Investigator Initiated Trial Investigator Brochure

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Contents

Introduction

As part of Alcon's commitment to deliver innovative products to patients worldwide, Alcon supports ethical independent clinical research conducted by qualified third party investigators. IIT research enhances our understanding of the benefit/risk profile of Alcon products and can offer new opportunities to develop solutions to address unmet medical needs.

An IIT is 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. Study sponsors retain full responsibility for and control over the study design, initiation, management, data analysis, monitoring, and reporting.

The purpose of this brochure is to describe clearly Alcon's essential requirements for IIT funding, and to highlight the study sponsor obligations when supported by Alcon.

Requirements to Request Alcon IIT Funding

Below are the key requirements for requesting Alcon support for an IIT study. Please direct any questions to your local Alcon Medical contact.

Investigator qualifications

The Investigator's curriculum vitae must be submitted for an assessment of the Investigator's qualifications to conduct the study. These qualifications include, at minimum:

- Current valid license to practice medicine [except for in vitro studies]
- If the IIT is a clinical study, Good Clinical Practice (GCP) training within the previous 2 years

Study criteria

The proposed study must have a legitimate research purpose that:

- Has innovative scientific merit
- Complements Alcon generated research
- Is aligned with the Alcon product scientific/development strategy, and
- Will enhance understanding of the risk/benefit profile of a product or could help to address an unmet medical need.

Resources

The Investigator must have the right infrastructure in place with capability to complete the study.

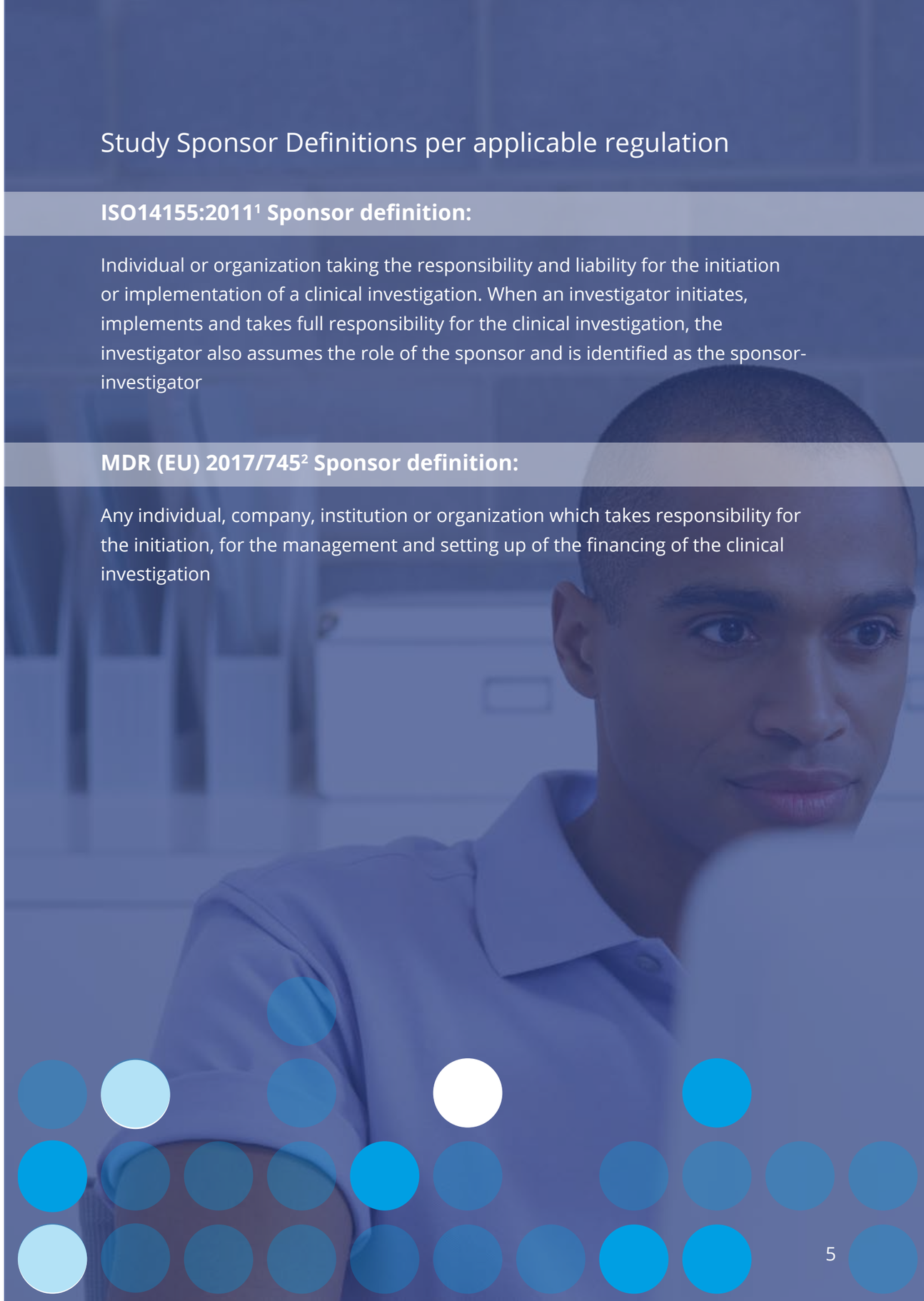
Study Sponsor Definitions per applicable regulation

