

# Research practices

The research and development of new medicines and vaccines makes a significant contribution to society through the prevention and treatment of disease. R&D is at the core of our business, with 85 per cent of our revenues derived from the sale of prescription medicines and vaccines.

## Headlines

- Developed non-animal techniques to test batches of our new cervical cancer vaccine
- Improving our internal monitoring process for payments made to healthcare professionals
- Conducted 203 audits of GSK-sponsored clinical trials
- Initiated a project to improve the usability of our Clinical Trial Register which now includes results for 3,089 GSK clinical trials
- Entered into a new patient safety collaboration in partnership with companies, academic institutions and the US government

All R&D must be conducted to high ethical and scientific standards. We aim to make our medicines as safe as possible by evaluating the risks and benefits at every stage from initial research, through to clinical trials and then after a new product is approved for sale. In addition the safety of volunteers who participate in our research is of paramount importance. We take these responsibilities extremely seriously. High ethical standards are also essential for us to obtain regulatory approval for new medicines and for patients and doctors to put their trust in our research programmes and products.

We recognise that biomedical and pharmaceutical research raises ethical concerns such as the use of new technologies, animal research and the conduct of clinical trials.

This section explains how we address these concerns during the discovery and development of medicines and vaccines. It covers:

- New technologies
- Use of animals in research
- Accountabilities and responsibilities for medical governance
- Conduct of clinical trials
- Clinical trial transparency
- Monitoring the safety of our medicines

For more on our R&D pipeline and the contribution our products make to health, see [page 24](#).

## Advocacy and engagement

We regularly engage with policy makers and other stakeholders on issues relating to research practices.

GSK was the first pharmaceutical company to launch an online clinical trial results register and we believe GSK has posted more clinical trial result summaries than any other clinical trial sponsor. As a result we are regularly invited to take part in policy discussions on clinical trial registries by the WHO and other organisations. In 2007 we participated in discussions in the US on appropriate elements of a national registration system. We advocated the need for transparency while not inadvertently misleading patients and healthcare professionals or disclosing proprietary information. These discussions have informed new legislation in the US.

GSK is engaged in [The European Partnership for Alternatives to Animal Testing \(EPAA\)](#) with the European Commission and companies from seven industry sectors across Europe. The aim of the EPAA is to replace, reduce and refine the use of animals in the safety assessment of medicines, chemicals and products. This partnership has led to constructive dialogue with regulators responsible for human safety. Issues addressed include the impact of the European REACH Directive on animal use, and vaccine batch safety testing, one of the major drivers of animal use at GSK.

## New technologies

New technologies such as stem cell and genetic research are helping to expand the boundaries of scientific understanding. These technologies hold out hope for new ways to treat serious diseases as well as better ways to evaluate the risks and benefits of the compounds we develop. For example, advances in genetic research are beginning to enable identification of patients who are more likely to experience a side effect from a medicine.

We recognise that new technologies can also give rise to ethical concerns. For example, some stakeholders are concerned about the use of embryonic stem cells in research.

### Cloning Technologies

GSK uses cloning technologies to replicate molecules and cells for research. These technologies have provided better ways to evaluate compounds, enabling greater insight into the risks and benefits of potential medicines and helping to create better medicines for patients. This technology is a fundamental component of drug discovery and development.

GSK does not use cloning technologies with the intention of reproducing entire human beings and we do not see a medical or research case for doing so.

### Stem cells

Stem cell research makes up a very small part of R&D at GSK. However we recognise the importance of being clear about our approach and the standards we apply to this area of research.

We published our policy on stem cell research in 2007. It sets out the standards we apply when using stem cells, including when using embryonic and foetal stem cells. It is available in the [background section](#) of our website.

### Collaborative research

New scientific knowledge and technologies can be applied to the process of drug discovery and development through collaborative research. This collaborative research combines resources, expertise and know-how from several partners. The benefit of this research is often realised by making the results widely available to the research community.

One example is our participation in the US Biomarkers Consortium, a public-private biomedical research partnership managed by the Foundation for the National Institutes of Health.

