

Roche Global Policy on Registration of Clinical Trial Protocols and Publication of Clinical Trial Results

Executive Summary

Roche believes it has an ethical obligation to ensure that results of all clinical trials which are likely to have scientific or medical significance are available to the medical community. Therefore, Roche will participate in both a clinical trial protocol registry to disclose certain details of new studies at or before their inception and a clinical trial results database to publish key results from completed trials. The goals of this policy are two-fold:

- 1. To assist patients, in consultation with their physicians, to find clinical trials that may be appropriate for them (in the clinical trial protocol registry)*
- 2. To make a balanced view of clinical trial results available to practicing physicians and other health care professionals in a format that is both readily accessible and comprehensible (in the clinical trial results database)*

The key features of the proposed registry and database are described in this policy document.

Global Policy

Roche remains dedicated to transparency in clinical trials. The company adheres to the principles of Good Clinical Practice and the Declaration of Helsinki, and follows clear guidelines to ensure this policy.

Roche will establish both a clinical trial protocol registry to disclose information about new studies at or before their inception and a clinical trial results database to publish key clinical trial results.

The **clinical trial protocol registry** will consolidate and expand information which has previously been communicated through local registries and serve as a central global repository for information on ongoing clinical studies. It will provide basic study information in layman's terms to inform the public, in particular patients and healthcare professionals, as to the trial's purpose and conditions of participation.

The **clinical trial results database** will ensure that results from Roche-sponsored clinical trials that might affect the practice of medicine are reported in a fair and balanced manner. This public database reflects Roche's belief in the ethical obligation to accurately communicate all research results, whether positive or negative.

The registry will contain information on all Roche-sponsored clinical trials, Phase II to IV worldwide, and the database will contain information on the outcome of these studies once the product has reached the market. As appropriate, Roche will provide links to its global registry and results database in local registries and databases.

Clinical Trial Protocol Registry for Disclosure of Information about Ongoing Studies

- A publicly available clinical trial protocol registry will provide basic information to inform patients and healthcare workers about available and appropriate clinical trials.
- Each clinical trial will be labelled with a unique identifier to facilitate cross-reference.
- Information will be provided for all Roche sponsored trials, Phase II, Phase III and Phase IV.
- Trial information will be included in the registry as soon as the study design has been finalized, and Independent Ethics Committee (IEC)/Institutional Review Board (IRB) or Competent Authority (CA) approval has been obtained, unless local law requires earlier registration. Such registration will always take place at or before inception of the trial.
- Since the goal is to help patients find clinical trials that they might want to join, information will be presented in a language that a person with a basic knowledge of medical language can understand.
- Clinical trial protocol information will be communicated through a publicly available clinical trial protocol registry. We intend to establish a clinical trial protocol registry that is hosted by an independent, neutral entity.

Clinical Trial Results Database for Disclosure of Information about Completed Studies for Marketed Products

- All clinical trials listed in the registry will also be listed in a clinical trial results database and cross-referenced to ensure transparency.
- Regardless of outcome, Roche will publicly disclose the results of all Roche sponsored trials, Phase II, Phase III and Phase IV.
- Since the primary purpose of this database is to provide balanced information to health care professionals, the data will be presented in scientific terms.

What information will be disclosed? The clinical trial results of the primary and secondary outcome measures as specified in the study protocol, as well as safety results will be provided in summary form. Additionally, a description of the trial design and methodology for each study will be included.

When will information be disclosed? For Phase II and III clinical trials, the results will be disclosed within one year of the time that a drug or new indication is first approved in any market. For trials conducted after approval, in the approved indication, the results will be disclosed within one year after the trial has been completed (defined as last patient, last visit). The same timeline will apply to trials for new indications in approved drugs that do not lead to a new marketing application or change in the labelling.

