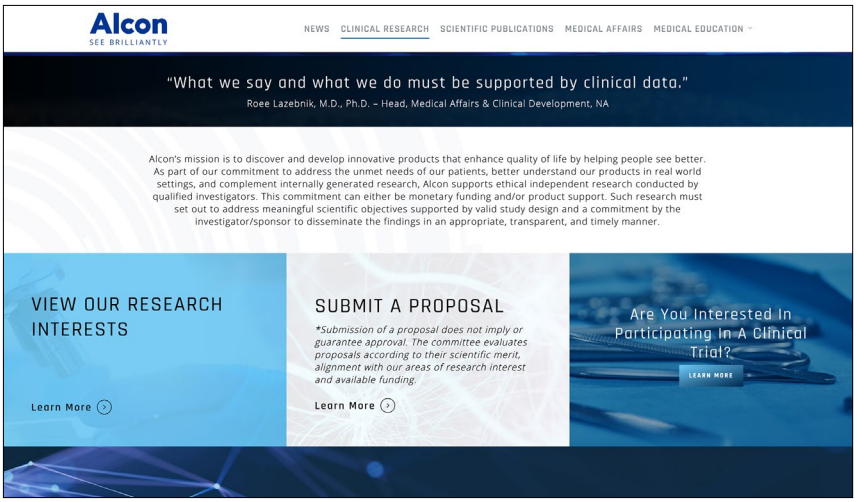
Step 1: Select Region



Step 2: Select Clinical Research



Step 3: Click Submit A Proposal

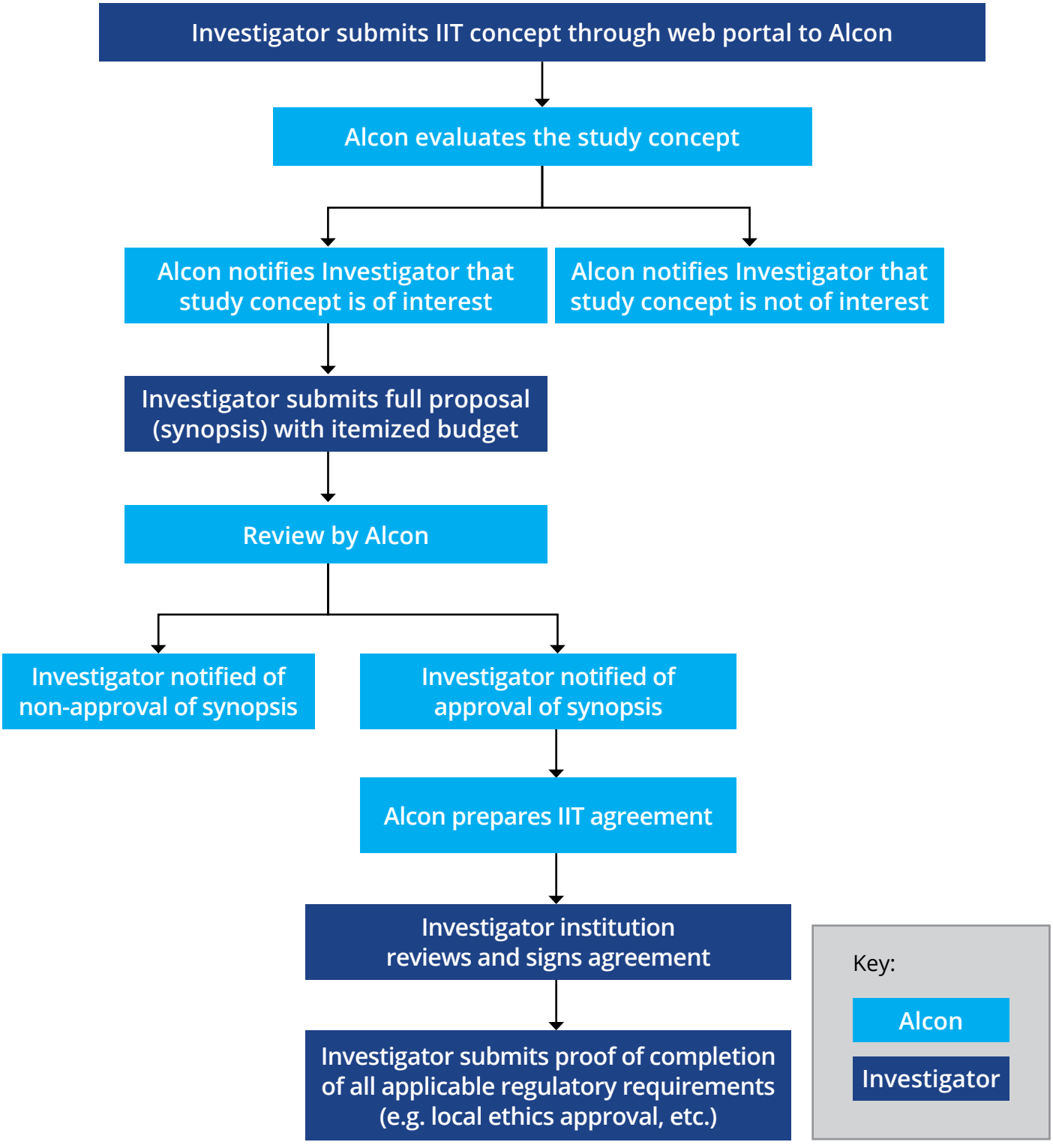


IIT Review and Approval Process

The submission of the IIT proposal and its consideration for approval will be a two-step process:

1. Submission of a concept sheet
2. If concept sheet is endorsed, submission of an IIT proposal (synopsis)

An overview of the application process required for submission of a proposal shown below:



What is a Concept Sheet?

- The concept sheet should provide primary information that will allow an initial assessment of interest in the proposed project
  - Study area, type of device and targeted population to be studied
  - Main objective of the study
  - Describing innovative part of the trial vs current knowledge (i.e. the unmet medical need that this study will address)
  - Estimated budget for study

What Will be Evaluated During the Concept Review?

- Alignment with the overall Alcon product scientific/development strategy
- Innovative aspect of the proposed project
- Pre-assessment of the regulatory status of the product, on/off-label (proposals exploring uses that are contraindicated will not be endorsed)
- Adherence to ethical standards
- Alcon budget availability

Key Elements to Provide in the Full Proposal (Synopsis)

- Synopsis including: title, background and hypothesis, primary objective, study design, inclusion/exclusion criteria, sample size and sample calculation rationale, primary endpoint, secondary endpoints, study duration, key supporting references.
- Curriculum Vitae of the principal investigator
- Detailed budget of the funding requested allowing Fair-Market Value (FMV) assessment