Biomarkers are characteristics that can be measured and used as an indicator of disease or responses to treatments. They can be used in early research and play an important role in clinical research and practice, for example by enabling scientists and physicians to more quickly and accurately determine the presence or status of disease or the effect of a medicine. This can speed up the research process and enable more effective and timely medical interventions.

The Biomarkers Consortium will harmonise approaches to identifying viable biomarkers. It will help to verify their individual value and formalise their use in research and regulatory approval.

## Animal research

Animal research and testing is an essential component of understanding disease and evaluating the safety and effectiveness of new vaccines and medicines.

Safety regulations require us to test all new medicines on animals before they are tested in clinical trials using humans. Most vaccines have to be tested on animals each time a new batch is produced.

## Our approach

Ultimately GSK would like to see the important benefits of research being achieved and applied to humans without the need for animals in research. We do not believe this can be achieved in the foreseeable future, therefore GSK remains committed to the 3Rs – reduction, refinement and replacement of animals in research – and to achieving high standards of animal welfare. Our goal is to use animals only when scientifically necessary, use as few as scientifically feasible and to minimise pain and distress

### Animal research at GSK – in summary

**GSK has 17 animal research laboratories in Europe, Asia and the US. Some animal research is conducted by external contractors on our behalf, representing around eight per cent of our total animal use. We estimate that animal research accounts for around five per cent of all GSK research expenditure.**

**Almost all of the animals used by GSK are rodents, mainly rats, and mice. We also use cats, dogs, ferrets, fish, pigs, primates and rabbits.**

### The 3Rs

Implementing the 3Rs commits us to:

- Replacing animal studies with alternative methods wherever possible
- Reducing the number of animals used in each study
- Refining studies to minimise pain and maximise the information obtained from each animal

We implement the 3Rs by using advanced scientific methods, training, raising awareness, and sharing and encouraging best practice.

### Regulation and internal controls

Our animal research laboratories comply with national laws on animal welfare. Regulators carry out regular unannounced inspections of our sites. In addition:

- We aim for our laboratories to achieve independent accreditation by the Association for the Assessment and Accreditation of Laboratory Animal Care International (AAALACi)
- GSK laboratories, and any external laboratories conducting research on our behalf, must follow all legal and regulatory requirements and our core principles of care and welfare for animals. These core principles include a requirement for all proposed research and testing using animals to be considered by an ethical review committee

**Communicating our approach**

Some people hold strong views on animal research and testing. We believe it is important to explain the need for animal research and testing and to be transparent about what we do.

Our laboratories host visits from schools, colleges, animal welfare organisations and others. We engage regularly with animal welfare organisations and our investors, as well as contributing to the debate in the media.

**Protest**

We accept the right of lawful protest against animal research as a part of a free society, but condemn the use of violence and intimidation by some who are opposed to animal use. We welcome the shift in the UK away from extremism to debate.

