

Policy on Transparency and Publication of Clinical Study Data

Registration of Clinical Studies, Disclosure of Results in Publications and Results Databases and Access to Study Data and Documents

Executive Summary

The free exchange of scientific information is the basis for innovation in medicine, especially the exchange of scientific results from human, interventional, and non-interventional clinical studies¹. As a research-driven pharmaceutical company, Boehringer Ingelheim supports this principle by seeking publication of the scientific results from all our studies in peer reviewed journals and at scientific meetings, regardless of study outcome.

Boehringer Ingelheim publicly registers all sponsored clinical studies and discloses the results. Furthermore, to benefit patients, public health, and to foster scientific discovery, Boehringer Ingelheim is committed to responsible sharing of clinical study reports (CSRs), related clinical documents, and patient-level clinical study data after drug approval or after termination of the drug development program.

These transparency commitments apply to studies initiated after **January 1st, 1998**.

Publications

This policy applies to all publications relating to scientific information, e.g., manuscripts, abstracts, posters, oral presentations, and review articles published by peer-reviewed scientific journals or presented at scientific meetings and congresses.

Boehringer Ingelheim publishes the results of all sponsored human clinical studies in an accurate, scientific and balanced manner to enable healthcare providers, payers, and other stakeholders to make informed decisions about Boehringer Ingelheim's products:

- For pivotal Phase III clinical studies, we submit manuscripts with the key findings of protocol-specified outcomes to indexed, peer-reviewed journals no later than 12-18 months after study completion.
- For all other studies, we strive to publish the results in a timely manner.

For its publications Boehringer Ingelheim adheres to the Declaration of Helsinki of the World Medical Association, to Good Clinical Practice², as well as to applicable guidelines such as Good Publication Practice³, CONSORT⁴, STROBE⁵, and those from the International Committee of Medical Journal Editors (ICMJE)⁶.

Authorship Criteria

In accordance with the ICMJE criteria⁶ Boehringer Ingelheim requires for authorship credit that the respective individual has participated sufficiently in the development of the publication to take responsibility for the content. The following criteria must be all met:

1. Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the publication,
2. Drafting the publication or revising it critically for important intellectual content,

3. Final approval of version to be published,
4. Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Contributors who do not fulfill all authorship criteria, but nevertheless contribute to the development of the manuscript or research study, are acknowledged for their specific role in the project.

Authorship Agreements

Prior to the development of a publication, Boehringer Ingelheim and the external author(s) confirm in an authorship agreement to adhere to the Good Publication Practice Guidelines³ and the ICMJE Guidelines⁶ and define each other's responsibilities towards the development of the publication, as defined by the Council of Scientific Editors⁷. Boehringer Ingelheim does not pay any fees or honoraria for authorship of peer-reviewed articles or presentations. Only reasonable expenses incurred by authors (e.g., travel expenses) are reimbursed and disclosed as required by applicable law.

Author Access to Clinical Study Data

To ensure independent interpretation of clinical study results, Boehringer Ingelheim grants all external authors access to patient-level clinical study data and relevant material as needed by them to fulfill their role and obligations as authors under the ICMJE criteria.

Responsibilities and Boehringer Ingelheim Review

Authors are in editorial control of the publication's content and accept full responsibility for the publication by approval of the final version prior to submission for publication. Boehringer Ingelheim reviews a proposed publication only for proprietary information, information related to patentable inventions, and medical, scientific, and statistical accuracy. Commercial

functions will not be involved in this review. Boehringer Ingelheim may suggest revisions prior to submission for publication. It is the sole decision of the author(s) to accept or not accept these suggestions. Safeguarding intellectual property rights such as patent filings may require delaying the publication for a reasonable period of time.

Medical Writing/Editorial Support

Upon authors' request, medical writing and/or editorial support can be provided by qualified agencies or other third parties funded by Boehringer Ingelheim. This support is disclosed in the publication and, where necessary to fulfill legal or regulatory transparency requirements, to governmental or regulatory authorities.

Transparency on Clinical Study Data and Documents

Boehringer Ingelheim publicly registers all sponsored clinical studies prior to initiation and discloses study results independent of their outcome. In addition, Boehringer Ingelheim complies with the joint 'Principles for Responsible Clinical Trial Data Sharing' by EFPIA and PhRMA⁸.

