

# Novartis Investigator Initiated Trials (IITs) Guidelines

## Introduction and background

As part of our commitment to delivering innovative therapies to patients worldwide, Novartis believes in the need to support ethical independent clinical research conducted by qualified third-party investigators. The value of the scientific research that is produced by such investigators is key to complementing Novartis-sponsored research in helping ensure we better understand the benefit/risk profile of our therapies as well as explore new opportunities to address unmet medical needs. Such clinical research must set out to address meaningful scientific and/or clinical objectives supported by valid study designs in which the privacy rights, safety and welfare of patients is of paramount importance.

Like other health care companies, Novartis has over many years supported the funding of **Investigator Initiated Trials (IITs)** with defined processes and governance measures in place.

Within Novartis we define IITs as: *“Studies 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 conducted without the participation of Novartis, for which the IIT sponsor requests Novartis to provide either funding, drug product or both.”*

Novartis provides financial support and/or drug product for IITs pursuant to a written agreement, which requires that third-party sponsors comply with applicable local laws, rules, guidelines and regulations.

The overarching principles that govern evaluation of IITs include:

- The validity of the scientific question being addressed, ensuring that any data generated by an IIT complement the existing body of evidence and not simply be a repetition of a previous study/experiment.
- The robust nature of the IIT experiment/investigation being conducted in terms of ethical and design elements.
- A commitment by the investigator/sponsor to disseminate the findings in an appropriate, transparent, and timely manner.

The IIT study is conducted independent of Novartis. The investigator or affiliated study sponsor has responsibility for study conception, design, operational execution, data handling, data analysis/interpretation, subsequent reporting/ publication, and ensuring compliance with all local laws and regulations.

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These guidelines lay out the principles Novartis is committing to on a worldwide basis for all third-party sponsored IITs:

1. Rigorous ethical and scientific standards when engaging and reviewing study proposals from third-party independent sponsors, including investigator qualification and institutional site credibility. In study sites where Novartis is not satisfied that Good Clinical Practice (GCP) standards exist, we will not support IITs. Novartis will however consider, on a case-by-case basis, to help develop local sponsor capabilities in GCP, if local policy and regulations permit.
2. Robust medical and scientific governance systems in place at all levels of the Novartis organization (globally, regionally, locally) with no commercial funding or influence on any aspect of the IIT process. Under no circumstances will Novartis permit the involvement of sales and marketing associates in any aspect of IIT design, review and approval, operational execution, funding or transfer of value to a sponsor/investigator undertaking an IIT.
3. The review/approval process focuses specific attention on ensuring that patient safety is of paramount importance in the proposed IIT.
4. Worldwide training within Novartis on the policies and practices required for successful IIT support, including the rules of independence of the third-party investigators/sponsor and no undue influence from Novartis, when engaging in all aspect of the IIT process (conception, design, operational execution, and data management, including data handling and interpretation).
5. Financial transparency on amount of monies and transfer of value provided to any investigator or institution worldwide undertaking an IIT as part of a contractual agreement with Novartis.
6. Communication and enforcement with all third-party sponsors, their contractual commitment to publish their research findings in a timely manner, as well as the need to report safety information findings during the conduct of the IIT in accordance with Novartis and local regulatory requirements and timings.
7. Tracking and monitoring in an ongoing and transparent manner our IIT-contracted obligations and practices and sharing appropriate data with key stakeholders.

### **Selection and Qualification of Investigators/Sponsors of IITs**

Novartis will only undertake IITs with third-party sponsors/investigators that are able to demonstrate clear evidence of high ethical and scientific standards as it relates to clinical research in human subjects as stipulated by the International Conference of Harmonization (ICH) Efficacy Guidelines E6 - GCP.

In addition, investigators undertaking non-clinical studies using animal subjects will have to provide equivalent evidence of ethical standards and/or Good Laboratory Practices (GLP).

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For clinical research in human beings and before embarking on a contractual process of an IIT with a potential sponsor/principal investigator/sub-principal investigator, Novartis will require documentation that demonstrates the following:

- Recent evidence (within previous 3 years) of the potential investigator and site personnel being trained in GCP (e.g. a signed attestation by the potential investigator of having completed GCP training).
- Recent evidence (within previous 3 years) of the potential investigators experience in undertaking clinical research e.g., documentation from a Local Ethical Committee/Institutional Review Board confirming previous participation in clinical research, or documented proof of involvement in a previous clinical trial.
- Evidence of a current license to practice medicine and good medical standing (including no evidence of restrictions by a regulatory/government authority to undertake clinical research).
- Novartis medical staff will ensure the validity of all of the above requirements as well as those requirements stipulated in Novartis Standard Operating Procedures used in the conduct of IITs.

Novartis will not undertake a clinical IIT with an investigator that has not previously undertaken clinical research, either as a sponsor of clinical research themselves or by participating in research sponsored by Novartis or another credible sponsoring organization.

In countries/sites where Novartis is not satisfied that GCP standards exist, Novartis may work with an appropriate credible third party/stakeholder to help develop local sponsor capabilities in GCP and GLP, if local policy permits.

For non-clinical research using animal subjects, similar documentation demonstrating the qualification of the potential investigator site personnel is required.