**Our performance**

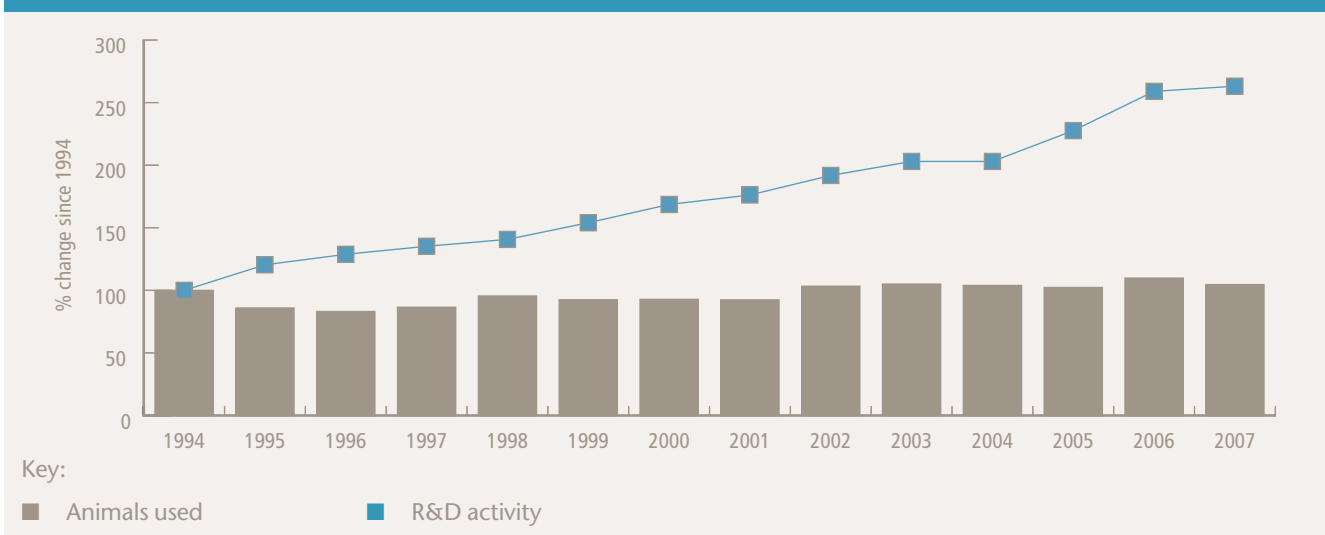
In 2007 the absolute number of animals used in our laboratories was 4.6 per cent greater than in 1994. The growth in R&D activity continues to greatly exceed any increase in animal use.

We estimate animal use by our external contractors to account for 7.9 per cent of all animal use for GSK, compared with 3.2 per cent in 2002. This change may represent an increase in animal research on our behalf by external contractors or may reflect improvements in our data collection from our diverse external collaborations<sup>1</sup>.

Animals used by GSK in 2007 (per cent)*	
Mice	67.1
Rats	25.3
Guinea pigs	6.4
Other rodents	0.2
Rabbits	0.3
Others	0.7

\*This does not include animals used by external contractors on our behalf. Of the animals used by external contractors on our behalf in 2007, 88.5 per cent were rodents and rabbits.

**Change in R&D activity compared to change in number of animals used in GSK research laboratories\***



\*These data do not include animal research conducted by external contractors on our behalf. R&D activity combines our R&D budget and our vaccine sales, the two main drivers of animal use.

<sup>1</sup>We started separately estimating our external animal use in 2002 and to 2007 have recorded external animal use as representing 3.2%, 4.3%, 6.7%, 6.3%, 8.2% and 7.9% of total animal use. The range of external interactions that may involve GSK, directly or indirectly, in animal use is so diverse, and is reported to regulators by third parties, that we refer to these data as an estimate.

## The 3Rs

### 3Rs projects

Recent GSK advances in replacing, reducing and refining animal use include:

- Continuing to replace non-human primates with mice in polio vaccine batch testing
- Decreasing the number of animals needed for vaccine testing. For example we included an *in vitro* (non-animal) test in the regulatory submission for our new cervical cancer vaccine, *Cervarix*. This means that new batches of *Cervarix* will not need to be tested in animals
- Implementing new technology to collect blood samples in animal studies. This approach, previously used in newborns and genetic screening, enables analysis to be carried out on much smaller blood samples than traditional techniques. This enables quality data to be obtained using fewer animals
- Working with governments to change regulatory requirements so fewer animals are required for routine testing. A proposal to reduce animal testing originating from GSK Biologicals was submitted to the European Vaccine Manufacturing Association and later presented to the European Directorate for the Quality of Medicines in 2007
- Developing *in vitro* alternatives to safety tests which check the potential impact of pharmaceutical process materials on workers' skin and eyes. No animals have been used in the evaluation of dermal or eye irritation for worker safety purposes since 2006
- Donating our collection of information on commonly used blood collection methods to the UK National Centre for the 3Rs' (NC3Rs). This now forms the central part of the NC3R's blood sampling website which is used by laboratory staff to choose the most appropriate technique for the humane and efficient removal of blood.