After drug approval or termination of a drug development program, Boehringer Ingelheim is committed to responsible sharing of de-identified patient level clinical study data and redacted clinical documents. This applies to data available in our Clinical Trial Data Database and for reports following the ICH E3 format⁹, respectively. Data sharing must respect the boundaries of the informed consent of study participants and ensure the protection of personal data of study participants and personnel. Furthermore, data sharing must respect the integrity of regulatory systems, protect commercially confidential information and intellectual property rights.

Boehringer Ingelheim's transparency commitments apply to studies initiated after **January 1st, 1998**.

Clinical Study Registries and Study Results Disclosure

Clinical Study Protocol Information

Over and above legal requirements, Boehringer Ingelheim registers protocol information for all clinical study types on www.ClinicalTrials.gov, including Phase I studies in healthy volunteers, studies without a control arm, and non-interventional studies for all prescription and non-prescription drugs performed in any country world-wide.

Boehringer Ingelheim is committed to extend protocol registration to studies initiated after **January 1st, 1998**.

Clinical Study Result Synopses

For all clinical study types, Boehringer Ingelheim posts study result synopses in ICH E3 summary format (for legacy studies if available) on its [Trial Results Website](#)¹⁰ within one year after study completion, once a product is approved in at least one country for 30 days or after termination of the development program. On its [Trial Results Website](#), Boehringer Ingelheim also provides lists of study related publications.

Boehringer Ingelheim is committed to extend posting synopses to all studies initiated after **January 1st, 1998**.

Structured Clinical Study Results

Once a product is approved for at least 30 days in the US in at least one indication, Boehringer Ingelheim posts structured study results on www.ClinicalTrials.gov within one year after study completion.

Starting with clinical studies completed in 2014, Boehringer Ingelheim also posts structured study results on www.ClinicalTrials.gov for products approved outside the US and for terminated drug development programs.

In line with the EU Commission Guideline 2012/C 302/03, structured results of EU studies will be made publicly available via the European Clinical Trials Database (EudraCT) (excluding Phase I studies), once this database will be available. From then on, Boehringer Ingelheim will be going beyond this obligation and will post results for Phase II and III studies with not yet approved products on ClinicalTrials.gov and corresponding results synopses via our [Trial Results Website](#) for EU and non-EU studies.

Summary of Clinical Study Results for Research Participants

To help inform and educate patients about the clinical studies in which they participate, Boehringer Ingelheim will work with other pharmaceutical companies and regulators to develop factual summaries of clinical study results to research participants.

Access to Clinical Study Reports, other Clinical Documents and to Clinical Study Data

Boehringer Ingelheim provides redacted clinical study reports (incl. appendices, but without line listings) and related clinical documents on request. Furthermore, Boehringer Ingelheim provides bona fide, qualified scientific and medical researchers access to de-identified, analyzable patient-level clinical study data, together with documentation describing the structure and content of the datasets.

These commitments apply to all documents and patient-level study data of clinical studies initiated after **January 1st, 1998**.

Access is provided after regulatory review has been completed or after termination of the development program and once the primary manuscript describing the results has been accepted for publication.

Prior to providing access, documents and data are being examined, and, if required, redacted, and de-identified to protect personal data of study participants, study personnel, and Boehringer Ingelheim employees, to respect the boundaries of the informed consent of study participants, and to protect Boehringer Ingelheim's commercial confidential information, including intellectual property rights.

In some cases, contractual obligations vis-à-vis third parties or other restrictions (e.g., copyright issues) may not allow sharing documents or data. In rare instances, Boehringer Ingelheim may also have to decline requests that would require excessive resources to provide documents or data compared to their scientific or medical importance. For requests that already have been answered by available clinical documents or are part of the Boehringer Ingelheim publication plan, we will provide the requestor available documents and prioritize related publications. Required redactions and de-identification of data may, in rare cases, have the effect that the scientific value of the documents and data will be reduced. Furthermore, the limitations of the informed consent of study participants might not allow data sharing. In such cases, Boehringer Ingelheim will try to address requests by providing summary data or otherwise.

Boehringer Ingelheim does not provide data and reports for pharmaceutical studies and associated analytical methods, and for studies pertinent to pharmacokinetics using human biomaterials, since there is a general understanding that the reports and data for such studies primarily contain commercially confidential information (CCI)¹¹ and intellectual property (IP).

