

# Investigator Sponsored Studies (ISS) – Principle –

## Rationale

We are a patient-centric organization and believe in science and innovation to advance patient care. The healthcare business of Merck KGaA, Darmstadt, Germany supports Investigator-Sponsored Studies, or ISSs, which are also known as Investigator-Sponsored Trials, Investigator-Initiated Research or Investigator-Initiated Studies, for innovative research and clinical studies. By supporting such independent research, Merck KGaA, Darmstadt, Germany seeks to stimulate the advancement of clinical and medical knowledge and patient care in areas of therapeutic interest, as a complement to our company-sponsored studies. In granting financial and/or material support to external investigators, Merck KGaA, Darmstadt, Germany shall give higher priority to research that is innovative and has the potential to address specific unmet medical or scientific needs within its areas of therapeutic interests.

Merck KGaA, Darmstadt, Germany ISS activities shall comply with applicable Merck KGaA, Darmstadt, Germany policies, the Merck KGaA, Darmstadt, Germany Code of Conduct, the Merck KGaA, Darmstadt, Germany Pharma Code, and Applicable Laws and Codes. Any request for support shall be unsolicited and initiated by a Sponsor (either institution or investigator) that is fully responsible for planning, designing, and conducting a study.

## Objective

By supporting ISSs, Merck KGaA, Darmstadt, Germany seeks to stimulate the advancement of novel scientific/clinical research and patient care in our therapeutic areas of focus. In awarding ISSs, Merck KGaA, Darmstadt, Germany shall give higher priority to studies which are: (1) innovative, (2) have the potential to address specific unmet medical needs and be patient centric, and (3) potentially synergistic with our ongoing clinical development programs.

This Principle defines the framework and operational boundaries for Merck KGaA, Darmstadt, Germany as funder and supplier of Merck KGaA, Darmstadt, Germany materials for ISSs.



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## 1. Background

At Merck KGaA, Darmstadt, Germany our aspiration is to enable scientific innovation and advanced patient care. With research-driven specialty businesses, our intent and core principles are to help patients, investigators, customers, partners, and communities around the world to advance human health. We are powered by a relentless strive to bring innovation that matters most to patients.

They are reflected in our approach based on guiding principles like scientific novelty, research excellence and clinical impact for patients.

### **Scientific novelty:**

Scientific curiosity and novelty is the basis of all research at Merck KGaA, Darmstadt, Germany as this ensures bringing new approaches and new treatment to our patients. Our experts constantly strive to develop first-in-class or best-in-class molecules and compounds that bring incremental value to patients and health care systems. Our focus is on developing innovative products for hard-to-treat diseases with substantial unmet medical needs. Additionally, we work intensively on innovative therapeutic modalities and areas of high unmet needs.

To meet these goals Merck KGaA, Darmstadt, Germany not only relies on its own promising pipeline but also on research with the public and private sectors and non-profit organizations.

### **Research excellence:**

In addition to aspiring for innovative research, Merck KGaA, Darmstadt, Germany seeks to ensure that all internal and external research supported by Merck KGaA, Darmstadt, Germany is high quality. The company believes in supporting ethical, independent research conducted by qualified third-party investigators as an important means to foster innovation and improve patient care. The scientific research conducted by such investigators can be key to understanding the benefit/risk profile of the therapies we develop, as well as addressing unmet medical needs. Committed to the principle of "smarter together," Merck KGaA, Darmstadt, Germany welcomes the opportunity to work with and support external investigators.

For purposes of our ISS program, Merck KGaA, Darmstadt, Germany defines an ISS as an unsolicited request for funding and/or supply of an investigational or marketed product by a third-party investigator/institution that initiates and conducts an independent scientific investigation as the regulatory sponsor.



Merck KGaA, Darmstadt, Germany expects operational excellence in every ISS it supports. Investigators are expected to perform studies according to their standard institutional operating procedures, with scientific rigor and in compliance with all applicable laws/codes and regulations. That means that each investigator will sponsor, plan, design, conduct and monitor the study, manage the data, prepare the study report and any related publication(s), and oversee all regulatory and ethical matters related to the study as defined by International Conference on Harmonization's (ICH)-Good Clinical Practice (GCP) guidelines. Compliance with ICH-GCP ensures patient rights, safety and integrity are protected, and trial data is credible. In the event an ISS is not subject to ICH-GCP (e.g., in a non-interventional study), then applicable regulatory, ethical and legal requirements (such as Good Epidemiology Practice) must be followed, and the principals of ICH GCP observed where applicable. In addition, investigators undertaking non-clinical studies using animals must provide equivalent evidence of ethical standards and/or Good Laboratory Practices (GLP).

Merck KGaA, Darmstadt, Germany expects scientific excellence from these studies, meaning that each study should generate results with high scientific value for the medical/scientific and patient communities.

Intellectual property rights for the provided drug or device remain with the original inventor (i.e., Merck KGaA, Darmstadt, Germany).

### **Patient centricity**

We want to make a positive measurable impact on the lives of people living with serious diseases and chronic conditions, including their careers and families. Merck KGaA's, Darmstadt, Germany global vision is to be recognized as a trusted partner and innovator for approaches that help patients and improve health around the world. The purpose of ISSs is to increase scientific and clinical knowledge to support safe and effective use of our products and clinical utilization and to accelerate new treatment development and improve patient care.