### Training and awareness

We encourage a 3Rs culture at GSK. For example through:

- Regular training for staff involved in the care and use of animals
- Our internal 3Rs website was revised and relaunched in 2007
- A news bulletin on advances in the 3Rs. This was relaunched in 2007 so it is now easily accessible from the 3Rs website and is updated on a rolling basis
- Seminars and 'Recommended Practice' guidelines from our ethical review committees
- Our internal animal Welfare Awards for employees who have made outstanding advances in implementing the 3Rs

### Sharing best practice

We encourage research into the 3Rs and share our experiences and best practices. For example:

- We fund the UK NC3Rs prize which recognises the best new techniques for implementing the 3Rs
- Together with industry partners, we are funding a three-year job post at the NC3Rs to encourage sharing of best practice

More information on [how we implement the 3Rs](#) is available in the background of our website.

### AAALACi accreditation

Ten of our 17 animal laboratories are accredited by AAALACi. These are located in Belgium, Italy, Spain, the UK and the US. This accreditation now covers approximately 92 per cent of the animals used in GSK-owned laboratories. Accreditation is reassessed every three years. Our aim is to achieve AAALACi accreditation for all our laboratories.

### GSK's worldwide standards

It is very important that we apply the same high standards of care and welfare in all the countries in which we operate. We have revised our global animal research standards to ensure they more clearly define our requirements of GSK staff, contractors and collaborators, and that they are applied to all animal research commissioned by GSK. The standards are published on our [website](#).

In 2007, we standardised contractual language on animal care and welfare for inclusion in agreements with our collaborators. We established an ethical review process for all animal studies conducted at our new animal research laboratories in China. The new process was in place before the laboratories opened.

### Communicating our approach

In 2007, we made over 23 visits to UK and US schools and hosted ten site visits in the UK.

In the US we host regular Science Literacy teacher workshops on animal research with the Pennsylvania and North Carolina Associations for Biomedical Research. Four workshops were held in 2007.

We produced a DVD entitled 'Animals in Research: Make up your OWN mind' in partnership with the Physiological Society. A copy of this was sent to every secondary school in the UK in 2007.

## Medical governance

Medical governance at GSK is the system of principles, policies and accountabilities that ensures we apply generally recognised principles of good medical science, medical integrity, ethics and standards. It applies to all aspects of the development and marketing of medicines, vaccines and medicinal products.

It is important that we have clear accountability and responsibility for medical governance to ensure oversight of clinical research, pharmacovigilance and medical information and promotional practices at GSK.

We further clarified medical governance at GSK this year by providing a framework for medical governance across all our businesses. Our Chief Medical Officer (the most senior physician at GSK) has responsibility and authority for establishing an effective medical governance system. Our Corporate Executive Team members are responsible for the performance of, and compliance with, this system within their areas of responsibility.

## Clinical trials

### Our approach

#### Conduct of clinical trials

All GSK clinical trials, wherever they are carried out, are conducted according to the Good Clinical Practice (GCP) guidelines developed by the International Conference on Harmonisation (ICH) and the principles contained in the World Medical Association Declaration of Helsinki on the 'Ethical Principles for Medical Research Involving Human Subjects (2004)'.

The ICH guidelines cover issues such as the selection and training of trial investigators, gaining informed consent from trial participants, monitoring and quality assurance.

Trial protocols (the plan for how a clinical trial will be conducted) are reviewed by government regulatory agencies in the relevant countries when required.

All protocols are also reviewed by an independent ethical review committee of lay people, medical professionals and scientists. They assess whether a trial is justified and whether it is designed and will be conducted according to appropriate ethical standards. Ethics committees have the power to reject or stop a clinical trial.

We have a Global Safety Board (GSB) led by the Chief Medical Officer and composed of senior physicians and scientists. Its role is to:

- Oversee the safety of all investigational and marketed compounds
- Approve the first administration of investigational compounds to humans
- Define the doses and duration of treatments that are considered safe
- Approve the progression of compounds into pivotal trials (these are trials which provide the primary data on which regulatory approval is based)
- Assess any issues related to patient safety that arise during product development or marketing

Safety data are routinely collected throughout development programmes and are reported to regulators in line with applicable regulations. Data are also reviewed by GSK on an ongoing basis for any safety signals (events not necessarily caused by the treatment that require further exploration).