- List of equipment or devices requested
- Timelines
- Publication plan (meeting targeted, journal targeted)

What Will be Evaluated During the Final Review of Synopsis?

- **Project Description:**
  - Scientific merits of the study
  - Innovative study design
  - Adherence to ethical standards, GCP/ISO 14155, applicable regulations and business practices
  - Technical and practical feasibility
  - Regulatory status of the product, on/off-label use within the proposed study
- **Study Site and Principal investigator:**
  - Investigator's medical qualifications and technical expertise
  - GCP training in the last 2 years for clinical study
  - Appropriateness of study site resources to conduct the study
- **Funding:**
  - Alignment of requested funding with fair market value (FMV) of anticipated study costs
  - Alcon budget availability

Funding and Conducting the Study

Receipt of funding

IIT budgets submitted to Alcon will be subject to a FMV assessment prior to approval.

The purpose of IIT funds are to further the scientific research and knowledge within a particular therapeutic area.

IIT support may include study-related activity expenses or services but may not be given to pay for the recipient's ordinary operating expenses (i.e. expenses of activities that the recipient is already required to perform or customarily performs). The payments will be scheduled according to milestones for key achievements of the project until project completion and delivery of a final clinical study report and a draft publication. Milestones and projected timelines to deliver the milestones are agreed with the investigator and described in the agreement.

