

GSK Public policy positions

Public Disclosure of Clinical Research

The Issue

The pharmaceutical industry communicates the results of its clinical research by publishing in scientific journals; by presenting results at scientific congresses; and, in line with established industry commitments and evolving legal requirements, by posting information and results on internet-based public registers. This disclosure is in addition to submission of information to national or regional regulatory authorities as part of the product development or approval process.

Despite this, however, concerns have been raised by some stakeholders about:

- whether study results which may be viewed as “negative” for companies’ medicines are published in scientific literature;
- whether published studies accurately reflect the conduct of the study;
- whether some journal articles are “ghost-written” (where doctors put their name to articles written by pharmaceutical companies);
- the lack of access to the underlying patient level data that is collected during the study.

This paper outlines GSK’s approach to addressing these issues. It is an approach that dates back to 2004 when we became the first company to launch an internet-based clinical study register <http://www.gsk-clinicalstudyregister.com/> providing result summaries from our clinical trials of marketed medicines (i.e. pharmaceuticals and vaccines) irrespective of the study outcome. It has evolved significantly as we have sought new ways of enhancing the transparency of our clinical research, including that conducted by our consumer healthcare division. GSK’s disclosure policy goes beyond what is required by laws and regulations.

GSK’s Position

- Before the first subject is enrolled in a study, we post protocol summaries of GSK-sponsored interventional and non-interventional studies on internet registers. This includes phase I-IV clinical trials of both investigational and marketed medicines and consumer healthcare products. This commitment also includes pooled analyses/meta-analyses that evaluate our products.
- We post all studies that enrol participants on ClinicalTrials.gov (<http://www.clinicaltrials.gov>). In addition, we post studies that retrospectively analyse information from previous studies on our Clinical Study Register (<http://www.gsk-clinicalstudyregister.com/>).
- Irrespective of the outcome of the study, we post result summaries within 12 months of primary completion date for interventional studies and 12 months from the completion of analysis for non-interventional studies. We do not wait until approval or termination of the medicine before posting result summaries. At the time of results’ registration, we also post the full protocol and the statistical analysis plan.
- Our commitment includes posting results from studies of terminated compounds in order to help inform the scientific community about non-productive areas of research and to reduce unnecessary exposure of study participants to similar compounds in other clinical trials.
- GSK’s commitment to post protocol summaries, analysis plans and result summaries for all Phase I studies (in addition to Phases II-IV) to ClinicalTrials.gov, goes beyond what is currently required by laws and regulations in the US and EU. Equally, our policy of posting a similar level of detail for all our non-interventional studies to GSK’s Clinical Study Register goes beyond current legal and regulatory requirements.

- In order to support a broader understanding of our clinical research, in 2017 we began posting some plain language summaries to our Clinical Study Register. As we gain experience and feedback on these summaries we will increasingly include them alongside the result summaries of our clinical studies. We will also use these summaries to help communicate the results of our clinical research to those who participated in our studies.
- We consider the above postings on the internet to be supplementary to, and not a replacement for, the need to publish studies in peer reviewed journals. Our approach is to submit studies as more comprehensive manuscripts for publication in peer reviewed journals, with an increasing focus on open access journals that are indexed by online search engines such as Medline and Embase. The manuscripts are submitted within 18 months of study completion, regardless of market authorisation or termination.
- All interventional and non-interventional studies that evaluate our products, and non-product studies that provide important scientific knowledge or are relevant for patient care, are submitted for publication.
- GSK's policy prohibits "ghost writing" of journal manuscripts and abstracts by requiring authorship and acknowledgements for scientific publications consistent with the requirements of the International Committee of Medical Journal Editors (ICMJE). GSK and external medical writers are either named as authors or included in the acknowledgement section of manuscripts.
- Since December 2013, we have made Clinical Study Reports (CSRs¹) publicly available through our Clinical Study Register, once the medicine being studied is approved or terminated from development. We have also posted CSRs for interventional clinical trials (phase I-IV) for approved and terminated medicines dating back to the formation of GSK in 2000, as well all non-interventional studies conducted since 2009 that have evaluated the safety and efficacy of our medicines.
- The names of the investigators who participate in our clinical studies that were initiated after January 2009 are available on our Clinical Study Register. Since January 2010 we have disclosed the payments we make to US healthcare professionals and their institutions for research studies. We are working to a similar level of disclosure outside the US, initially at the aggregate level and moving to the individual level over time.
- In May 2013, GSK launched an online system to enable researchers to request access to anonymised patient level data from globally conducted GSK clinical trials (phase I-IV) of medicines started since 2000. Studies are listed on this system within six months of publication. This system is now also used by 12 other industry sponsors and we are working with them to attract other industry and non-industry sponsors to expand the site. Requests for access to Consumer Healthcare patient level data may also be submitted through this system.

Background

The Clinical Development Process

Evaluation of an investigational product is done through interventional clinical trials and is usually conducted in four main phases. Each phase addresses different questions that determine if testing should proceed to the next phase.

Phase I: Phase I studies are primarily concerned with assessing the investigational product's safety usually in a small number of healthy human volunteers (typically between 20 and 100 people) and are designed to determine what happens to the investigational product in the human body.

¹ CSRs are formal study reports that provide more details on the design, methods and results of clinical trials and form the basis of submissions to the US FDA, EMA and other regulatory agencies. Patient data in the CSRs and appendices with patient data listings are removed to protect patient confidentiality.

