

Public Disclosure of Clinical Research

The Issue

Pharmaceutical companies are legally required to disclose relevant data from clinical trials and other research to the appropriate national or regional regulatory authorities as part of the medicine development and approval process. After approval, companies have a continuing obligation to provide regulatory authorities with updated safety information from clinical research and other sources. This ensures regulators can accurately assess the safety and effectiveness of medicines and monitor their safety. Safety and efficacy information is also provided to healthcare professionals through prescribing information which is approved by regulators.

In addition to fulfilling these regulatory requirements, the pharmaceutical industry also communicates the results of its clinical research by publishing in scientific journals; presenting results at scientific congresses; and posting information and results on internet-based public registers and databases. Despite this, however, concerns have been raised by some about whether study results which may be viewed as “negative” for companies’ medicines are published in the scientific literature, whether published studies accurately reflect the conduct of the study, and whether some journal articles may be “ghost-written”, such that doctors put their name to articles written by pharmaceutical companies.

This paper addresses these issues and outlines GlaxoSmithKline’s (GSK) approach to the public disclosure of the results from our clinical research.

GSK’s Position

- GSK’s approach is to post protocol summaries on internet registers [eg. <http://www.clinicaltrials.gov/> and <http://www.gsk-clinicalstudyregister.com/>] when studies are initiated and to post result summaries following their completion - irrespective of the outcome of the study.
- This commitment includes all our clinical trials (phase I-IV) as well as our observational studies and meta-analyses that evaluate our medicines. It also includes posting results from studies of terminated compounds in order to help inform the scientific community about non-productive areas of research and reduce unnecessary exposure of study participants to similar compounds in clinical trials.
- We consider these postings on the internet to be supplementary to and not a replacement for, the need to publish studies in peer reviewed journals. We aim to publish the studies described above as more comprehensive manuscripts in peer reviewed journals that are indexed by online search engines. Where studies are not published we will provide context and interpretation on our own Clinical Study Register.
- The names of the investigators who participate in our clinical studies that were initiated on or after January 2009 are also available on our Clinical Study Register.

GLOBAL PUBLIC POLICY ISSUES

GlaxoSmithKline's Position

- 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 or external medical writers are either named as authors or included in the acknowledgement section of manuscripts.

BACKGROUND

The Clinical Development Process

Evaluation of an "Investigational Medicinal Product" (IMP) or "Investigational Vaccine" (IV) is done through trials and is usually conducted in four main phases. Each phase addresses different questions that determine if the testing of the IMP or IV can 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 IMP or IV in the human body.

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 medicine addresses the illness it is intended for, as well the amount and frequency of dosing necessary to achieve the optimal benefits for patients with the smallest number of 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. Anti-infective studies can be conducted relatively fast: but Phase III studies in chronic diseases and for vaccines may require years.

Phase IV: Trials of a medicine or a vaccine may continue after it has been approved for marketing. Known as Phase IV trials, they may further evaluate the effect of the medicine or vaccine 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, **observational 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 medicines.

GSK & Clinical Research Data

The guiding principle for GSK is to disclose publicly the results of GSK-sponsored clinical research that evaluates our medicines irrespective of whether the results are likely to be perceived as positive or negative.

GLOBAL PUBLIC POLICY ISSUES

GlaxoSmithKline's Position

Internet-based Registration of Ongoing Clinical Trials

Publicly available internet-based registration of **ongoing** clinical research can provide a stimulus for increased participation. It also provides an important reference point so interested parties can track the subsequent public disclosure of the results.

We post protocol summaries of all GSK-sponsored clinical trials (phase I-IV) of investigational and marketed medicines on either external/national registries such as <http://www.clinicaltrials.gov/> or else on GSK's own Clinical Study Register [<http://www.gsk-clinicalstudyregister.com/>] whenever practicable before the first subject is enrolled. We also post protocol summaries for observational research that evaluates our medicines and pooled analyses/meta-analyses of our clinical trials on the GSK Clinical Study Register.