## Scientific and Medical Governance

Novartis medical associates may be involved in non-promotional interactions with health care professionals (HCPs) with the aim of exchanging scientific/educational information with HCPs as experts in order to enhance patient care and the practice of medicine. Such interactions must not interfere with the independence of the HCPs decision making in the care of their patient.

As part of scientific interaction aiming to enhance patient care and the practice of medicine, Novartis will consider supporting studies independently conceived, designed and planned by investigators or third-party sponsors. While Novartis may communicate its general areas of research interest, individual IIT requests must be unsolicited. These unsolicited requests may be derived and submitted by an investigator independently following a scientific discussion or meeting with the medical organization. Novartis medical colleagues may respond to investigator-expressed interests with a science-based discussion intended to:

- a. Rationalize the scientific interest of Novartis in specific novel pathways for which Novartis has specific therapies or development programs, and
- b. Avoid unintended duplication in areas where there is known ongoing work with other collaborators.

In addition, as part of the review and conduct of potential IITs:

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- Novartis must not direct the scope, objective, design, and operational conduct of any IITs. Novartis may provide comments to ensure that the study is based on sound scientific hypotheses, and protects the safety of subjects in terms of dosing, schedule and potential interactions of approved or novel drugs in combination studies.
  - There will be no marketing and sales influence (actual or perceived) on the selection of an investigator, on the choice to support his/her IIT, nor on any aspect of IIT design or execution.
  - All IIT funding will be initiated and controlled via the medical departments within Novartis, with financial oversight. Novartis support to the study is limited to coverage of financial expenses and/or with the supply of Novartis products, without exceeding fair market value.
  - Based on scientific merit and request by the IIT investigator, Novartis may consider on a case-by-case basis additional support (e.g., laboratory analysis not available outside of Novartis).
  - The investigator takes full responsibility for the design, initiation, management, data analysis and reporting of the study (including local regulatory obligations).

The entire IIT process is regulated by Novartis standard operating procedures that follow ethical research principles and can be summarized as follows:

- The IIT request is initiated by an investigator submitting a signed study concept sheet to the Novartis medical or appropriate research department initiating a review process that documents and tracks all decisions taken. This will apply to Material Transfer Agreements.
- Within this process, IIT proposals are appropriately evaluated by a formalized multidisciplinary team (which does not include Marketing and Sales personnel). The review and approval of an IIT is based on the following principles:
  - Maintaining independence of the investigator and their study concept
  - Good ethical and medical principles
  - Sound scientific design and methodology
  - Investigator's qualifications and expertise
  - Ensuring that the IIT proposal is aligned with the Novartis Medical strategic scope for that therapeutic product
- The research proposal and provision of support between Novartis and the institution and/or investigator must be appropriately documented in a contractual agreement that defines roles and responsibilities. The agreed financial support is linked with defined milestones such as patient recruitment and completion of the final study report and shall only be paid if these milestones are achieved.
- The progress and results of the IIT will be collected, analyzed, and adequately reported to Novartis by the investigator, including, at a minimum, submission of periodic progress, final study report and safety information.

## Training Principles and Commitment

Novartis is committed to ensuring our policies regarding IITs are followed across the organization. In that regard, Novartis is committed to communicating and enforcing the aforementioned principles and procedures for IITs to all relevant associates.

All Novartis associates worldwide involved in customer-facing roles (e.g., sales representatives, marketing associates) will continue to receive the appropriate training on our IIT policies.

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In addition, Novartis will mandate training to sales and marketing associates to ensure that they understand that under no circumstances can they be involved in soliciting, planning, approving, or executing IITs. Furthermore, sales and marketing associates will be trained on the appropriate steps to take if they receive an unsolicited request from an HCP to conduct an IIT, or support the conduct of an IIT.

Furthermore, Novartis will ensure that associates involved in the detailed IIT processes across the globe (e.g., medical associates, IIT cross-functional review team members) receive in-depth training on these policies and processes.

All training will be documented and associates must certify that they have completed and understood the training. Novartis will regularly review this training to assess and, if necessary, improve its effectiveness.

## Principles of Financial Transparency

Novartis is a research-based company and committed to both data and financial transparency. We believe that sharing information in all areas of clinical research, without compromising patient data or confidentiality, supports sustainable innovation and accountability. Therefore, when Novartis provides direct or indirect financial support, including Novartis products, to a third-party sponsor (e.g., investigators or research institutions) we believe that the scientific community and patients have a right to access information about the following:

- The type of IITs we support (e.g., clinical and non-clinical, interventional and non-interventional, disease areas) and their geographical and site location.
- The institutions and investigators who we support through financial commitments to undertake IITs.

This means that in Novartis we track all value transfers provided to an investigator or an institution and ensure that our interactions are properly documented in a written contract. We also encourage institutions and investigators that benefit from Novartis research support to publicly share appropriate research results. All signed IIT agreements across the world are filed in the centralized Novartis Global IIT Repository.

## Tracking and Monitoring Systems

To hold ourselves accountable to high ethical standards, we will monitor and audit Novartis associates adherence to our policies, standards, and effectiveness of training on IITs as part of our global risk assurance program and compliance framework.

Novartis will monitor the IIT investigators compliance and adherence to their contractual obligations related to disclosure of IIT findings, agreed upon milestones, and safety information reporting.

In 2014, Novartis will begin conducting surveys of investigators to request feedback and information on Novartis associates' conduct and adherence to these principles that will help shape future guidelines and practices.