Access to Clinical Study Reports and Related Clinical Documents

Access to clinical study reports and related clinical documents will be provided to a requestor based on a brief 'Document Sharing Agreement', which requires, in particular, the requestor's commitment to use the documents only for scientific purposes and to not misuse it, e.g., for their own or third party's commercial interests or in support of generic or other competitive marketing authorization applications or other regulatory proceedings.

Access to Analyzable Patient-level Clinical Study Data

Access to patient-level clinical study data requires that the requestor submits a study proposal with a sound scientific

analysis rationale of potential public interest, which will be reviewed and approved/rejected by an independent external review panel consisting of acknowledged experts. For approved requests, access is provided based on a 'Data Sharing Agreement' where the researcher – in addition to the conditions of the 'Document Sharing Agreement' – agrees to certain contractual obligations.

The 'Data Sharing Agreement' includes obligations such as the commitment to use the data only for the purposes described in the study proposal, to not attempt to identify study participants, to comply with applicable legal and Good Clinical Practice (GCP) requirements for handling, analyzing, and reporting clinical study data, and to be "transparent" regarding the planned analysis and disclosure of results. It also includes the requirement to provide a copy of the draft manuscripts to give Boehringer Ingelheim an opportunity for input regarding accuracy and for providing supplementary scientific information (no veto-right and no obligations by Boehringer Ingelheim). In case the requestor interprets the analysis results to be potentially relevant for the risk-benefit assessment of the Boehringer Ingelheim drug, he/she will inform Boehringer Ingelheim without delay in order to ensure appropriate regulatory action in the interest of patient health and safety.

Further details on the document and data sharing process are being published separately.

Effective Date

Implementation of this policy will begin as of January 1st, 2014. Requests for access to clinical study reports, other clinical documents and patient-level clinical study data will be accepted starting that date.

- 1 Note: In the context of this policy, the terms 'Clinical Studies' and 'Clinical Study Data' are not limited to conventional randomized controlled trials, but is meant to include other types of interventional (e.g., large pragmatic trials) and non-interventional studies (e.g. cohort studies, case-control studies) and registry data. Non-trial activities are not included.
- 2 International Conference on Harmonisation (ICH) of technical requirements for registration of pharmaceuticals for human use. Guideline for Good Clinical Practice E6(R1), www.ich.org/products/guidelines/efficacy/efficacy-single/article/good-clinical-practice.html
- 3 Good publication practice for communicating company sponsored medical research: the GPP2 guidelines. Graf C. et al. BMJ 2009; 339: b4330
- 4 Schulz KF, Altman DG, Moher D; CONSORT Group. CONSORT 2010 statement: updated guidelines for reporting parallel group randomised trials. BMJ. 2010 Mar 23;340:c332
- 5 STROBE Statement - STrengthening the Reporting of OBServational studies in Epidemiology ("STROBE"). www.strobe-statement.org. 2007.
- 6 ICMJE Recommendations for the Conduct, Reporting, Editing and Publication of Scholarly Work in Medical Journals. International Committee of Medical Journal Editors. http://www.icmje.org/new_recommendations.html. August 2013.
- 7 Integrity in Scientific Journal Publications, 2012 Update. Council of Science Editors. <http://www.councilscienceeditors.org/i4a/pages/index.cfm?pageid=3313>
- 8 Principles for Responsible Clinical Trial Data Sharing - Our Commitment to Patients and Researchers. Jointly published on July 24th, 2013 by EFPIA and PhRMA. www.efpia.eu or www.phrma.org
- 9 Since 1998, Boehringer Ingelheim's Clinical Trial Data Database is routinely used for the majority of clinical studies. The ICH Guideline "Structure and Content of Clinical Study Reports (E3)" was implemented within Boehringer Ingelheim via SOP on Oct. 1st, 1998.
- 10 BI-Trial Results Web Application. http://trials.boehringer-ingelheim.com/trial_results.html
- 11 This understanding is confirmed for example by the Draft EMA POLICY 0070. Publication and access to clinical-trial data. June 24th, 2013. http://www.ema.europa.eu/ema/index.jsp?curl=pages/includes/document/document_detail.jsp%3fwebContentId=WC500144730&mid=WCOB01ac058009a3dc