Phase II: An investigational product that passes the Phase I testing hurdle then moves on to Phase II, which usually includes the “proof of concept” stage. Here for the first time, it is generally administered to carefully selected patients suffering from the disease which the product will potentially treat. Generally 100–300 patients are enrolled in these Phase II studies. Prophylactic vaccine trials enroll up to several hundred healthy volunteers. Therapeutic vaccine trials enrol volunteers who are already infected or have the disease.

The aim of the studies is to determine if the investigational product addresses the illness it is intended for, as well as the amount and frequency of dosing necessary to achieve the optimal benefits for patients with the fewest side effects.

Phase III: In Phase III studies, the investigational product is given to hundreds and frequently thousands of patients. Phase III studies require differing periods of time to complete, depending on the disease being studied.

Phase IV: Trials of an investigational product may continue after it has been approved for marketing. Known as Phase IV trials, they may further evaluate the effect of the product for the approved use; assess other potential uses; or yield additional safety data. Regulatory agencies may require these trials to address specific questions.

Other types of clinical research, such as non-interventional research (using data collected during the provision of routine healthcare) and analyses of data that is combined from a number of clinical trials (e.g. meta-analyses), are increasingly seen as important evidence in the evaluation of the risks and benefits of products.

GSK & Clinical Research Data

The guiding principle for GSK is to disclose publicly the results of GSK-sponsored clinical research that evaluates our products, irrespective of whether the results are likely to be perceived as positive or negative. Likewise, we require investigator sponsored studies supported by GSK to be conducted and publicly disclosed consistent with our policies.

To inform investigators of the outcome of a GSK-sponsored trial, GSK provides them with a summary of the overall trial results which we encourage them to share with study participants.

Internet-based Registration of Ongoing Clinical Trials

Publicly available internet-based registration of ongoing clinical research can help to increase participation. It also provides an important reference point so interested parties can track the subsequent public disclosure of the results.

Publication and Internet-based Posting of Clinical Research Results

Traditionally, research results have been publicly disclosed via publication in peer reviewed scientific literature; however, there are well recognised constraints associated with this approach. With limited journal capacity, some studies or analyses may not be considered a priority by some journals, and therefore may not be accepted for publication.

Posting result summaries on internet-based registers is part of a solution as it ensures that the results of clinical studies are available in the public domain whether or not they are accepted for publication.

Regulatory requirements to disclose research results have therefore arisen and numerous public registers [e.g. <http://www.clinicaltrials.gov/>] have been established to serve as repositories for this information.

Where we are not the sponsor of a study, for example, where we support a study by providing a GSK product, we require external researchers to post protocol and result summaries on internet-based registers and submit the results for publication in a searchable peer-reviewed journal.

Authorship

Authorship and acknowledgements for manuscripts follow ICMJE criteria (<http://www.icmje.org>) and are determined based on the level of intellectual contribution to study design, data acquisition, analysis and interpretation, and writing or revising the manuscript. Some journals, however, have a more narrow definition of authorship and this convention is followed for such journals.

The named primary author for a paper must actively participate in the drafting process and lead the content development of manuscripts. The primary author works closely with co-authors and together they have final approval authority for the manuscript. Any GSK staff or contractors such as professional medical writers who contribute to the development of manuscripts for authors (e.g. assistance in assembling initial drafts, tables and figures, collating co-author comments and revising the document based on author input) are named in the article either as authors when their contribution meets authorship criteria, or by description of their contribution within the acknowledgements section.

GSK will provide authors full access to data supporting the publication including access to data tables, final study reports, case report forms and raw data as needed.

GSK does not suppress or veto submission of manuscripts; though the timing of submissions may on occasion need to be delayed to allow GSK the opportunity to seek necessary intellectual property protection.

GSK generally does not support publication of data from an individual centre in a multi-centre trial. It is GSK's position that the results from the entire trial should be published before information from individual centres is published, and that individual centre data should always reference the primary publication of the entire study.

Access to Patient Level Data

Publication of clinical studies in the scientific literature and result summaries on registers typically only contain aggregated data. These publications therefore have limitations for those who wish to examine the data more closely or to combine it with other studies in meta-analyses. To address these limitations, there needs to be greater access to underlying patient level data. In May 2013, we therefore established an online system to allow researchers to request access to anonymised patient level data from GSK sponsored clinical trials.

Clinical studies for our medicines are listed on the website within 6 months of publication of the first scientific paper from the study. Studies that have not been accepted for publication and are no longer being progressed are also available, as are studies of approved medicines for indications that are terminated from development.

Anonymised patient level data is made available from GSK medicines' studies provided that an external Independent Review Panel approves an associated research proposal and the investigator signs a Data Sharing Agreement. The Independent Review Panel accepts or rejects proposals based on the scientific rationale and relevance to medical science or patient care. The Panel also considers the qualifications of the investigators, the management of potential conflicts of interest and publication plans.

Access to the data is provided in a secure manner to help ensure patient privacy is protected and the data is used only for the intended purpose.

Together with other sponsors of clinical trials, GSK is encouraging a broader sharing of clinical trial data to enable researchers to combine data from multiple sponsors (both industry and non-industry), and to help ensure that the contribution of study volunteers to medical innovation is fully realised.

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