Clinical Trials Disclosure and Transparency Policy

Purpose

This policy describes Shire's position on Clinical Trial (CT) transparency, disclosure and data sharing activities related to Shire-sponsored research and projects to ensure full compliance with all applicable external laws, guidelines and standards, while mitigating the risk of personal data identification at a patient level and positioning Shire as a leader in the area of rare diseases and highly specialized conditions with ongoing dedication to maximum CT transparency. Shire follows the data sharing principles that were jointly adopted by the Pharmaceutical Research and Manufacturers of America (PhRMA) and the European Federation of Pharmaceutical Industries and Associations (EFPIA).

This policy is written in accordance with CT transparency regulations, standards and principles for responsible CT data sharing.

Scope

This policy is applicable to CT registrations and results disclosure of Shire-sponsored studies on externally-facing public websites (i.e., ClinicalTrials.gov, EudraCT, EnCePP/EU PAS and Shire's clinical trials disclosure website at www.shiretrials.com), as well as CT data and document sharing (i.e., patient level data [PLD], clinical study reports, [CSR] synopses, and plain language summaries [PLS]) developed by or in collaboration with Shire. This policy applies to all Shire personnel (including service providers to whom Shire has delegated tasks) and external contributors involved in CT registration, results posting and data/document sharing.

Policy

Public Access to Clinical Study Information

Registration

Since 2007, Shire has registered all interventional Phase II/III/IV Shire-sponsored CTs conducted in patients and/or healthy volunteers on ClinicalTrials.gov. Beginning in January 2015, Shire's disclosure policy has applied to the registration of all interventional and non-interventional Phase I/II/III/IV Shire-sponsored CTs, conducted in patients and/or healthy volunteers (regardless of study outcome or where the study is/was conducted) on applicable public registries and public websites (ClinicalTrials.gov, EudraCT, ENCePP/EU PAS and Shire's Clinical Trials Disclosure website at www.shiretrials.com), with the exception of clinical pharmacology studies on healthy volunteers. Shire will only register clinical pharmacology studies in healthy volunteers that the Shire protocol review committee (PRC) determines should be registered.

Results Disclosure

According to applicable regulatory requirements, unless otherwise allowed, Shire commits to making the results of all CTs publicly available within 6 months (for pediatric studies) and 12 months (for adult studies) of study completion. This includes results of CTs of unapproved treatments, CTs for unapproved uses of approved treatments, and phase I/II/III/IV Shire-sponsored CTs conducted in patients and/or healthy volunteers (regardless of study outcome or where the study is conducted). These will be posted on applicable externally-facing public websites (i.e., ClinicalTrials.gov, EudraCT, EnCePP/EU PAS, and Shire's Clinical Trials Disclosure website at www.shiretrials.com). Since January 2017, Shire has also been posting redacted protocols and statistical analysis plans on ClinicalTrials.gov, concurrently with disclosure of trial results. The policy covers results disclosure of interventional trials (other than Phase I) on ClinicalTrials.gov as per FDA Amendment Act. This includes products and treatments that were completed after September 27, 2007 or initiated on or before that date, and which were still ongoing as of December 26, 2007. Shire posts results of all Shire-sponsored studies on EudraCT in accordance with the timing and modality set forth by the EMA. CT results will also be posted on the Shire Clinical Trials Disclosure website at www.shiretrials.com, in addition to redacted synopses of CSRs dating back to January 1, 2014.

Clinical Study Reports (CSRs)

Shire is committed to protecting patient privacy, especially for trials involving patients with rare diseases, by continuing to implement an approach that balances data utility while mitigating the risk of personal data identification at a patient level. Redacted and anonymized full CSRs for clinical trials on products covered in a CTA and approved in the EU are accessible on the EMA Clinical Data Website (this only covers EU trials).

Scientific Publication of CT Results

Shire is committed to making every effort to submit manuscripts of clinical studies for publication within 12 months after the completion of clinical trials for marketed products (regardless of the outcome of the clinical trial). This commitment also pertains to investigational medicines whose development programs have been discontinued. As of January 1, 2018, Shire-supported research manuscripts will be submitted to journals that are visible to the public via Open Access.

Responsible Data Sharing

Patient Level Data (PLD)

Providing researchers access to clinical study data may help advance medical science or facilitate creation of further knowledge and understanding. In 2014, Shire began accepting requests from researchers for PLD for Shire-sponsored phase I/II/III/IV studies conducted in patients and/or healthy volunteers (regardless of study outcome or where the study is conducted). Researchers are able to request access to PLD from Shire clinical studies for compounds and indications approved in the United States and European Union on or after January 1, 2014. Data Requests outside the scope of this policy may be considered in appropriate circumstances. For data from clinical trials involving patients with rare diseases,

Shire will continue to protect patient privacy by retaining its current approach that balances data utility while mitigating the risk of personal data identification.

Submission of Data Requests: All research proposals must be submitted by completing a Data Request Form which requires basic information.

- Detailed research proposal includes:
  - Background and rationale
  - Research design and objectives
  - Scientific hypothesis
  - References supporting the research proposal
  - The data, information, studies and study populations requested for research
  - Consideration for Ethical Committee or Institutional Review Board approval
  - Statistical analysis plan
  - Publication plan
  - Source of the resource funding
- Curricula Vitae of all researchers including the biostatistician
- Assessment of potential conflicts of interest outside the funding of the proposed research

Data Request Review: Once Shire assesses the validity of the researcher's data request and determines appropriate consent(s) exists for requested product(s) and indication(s), an internal team made up of subject matter experts will review the eligibility of the proposed research against the criteria below and render a decision. In cases where the validity of the researcher or proposed request is in question, Shire will defer the request to an external Independent Review Panel (IRP) for a final, objective opinion. IRP membership consists of non-Shire healthcare professionals and clinical biostatisticians. An IRP list of members is available on the Shire Clinical Trials Disclosure website at www.shiretrials.com.

Access to Data: The request will be reviewed based on the following criteria:

- The scientific rationale, statistical validity, and relevance of the proposed research to medical science or patient care
- The ability of the proposed research plan (design, methods and analysis) to meet the scientific objectives
- The publication plan for the research
- Real or potential conflicts of interest that may impact the planning, conduct or interpretation of the research, and proposals to manage these conflicts of interest
- The qualifications, experience, and resources of the research team to conduct the proposed research

For approved requests, the researchers will sign a Data Sharing Agreement and will be provided access to the approved data on a password protected website. Due to the complexity of the process to de-identify data, it may take up to 9 to 12 months to provide the requestor with access to data after the submission of the Data Request.

Sharing CT Results with Study Participants and Public

Shire launched a program in 2014 to make summarized study results for select studies available in plain language so the outcome of the clinical study is available to study participants. Shire will continue development of summarized study results in plain language for certain studies over a pilot period and will voluntarily expand current disclosure standards, laws and regulations by making them available not only to study participants, but also to the general public via Shire's Clinical Trials Disclosure website at www.shiretrials.com.

Data Sharing Limitations

There are circumstances in which patient-level data cannot reliably be de-identified (e.g., in small studies of rare diseases), which may pose challenges, as patient privacy or confidentiality must universally be safeguarded. In such cases, Shire will continue to protect patients' privacy by retaining its current approach that balances data utility while mitigating the risk of personal data identification. In addition, this may also include clinical study report sections that contain certain commercially confidential information and intellectual property. It may also apply to circumstances where legal, contractual or consent provisions prohibit data transfer to a third party (i.e., co-developed or out-licensed projects or the limitations of the informed consent of study participants might not allow data sharing).