ISO14155:2011[1] Sponsor definition:

Individual or organization taking the responsibility and liability for the initiation or implementation of a clinical investigation. When an investigator initiates, implements and takes full responsibility for the clinical investigation, the investigator also assumes the role of the sponsor and is identified as the sponsor-investigator

MDR (EU) 2017/745[2] Sponsor definition:

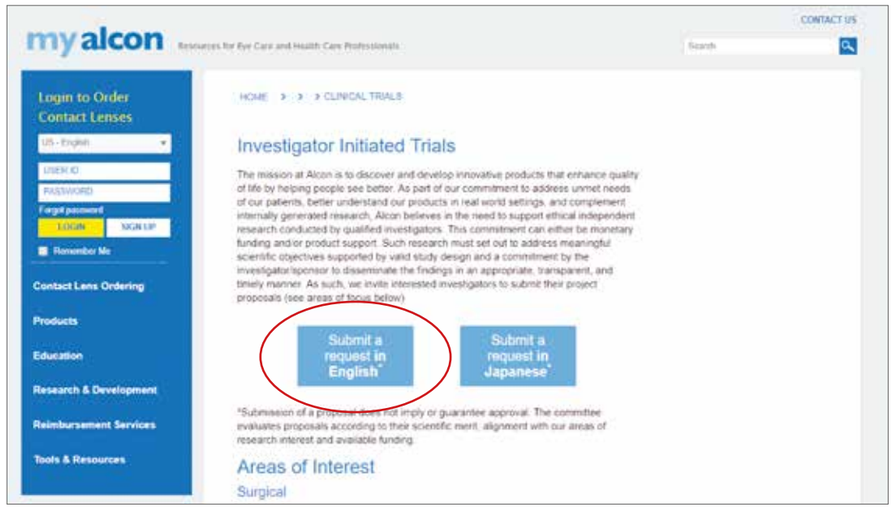
Any individual, company, institution or organization which takes responsibility for the initiation, for the management and setting up of the financing of the clinical investigation



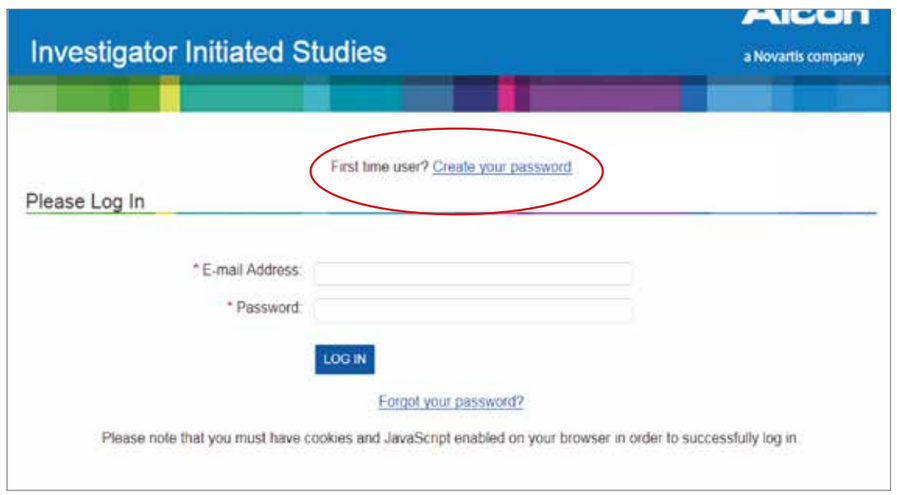
IIT Application Process

Go to https://2.myalcon.com/professional/alcon-research-development/clinical-trials/investigator-initiated-studies to locate the IIT Application Portal