On an exceptional basis, for ongoing phase I trials - although not in line with WHO and ICMJE requirements - GSK may delay registration of certain data elements (compound, name, outcome, measures and/or the official title). This is because early disclosure of compound names and trial outcome measures could, in some circumstances, prevent patentability or negatively impact the protection of intellectual property.

Internet-based Registration of Clinical Research Results

Traditionally, research results have been publicly disclosed by seeking to publish studies 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.

Registering 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. GSK has pioneered these registers – we were first company to launch an internet-based clinical study register [<http://ctr.gsk.co.uk/welcome.asp>] which focussed on providing result summaries from all our clinical trials (phase I-IV) of marketed medicines irrespective of the study outcome.

Our objective is to publicly disclose clinical research results on the GSK CSR for all **new** medicines and vaccines at the time of first approval and to disclose the results on the GSK CSR of studies completed on an **already approved medicines** within one year of study completion.

We recognize that information from terminated research programmes can also help inform the scientific community on the most productive areas of research to progress and help to reduce unnecessary exposure of study participants to similar compounds in clinical trials. In January 2009, we therefore decided to extend our disclosure commitment to all our studies of terminated compounds; our objective here is to post results within 12 months of the decision to terminate development.

We believe it is important that the results of all types of clinical research of our medicines are disclosed via internet-based registers. In January 2009, we therefore also extended our commitment to include all our observational studies and meta-analyses of our medicines.

Where the sponsor of these studies is not GSK, external researchers are encouraged (via written agreements) to post protocol and result summaries on internet-based registers and submit the results for publication in a searchable peer-reviewed journal.

GLOBAL PUBLIC POLICY ISSUES

GlaxoSmithKline's Position

Publication in Scientific Literature

In GSK's view, posting result summaries should be seen as supplementary to and not a replacement for, the need to publish studies in peer reviewed journals. We therefore aim to publish all our clinical research of our medicines as more comprehensive manuscripts in peer reviewed journals. Our approach is to prioritise studies for submission based on their likely impact on medical care and to submit studies of all new medicines and vaccines within 12 months of approval and studies of already approved medicines within 18 months of the completion of the study.

Where possible, we also want to enable researchers and medical practitioners to retrieve the published paper using search engines such as Medline and Embase. Our approach is therefore to submit manuscripts to journals that are indexed by online search engines. Where studies are not published we will provide context and interpretation on the GSK CSR.

Authorship and acknowledgements for these manuscripts follow ICMJE criteria and are determined based on the level of 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 retains final approval authority for the manuscript. Any GSK staff or contractors such as professional medical writers who contribute to the development of manuscripts for external 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.

To inform investigators of the outcome of a GSK-sponsored trial and to help ensure that the results are submitted for publication in a timely manner, GSK will provide investigators with a summary of the overall trial results and, if required to support planned publications, will provide relevant reports, figures or tables. GSK honours reasonable requests to allow investigators to review the complete study database at a GSK site or other mutually agreeable location.

To help ensure that clinical study results are reported in an objective, accurate and balanced manner, GSK reviews proposed manuscripts prior to submission. While GSK does not suppress or veto submission of manuscripts, the timing of submissions may need to be delayed to allow GSK the opportunity to seek necessary intellectual property protection.

GSK generally does not support publication of single centre data derived from 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.

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GLOBAL PUBLIC POLICY ISSUES

GlaxoSmithKline's Position

Appendix: Minimal Data Set for the Registration of Ongoing Trials¹

1. Unique trial number
2. Trial registration date
3. Secondary IDs
4. Funding source
5. Primary sponsor
6. Secondary sponsor
7. Responsible contact person
8. Research contact person
9. Title of the study
10. Official title of the study
11. Research ethics review
12. Condition
13. Interventions
14. Key inclusion and exclusion criteria
15. Study type
16. Anticipated trial start date
17. Target sample size
18. Recruitment status
19. Primary outcome
20. Key secondary outcomes

¹ Is this trial fully registered A statement from the International Committee of Medical Journal Editors *The Lancet*, Volume 365, Issue 9474, 28 May 2005-3 June 2005, Pages 1827-1829. Lancet