You will need to have the following items in place and provided to Alcon for release of product and/or funding:

- ❑ An institutional review board (IRB)/ethics committee (EC) approval of the protocol as applicable
- ❑ Health Authorities approval (as applicable)
- ❑ Final protocol and informed consent form (as applicable)
- ❑ Fully executed IIT Agreement with Alcon

Conducting the IIT

Study status, reporting and registration in a public database

According to the Alcon IIT Agreement, you will inform Alcon of any updates to the status of the IIT, such as the enrollment status and confirmation that safety data are being transferred to Alcon on an ongoing basis, as defined in the IIT Agreement. You must also verify that all applicable regulatory requirements have been completed; this includes protocol and informed consent form approval by the local EC and clinical trial registration in a public database, such as www.clinicaltrials.gov.

Safety Reporting Requirements

One of the most important requirements of an IIT Investigator is the ability to monitor and report safety data to the appropriate authorities and to Alcon, in a timely and accurate manner. IIT Investigators are responsible for ensuring that all adverse events (AEs and SAEs) and device deficiencies/quality complaints/malfunctions are recorded and appropriately reported to Alcon and the relevant health authorities according to applicable laws and regulations in each country where the Study will be conducted and in accordance with the IIT Agreement.

The timelines for providing the above information to Alcon may differ depending on where the study is being conducted according to local regulatory requirements. The timelines will be specified in the IIT Agreement.

In turn, Alcon will ensure that any important safety findings or urgent safety measures for the Alcon product that is the focus of the IIT are shared with you.

Study Results and Publications

Alcon requires the final study report to be provided within 12 months of the last patient last visit (LPLV). For Final Study Reports written in languages other than English, a full English translation is required for IITs that used an Alcon product.

As part of Alcon's commitment to publishing research, you are required to publish the results of IITs. As the Investigator, the content of any publication is your responsibility, and Alcon will not be involved in authorship selection or writing and cannot be included as a co-author of IIT publications. You should submit any publications to Alcon for review as specified within the IIT Agreement. Alcon support must be disclosed in any type of publication.

In order to receive the final milestone payment, you must produce a final study report within the specified timelines and attempt to publish study data, e.g. submission of a manuscript, an abstract, and/or a poster to a congress or a journal for publication.

Key Responsibilities of Alcon and the Investigator

Responsibilities	Alcon	Investigator
Development of the research protocol		✓
Review of the Research Protocol	✓	
Distribution of updated, approved product information	✓	
Submission to IRB/EC at study start and annual renewal		✓
Submission to local HA, if required		✓
Registry of IIT in a public database, such as www.clinicaltrials.gov as appropriate		✓
Implementation and monitoring of clinical research (including data monitoring)		✓
Contracting with third-party vendors (clinical research organizations, medical writing, or other analyses, patient insurance, statistical, courier, etc.) and the management and oversight of any other participating sites or contractors		✓
Conduct of research (patient inclusion, exams conduction, etc.)		✓
Ensure that the IRB/EC/local HA approved protocol is adequately followed (in accordance with GCP, ISO 14155, MDR directive, and/or other applicable guidelines and local/international standards)		✓
Submission of protocol amendments		✓
Review of protocol amendments	✓	
Maintaining clinical records of the study and assurance of the veracity of collected data and other attributions related to GCP		✓
Reporting of safety data to the manufacturer of the study product, as required, based on the study type		✓
Perform safety reconciliation, as required based on study type		✓
Reporting of safety data to HAs, as appropriate		✓
Post study results in public database, such as www.clinicaltrials.gov as appropriate		✓
Analysis of study data, prepare interim and final study reports and forward them to Alcon		✓
Submit draft publications to Alcon prior to submission to scientific congress or journal		✓
Review draft abstracts and manuscript for technical accuracy of the products description and appropriate funding disclosure	✓	
Independently publish the clinical trial results		✓
Report study results to HAs, if required according to local regulations		✓

Abbreviations

AE = Adverse Event

EC = Ethics Committee

FMV = Fair Market Value

GCP = Good Clinical Practice

HA = Health Authority

IIT = Investigator Initiated Trial

IRB = Institutional Review Board

MDR = Medical Device Regulation

SAE = Serious Adverse Event

Alcon