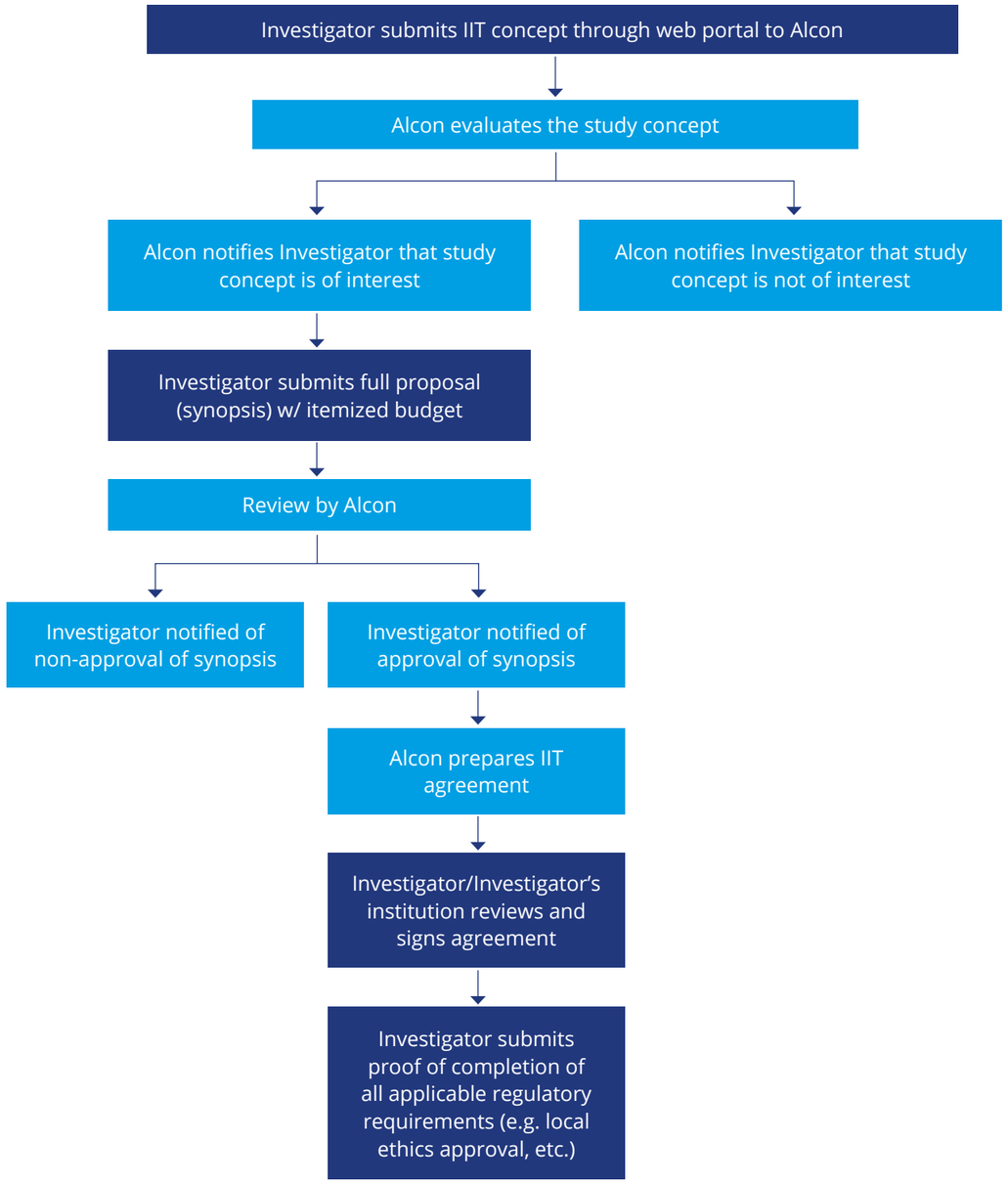
Step 1: Click Submit a request in English



Step 2: If a new user, enter registration information and then click Save.