Generally, ISSs complement our clinical studies by providing supplemental information about our products, such as when our company-sponsored studies do not provide information about certain subsets of patients within or adjacent to the approved indications. ISSs may also enable us to better understand the generalizability of the results of our company-sponsored studies which typically take place under strictly controlled settings.



## 2. Merck KGaA, Darmstadt, Germany Position

Merck KGaA, Darmstadt, Germany generally supports ISSs within the following framework.

### **Selection Qualifications of Investigators Conducting ISSs**

For all ISSs, all investigators must be able to demonstrate adequate qualification, experience and resources to conduct the proposed study, including the ability to fully comply with any and all applicable laws and codes including:

- A. Ethics committee/Institutional Review Board (IRB)/Health Authority approval or clearance requirements, as applicable;
- B. Global and local regulatory, ethical and legal requirements and standards, such as Declaration of Helsinki, GCP or Good Epidemiological or Pharmacoepidemiological Practice (GEP or GPP), including the requirement to obtain informed consent from study participants, as applicable;
- C. All applicable Pharmacovigilance responsibilities such as adverse event reporting requirements; and
- D. Posting and reporting requirements for the study in a publicly accessible database or registry, when required by applicable laws and codes.

### **Criteria for support**

Merck KGaA, Darmstadt, Germany may support an ISS only if the following general criteria are met:

- A. The proposed study is of legitimate scientific value either to Merck KGaA, Darmstadt, Germany or the medical/scientific community at large, is aligned with Merck KGaA's, Darmstadt, Germany ISS program strategy for each therapeutic area, and designed to provide meaningful information or conclusions.
- B. The study proposal has been considered by Merck KGaA, Darmstadt, Germany and any applicable alliance partner pursuant to its scientific review and approval processes.



- C. The amount of any financial support is commensurate with, and does not exceed, the legitimate fair market value of the costs associated with the proposed activities to be carried out in the study (or the portion of the study to be funded).
- D. The number of investigators and study participants shall be appropriate to meet the legitimate needs of the study objectives and timelines.
- E. In providing financial and/or material/medication support for an ISS, no preference shall be given to reward, in exchange for, or to induce recommending, prescribing, dispensing, purchasing, supplying, selling, administering, referring, arranging for, or ordering any particular medication.
- F. Any provision of technical equipment by Merck KGaA, Darmstadt, Germany or financial support to purchase of such equipment, may only be made if such equipment will be used solely for performing the ISS and if the equipment will be returned to Merck KGaA, Darmstadt, Germany after the end of the study.
- G. The Sponsor of an ISS shall act as the regulatory sponsor of the study as defined by current ICH-GCP guidelines, shall maintain control over the conduct and management of the study at all times, and must ensure the appropriate adherence to planned timelines.
- H. Merck KGaA, Darmstadt, Germany shall not exercise control over the design or conduct of the study. During Merck KGaA's Darmstadt, Germany view of the ISS proposal or protocol Merck KGaA, Darmstadt, Germany may suggest modifications to the proposal or protocol to protect the health and safety of study participants or improve the scientific integrity or quality of the study, and Merck KGaA, Darmstadt, Germany may make such modifications a condition of approval of the ISS. For the avoidance of doubt, such suggested modifications would not jeopardize the "independence" of the ISS.
- I. Where an ISS involves use of a Merck KGaA, Darmstadt, Germany pharmaceutical product for the study, Merck KGaA, Darmstadt, Germany shall either provide the Merck KGaA, Darmstadt, Germany pharmaceutical product (and a placebo to match a Merck KGaA, Darmstadt, Germany pharmaceutical product if needed and if reasonably available), or provide funding for the cost of the pharmaceutical product or placebo for the study, if not otherwise prohibited by applicable laws and codes. The investigator is prohibited from charging for any such product.
- J. The investigator – sponsor of the study has the appropriate infrastructure and experience to conduct the study as proposed



### Type of studies eligible for ISS support

- A. Studies evaluating a Merck KGaA, Darmstadt, Germany marketed or investigational product during any pre-clinical or clinical phase of development
- B. Clinical studies, pre-clinical and non-clinical studies, and laboratory research
- C. Interventional as well as non-interventional (observational) studies
- D. Studies related to non-drug investigations – e.g., techniques or epidemiologic/ disease focus

### 3. Outlook

In order to continually improve our ISS program, Merck KGaA, Darmstadt, Germany will periodically review this Principle against the new and emerging scientific, legal, regulatory and ethical standards.

### 4. Glossary

Abbreviation	Definition
<b>GCP</b>	Good Clinical Practice
<b>ICH</b>	International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceutical Products for Human Use
<b>ISS</b>	Investigator-Sponsored Studies A research study that Merck KGaA, Darmstadt, Germany supports through a grant, but for which Merck KGaA, Darmstadt, Germany, (including subsidiaries) does not serve as the study sponsor.



- **“Principle”: Corporate definition**

A Principle specifies the basic rules for corporate governance which need to be complied with by all subsidiaries of Merck KGaA, Darmstadt, Germany. Its purpose is to ensure a consistent corporate governance framework worldwide. A Principle defines corporate governance structures and corporate governance responsibilities. It does not address organizational responsibilities.

For reference, the link to other Merck KGaA, Darmstadt, Germany policies:

<https://www.emdgroup.com/en/research/our-approach-to-research-and-development/healthcare/positions-policies.html>

- **ISS details**

For details regarding ISSs the link to the respective webpage is given below:

<http://www.ist.emdserono.com>