#### Working with healthcare professionals

Our policies governing interactions between GSK R&D staff and healthcare practitioners require that:

- All clinical trial investigators must be selected solely on their qualifications to conduct clinical research. Their history of using GSK products must not be taken into account when deciding whether to include or exclude them in a particular trial
- Payments to practitioners are governed by contracts and any compensation reflects fair market value for the work performed

- No payments can be offered or made that could influence their judgement on whether to enrol or maintain a participant in a clinical study
- Gifts to healthcare professionals are not permitted

#### Clinical trials outside Western Europe and North America

Most clinical trials take place in Western Europe and North America but GSK also undertakes trials in regions such as Central and Eastern Europe, South Africa, Latin America and parts of Asia.

We seek to conduct clinical trials where:

- The population is relevant to the scientific question and where the results can be generalised to broader populations
- There are qualified investigators capable of carrying out the research
- There are people who qualify for participation in the research
- The research can be carried out as quickly and efficiently as possible

All GSK-sponsored clinical trials are conducted to the same ethical standards irrespective of the location. In some of the Least Developed Countries additional steps may be needed. For example, matching the objectives of informed consent to local culture may be necessary, for instance by involving local leaders and/or family members.

Our policy states that trials should not be conducted in countries when we know at the outset that there is no intention to register the product being evaluated in those countries.

You can read our position on [clinical trials in the developing world](#) in the background section of our website.

In some circumstances we believe it is appropriate to help build research capacity in these countries, for example through providing GCP training or research-related technical or clinical equipment.

#### Training for clinical trials

All employees involved in designing, conducting recording and reporting GSK-sponsored clinical research studies are trained in GCP. Training is mandatory and employees must have completed the required training before undertaking these roles.

We keep detailed training records which are routinely requested by regulatory authorities when undertaking an inspection of GSK clinical research studies.

#### Auditing for clinical trials

GSK's internal audit department audits the conduct of clinical trials. Audits cover GSK systems and processes, as well as external clinical research organisations and investigators performing clinical research on our behalf.

Trials are selected for audit on a risk basis. Risk factors include the complexity of the study, the patient population, the location of the study, previous audit history and any unusual findings during the conduct of the study.

Results are reported quarterly to the R&D Compliance Board, and annually to the Risk Oversight and Compliance Council and the Audit Committee of GSK's Board of Directors. Members of our Global Safety Board (GSB) receive individual audit reports on any safety related findings.

Any concerns or issues identified are fully investigated and appropriate corrective action taken. For GSK staff corrective actions may include development of new training programmes or retraining for the individuals concerned. In more severe cases appropriate disciplinary action will be taken, up to and including dismissal.

For external investigators, GSK may retrain the investigator, or stop working with the investigator, and trial data from noncompliant investigative sites will be excluded from the analysis.

Regulatory authorities also carry out inspections of GSK and investigators used by GSK to conduct clinical studies.

## Our performance

### Working with healthcare professionals

We are improving our internal monitoring process for payments made to healthcare professionals for services rendered. This will provide increased assurance that staff are complying with our policies outlined above.

### Training for clinical trials

In 2007 there were 50, 279 training activities related to GCP. Each 'training activity' represents a successful completion of an e-learning module or instructor-led course related to GCP by one of our employees or contractors.

### Auditing for clinical trials

In 2007 we conducted 203 audits. These included:

- 144 audits of investigator sites conducting GSK-sponsored trials. This represents approximately 5 per cent of investigator sites participating in pivotal clinical trials
- 16 audits of internal GSK systems and processes used in managing clinical trials and data
- 29 audits of clinical research organisations carrying out clinical trials on GSK's behalf
- 14 audits of GSK local operating companies involved in clinical research activities

In addition, 26 investigations were conducted in response to suspected irregularities at investigator sites.

