

Disclosure of Clinical Trial Information

The Issue

Pharmaceutical companies are legally required to disclose all relevant data from clinical trials to the appropriate national or regional regulatory authorities as part of the pharmaceutical drug development and approval process. After approval, companies have a continuing obligation to provide regulatory authorities with updated safety information from clinical trials. This ensures regulators can accurately assess the safety and effectiveness of new prescription products 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 routinely communicates the results of its clinical trials to healthcare practitioners and others who use or evaluate the use of its prescription products by presenting results at scientific congresses, publishing clinical trials in scientific journals and posting information and results on various internet-based public registers and databases. Despite this, however, concerns have been raised about the perceived approach of the pharmaceutical industry towards disclosing clinical trial results. In particular, doubts have been raised about whether trial results which may be viewed as negative for companies' prescription products are disclosed, potentially leading to a distorted evidence base for those products. In addition there have been concerns about "ghost writing" journal articles, where 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 (including publication in scientific journals) of clinical trial information relating to GSK prescription products ie. pharmaceuticals and vaccines.

GSK's Position

- GSK publicly discloses the results of GSK-sponsored clinical trials that are relevant for patient care irrespective of whether the results are positive or negative for GSK prescription medicines and vaccines.
- Whenever possible, public disclosure is via publication in scientific peer-reviewed publications. In addition GSK provides clinical trial results via the GSK Clinical Trial Register [<http://ctr.gsk.co.uk/welcome.asp>]. Here, GSK provides the results of all trials (phase I-IV) of **marketed** prescription medicines and vaccines. GSK will also post trial results of investigational medicines and vaccines that do not make it to market when relevant to patient care (eg. when related to an important safety issue).

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GlaxoSmithKline's Position

- GSK also posts protocol summaries of all **ongoing** GSK-sponsored clinical trials (phase I-IV) of prescription medicines and vaccines to [clinicaltrials.gov](http://www.clinicaltrials.gov). [<http://www.clinicaltrials.gov/>]. The trials we post here match the requirements of the International Committee of Medical Journal Editors which recommends the posting of all trials.
- On an exceptional basis, our policy is to delay registration of certain data elements (compound name, outcome measures and/or the official title) relating to ongoing Phase I trials. This is because early disclosure of compound names and trial outcome measures can, in some circumstances, prevent patentability or reduce the incentive to invest in novel ways of assessing the effects of investigational medicines and vaccines.
- GSK's authorship policy prohibits "ghost writing" of journal manuscripts and abstracts. Authorship and acknowledgements for scientific publications follow International Committee of Medical Journal Editors (ICMJE) criteria. It requires that the named primary author for a paper must actively participate in the drafting process; must lead the content development of manuscripts; and should retain final approval authority for the manuscript.

BACKGROUND

The Clinical Trial 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 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, the "proof of concept" stage. Here for the first time, it will be 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 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 throughout the world. Phase III studies require differing periods of time to complete, depending on the disease being studied. Results of anti-infective studies can be obtained in a period of 30 days or less, but Phase III studies in chronic diseases and for vaccines may require years.

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GlaxoSmithKline's Position

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.

GSK & Clinical Trial Data

The guiding principle for GSK is to disclose publicly the results of GSK-sponsored clinical trials that are relevant for patient care irrespective of whether the results are positive or negative for GSK prescription medicines and vaccines. As a minimum, GSK follows the PhRMA Principles on the Conduct of Clinical Trials and the Communication of Clinical Trial Results [http://www.phrma.org/principles_and_guidelines/] and is committed to timely communication of results for all prescription products approved for marketing.

Internet-based Registration of Clinical Trial Results

GSK cannot guarantee that clinical trial results will be disclosed publicly in the scientific literature as publication in journals and at many conferences is subject to peer-review and is at the discretion of journal editors and conference organisers. Therefore, in addition to submitting abstracts and manuscripts to conferences and journals GSK provides GSK-sponsored clinical trial results via the GSK Clinical Trial Register (CTR), which is publicly accessible through the Internet [<http://ctr.gsk.co.uk/welcome.asp>]. This database includes protocol information, summary results and, when available, publication references of all (phase I-IV) GSK-sponsored clinical trials of marketed prescription products.