If a study is under review by a peer-reviewed journal that prohibits pre-publication of results, the results will be posted at the time of the journal publication. An explanation will be placed on the database, in accordance with the timelines proposed in the preceding paragraph, while publication of the manuscript is pending. In addition, in some instances, there may be a delay in posting complete trial summaries due to the need to seek intellectual-property protection or to comply with confidentiality provisions in agreements with other parties. In such cases, an explanation will be placed on the database.

Are there any circumstances in which results of clinical trials covered by this policy would not be published? There are certain situations in which it would be improper to publish clinical trial results. One example would be the case of a study that ended prematurely where no conclusions can reasonably be drawn due to insufficient data. Another example would be a case where the study results were found to be invalid. This could be due to a flaw in the study design, or in the data itself, possibly connected to improper collection of data, storage or shipping conditions of samples, lab error, etc. In these and other circumstances where it is not appropriate to publish the data, the reason(s) for this decision will be detailed in the database.

How will information be disclosed? In all cases, Roche will disclose clinical trial results in a publicly available clinical trial results database. We intend to establish a clinical trial results database that is hosted by an independent, neutral entity. These clinical trial results will also continue to be published through peer-reviewed medical journals, subject to the discretion of the journal editors. References (and links when available) will be provided in the clinical trial results database for study results disclosed in the scientific literature.

How will the protocol registry and trial results database be cross-referenced? Roche will include in the clinical trial results database a reference to the clinical trial at inception. Roche will also update the clinical trial protocol registry to reflect when and where the results are published.

How will disclosure be verified? Adherence to the Roche Global Policy on Registration of Clinical Trial Protocols and Publication of Clinical Trial Results will be audited periodically by our internal auditing group. This will occur as a matter of course as clinical trials are audited. In addition, other audits will specifically address the registration of trials prior to or at the time of initiation, and the subsequent publication of data once each listed trial has been completed and the results analyzed.

What is the effective date for implementation? These standards will be applied to any clinical trial, Phase II - IV that is completed after October 1, 2004. In addition, the database will be populated retrospectively with results of Phase II - IV trials with marketed compounds having first approval after October 1, 2002.

The goal of this policy is to provide a balanced view of clinical trial results in a form that practicing physicians and other health care professionals can easily access and understand. Addressing the needs of lay-people for access to a simplified version of study summary results is outside the scope of this policy. We wish to both encourage and reinforce the traditional physician-patient relationship, and we believe that the optimal way for patients to receive useful information on use of their prescription drug products is through this important association.

Entry into Force

These Guidelines were adopted on January 5, 2005 and entered into force the same day.

Definitions of Terms

Clinical Trial¹

Any investigation in human subjects intended to discover or verify the clinical, pharmacological and/or other pharmacodynamic effects of an investigational product(s), and/or to identify any adverse reactions to an investigational product(s), and/or to study absorption, distribution, metabolism, and excretion of an investigational product(s) with the object of ascertaining its safety and/or efficacy. The terms clinical trial and clinical study are synonymous.

Clinical Trial Protocol Registry

Website for posting basic clinical trial protocol information at, or prior to, inception.

Clinical Trial Results Database

Website for posting clinical trial results for marketed products.

Impact on the Practice of Medicine

Data is of such scientific or medical importance that knowledge of it would influence the decision(s) made by a practicing physician and/or other qualified health care workers. The results may influence these decisions with regard to the drug itself, or with regard to drugs in the same class.

Published

If data is of sufficient quality, publication will be pursued in a peer-reviewed journal and/or in abstract form. If not, data will be published on a publicly accessible website.

Sponsor¹

An individual, company, institution, or organization that takes responsibility for the initiation, management, and/or financing of a clinical trial.

The scope of this policy includes all Roche sponsored trials. To be considered a Roche sponsored trial, Roche may either act as sole sponsor or as lead sponsor.

Roche as Sole Sponsor

In this instance, Roche will assume all the responsibilities of a sponsor as defined above.

Roche as Lead Sponsor

In this case, Roche will retain core responsibilities which will be defined in a case-by-case manner for the individual project. The clinical trial partner(s) will assume the remaining responsibilities.

¹ ICH GCP E6