Overview of IIT Submission and Review Process



Key Elements to Include in the Concept Sheet

To allow an initial assessment of Alcon interest in a proposed study, submit a concept sheet with the following information:

- Study area, type of device, and targeted population to be studied
- Main objective of the study
- Description of the innovative part of the trial vs current knowledge
- Type of support to be requested from Alcon, including approximate amount of funding and/or number and type of products needed

Evaluation Criteria for the Concept Review

- Alignment with the overall Alcon product scientific/development strategy
- Innovative aspects of the proposed study
- Regulatory status of the product
- Alcon budget availability

Key Elements to Provide in Full Study Proposal

If notified that the study concept is of interest to Alcon, submit a full study proposal including:

- **Synopsis** that describes:
  - Title
  - Background and hypothesis
  - Primary objective
  - Study design
  - Inclusion/exclusion criteria
  - Sample size and sample calculation rationale
  - Primary and secondary endpoints
  - Study duration, and
  - Key supporting references.
- **Curriculum Vitae** of the principal investigator
- Detailed **budget** for any funding requested
- List of products requested
- **Timelines**
- **Publication plan** (meeting and/or journal targeted)

Evaluation Criteria for the Full Proposal

Project Description:

- Scientific merit of the study
- Innovative study (does not replicate already published study)
- Alignment with the overall Alcon product scientific/development strategy
- Adherence to ethical standards, GCP/ISO 14155, and applicable regulations
- Technical and practical feasibility
- Regulatory status of the product

Study Site and Principal investigator:

- Investigator's medical qualifications and/or technical expertise in the field of research
- If the proposal is for a clinical study, Good Clinical Practice training in the last 2 years
- Appropriateness of the study site resources to conduct the study

Funding:

- Budget and funding request reasonableness with respect to projected study costs and aligned with Fair Market Value
- Alcon budget availability

Funding and Conducting the Study

Receipt of funding/Alcon device

IIT budgets submitted to Alcon are assessed for reasonableness. The purpose of Alcon's IIT funding is to further scientific research and knowledge within a particular therapeutic area.

Alcon does not provide IIT funding to:

- Provide experience with a study product or a treatment protocol or
- Pay for ordinary operating expenses (i.e. expenses of activities that the recipient is already required to perform or customarily performs).

If funding is approved, payments are scheduled according to milestones for key achievements reached 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 in advance with the investigator and documented in the IIT Agreement.

The following must be in place and provided to Alcon prior to Alcon providing funding:

- Fully executed Alcon IIT Agreement

The following must be in place and provided to Alcon prior to Alcon providing product

- Final protocol
- Data consent form or Patient Informed Consent (PIC) for clinical studies
- Institutional review board (IRB) or ethics committee (EC) approval of the protocol and PIC, as applicable according to local regulation on clinical studies
- Health Authority (HA) approval for clinical studies on investigational product

Study status, reporting, and registration in a public database

For clinical studies, the investigator must keep Alcon informed of any updates to the status of the study, such as enrollment and confirmation that safety data are being transferred to Alcon on a timely and ongoing basis. The investigator must also verify that all applicable regulatory requirements have been completed, including (without limitation):

- approval of the study protocol and informed consent form by the local IRB or EC and
- clinical trial registration in a public database, such as **www.clinicaltrials.gov**

Safety Reporting Requirements

A critical expectation of an IIT Investigator is to monitor and report patient safety data. IIT Investigators are responsible for recording and appropriately reporting to Alcon and the relevant health authorities, in a timely and accurate manner, all adverse events (AEs and SAEs) and device deficiencies/quality complaints/ malfunctions in each country where the study is conducted. This must be done in compliance with local legal requirements and in accordance with the Alcon IIT Agreement.

The timelines for providing this information will be specified in the IIT Agreement and may differ depending on where the study is being conducted.

Alcon will share with investigators any important safety findings or urgent safety measures for any Alcon product that is the focus of the IIT as well as safety information needed for performing AE reconciliation, as required in the Alcon IIT agreement.

Study Results and Publications

Alcon requires the final study report to be provided to Alcon 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, IIT investigators are expected to submit for publication the results of IITs funded by Alcon. In order to receive the final milestone payment, investigators must produce a final study report within the timelines specified in the Alcon IIT agreement and attempt to publish study data by submission of a manuscript, an abstract, or a poster to a congress or a journal for publication.

The content of any publication is the investigator's responsibility. Alcon will not participate in selecting authors or writing publications and Alcon associates cannot be included as co-authors of IIT publications. The Alcon IIT agreement does specify that publications are to be submitted to Alcon for a courtesy review in advance of being submitted for publication. Alcon support must be disclosed in any type of 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	✓	
For clinical study, Submission to IRB/EC at study start and annual renewal		✓
Submission to local Health Authorities for investigational device		✓
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		✓
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
PIC = Patient Informed Consent
SAE = Serious Adverse Event

References

1. ISO 14155:2011 – Clinical investigation of medical devices for human subjects – Good Clinical Practice. https://www.iso.org/standard/45557.html (accessed Sept 2018)

2. Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices https://eur-lex.europa.eu/eli/reg/2017/745/oj (accessed May 2019)

Notes

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