This approach applies to the clinical trials of marketed medicines and vaccines in approved and non-approved indications, and treatment regimens completed since the formation of GSK in December 2000. In the event that a product is withdrawn for any reason from the market then GSK would not remove the clinical trial data from our CTR.

Our objective is to publicly disclose trial results on the GSK CTR for all **new** prescription medicines and vaccines within 10 months of the product's first launch date and to disclose the results on the GSK CTR of trials completed on an **existing marketed product** within one year of trial completion.

When relevant to patient care (e.g. an important safety issue) GSK will also post trial results of investigational medicines and vaccines that do not make it to market.

Some journals consider the posting of trial summaries as a form of publication which prevents acceptance of a manuscript of the trial to their journal. Although we may delay posting to comply with journals' policies in this area, we believe that such policies do not serve the goal of transparency which we and other stakeholders are trying to achieve.

Internet-based Registration of Ongoing Clinical Trials

Publicly available internet-based registration of **ongoing** clinical trials of investigational or marketed products can provide a stimulus for increased participation in clinical research. It also provides an important reference point so interested parties can track the subsequent public disclosure of clinical trial results. We post protocol summaries of all GSK-sponsored clinical trials (phase I-IV) of investigational and marketed prescription products to [clinicaltrials.gov](http://www.clinicaltrials.gov). [<http://www.clinicaltrials.gov/>] whenever practicable before the first subject is enrolled.

We routinely disclose the 20 data elements set out in the International Committee of Medical Journal Editors (ICMJE) minimal data set (see Appendix).

On an exceptional basis, although not in line with WHO and ICMJE requirements that all data elements should be disclosed at the outset of our trials, GSK may delay registration of certain data elements (compound, name, outcome measures and/or the official title) relating to ongoing phase I trials. This is because early disclosure of compound names and trial outcome measures could, in some circumstances, prevent patentability or negatively impact innovation by reducing the incentive to invest in novel ways of assessing the effects of investigational medicines and vaccines.

- *Potential Impact on Patentability*

Publication on a clinical trial register of the compound (intervention) name in combination with the indication (condition) can prevent valid patent protection being obtained. Each case will depend on its precise facts and the law of the country for which patent protection is sought. However, if relevant patent protection is not applied for before the registration of the trial the information will become part of the public domain information (prior art) against which the novelty and inventiveness of the patent application will be assessed. Under these circumstances, the information on the clinical trial register could prevent the grant of valid patent protection.

In theory, one way of avoiding this problem might be to apply for patent protection before information is published on the clinical trial register. However, in many countries, this is not possible as the patent application itself must contain data of the nature which the clinical trial is intended to generate. Countries with this requirement include Japan, Korea, China and Taiwan. Even in European countries, the application may be required to contain data. That data cannot be provided until well into the trial so the patent cannot be applied for before results are obtained from the trial.

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GlaxoSmithKline's Position

- Potential Impact on Innovation in drug development

Publication on a clinical trial register of primary and key secondary outcomes in combination with the condition could negatively impact biomedical innovation as third parties could “copy” innovative clinical development strategies and more readily embark on “fast follower” strategies. There would therefore be little or no incentive to develop innovative approaches in the first place. Reducing these incentives not only negatively impacts the research-based pharmaceutical industry by reducing potential returns on investments, it also compromises the ability of the research-based pharmaceutical industry to meet patients’ needs.

Publication in Scientific Literature

Whenever possible, GSK aims to publish the results of GSK-sponsored clinical trials of marketed prescription and investigational products in scientific and medical journals and in conference abstracts and proceedings. Authorship and acknowledgements for these publications 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 (eg. 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, with the agreement of investigators, 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.

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GlaxoSmithKline's Position

GSK generally does not support publication of single centre data derived from a multi-centre trial. It is GSK's position that the 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. To help identify multiple publications from a single GSK-sponsored study (e.g., conference abstracts and journal manuscripts), GSK includes a unique identifier for the study in manuscripts and abstracts submitted for publication, as well as in clinicaltrials.gov and GSK Clinical Trial Register records (see above).

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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