Issues identified at investigator sites included insufficient oversight of clinical trial activities by investigators. Oversight covers all areas of investigator responsibility including: knowledge of the protocol design; appropriate and documented delegation of tasks to skilled personnel; and availability to meet sponsor representatives at regular intervals during the study. Additional training for investigators and implementation of further internal controls are helping to reduce the frequency and significance of this issue.

Inspections of investigators, clinical research organisations, independent ethics committees/Institutional Review Boards and sponsors of clinical trials are also carried out by regulatory authorities to ensure the safety of trial participants, the quality of data, and that trials are conducted according to GCP. During 2007 there were more than 51 such inspections of GSK and investigators used by GSK to conduct clinical studies. None of the inspections resulted in any regulatory sanctions, or any findings that would indicate a direct threat to patient safety.

## Reporting research results

Pharmaceutical companies are legally required to disclose all relevant data from clinical trials to the appropriate regulatory authorities when seeking approval for a new product. After approval, sponsors have a continuing obligation to provide regulatory authorities with updated safety information from clinical trials, see patient safety below. Safety and efficacy information is provided to doctors through prescribing information which is approved by regulators.

In addition there is a need to use other ways to communicate the results of our clinical trials to healthcare practitioners and others who use or evaluate the use of our medicines.

## Our approach

We make the results of our clinical trials and information about ongoing trials widely available, through three channels:

- We publicly register summary protocol information for all ongoing GSK clinical trials (phase I-IV) worldwide. Currently this information is on the [ClinicalTrials.gov](http://ClinicalTrials.gov) website
- Whenever possible, we submit trial results for publication in peer-reviewed scientific and medical journals or in conference abstracts and proceedings
- We publish results and protocol information from GSK-sponsored trials of marketed medicines on our online Clinical Trial Register

Our Clinical Trial Register was launched in 2004 and is designed to supplement prescribing information and publications in the scientific literature. Anyone with access to the internet can view our Register at <http://ctr.gsk.co.uk>.

## Our performance

At the end of 2007 there were protocol summaries of all GSK actively recruiting clinical trials on ClinicalTrials.gov, 237 in total.

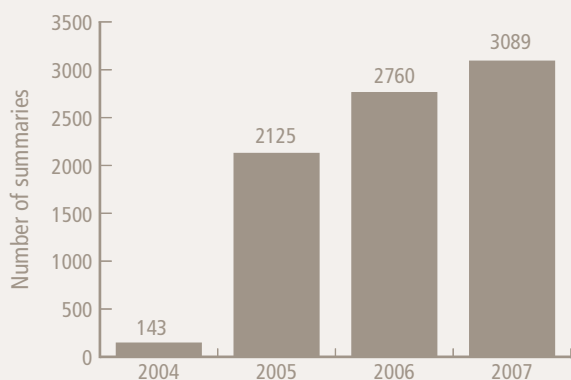
At the end of 2007 there were 3,089 clinical trial summaries on our Register. This includes clinical trials of our major marketed products which have been completed since the formation of GSK in 2000, or that were completed before this and are likely to inform medical judgement.

Our objective is to disclose on our Register the trial results summaries for all new products within 12 months of the product reaching the market. We aim to disclose the results of trials completed after a product is approved for marketing within one year of trial completion. We met this objective in 2007.

We are re-designing our Clinical Trial Register to improve its usability and make it easier for users to retrieve information.

- Improving the links between the protocol and results for each trial enabling users to move between the two
- Extending the search function to enable users to search by disease area or for trials relating to a particular medicine

### Number of summaries of GSK clinical trials on the GSK Clinical Trial Register (cumulative total)



## Patient safety

Patient safety is critically important for the health and wellbeing of the individuals who take our medicines and is paramount to the success of our business. We take the safety of our medicines and medical devices very seriously.

All medicines have potential risks as well as benefits although not everyone who takes a medicine will experience side effects. It is important that we identify, evaluate and minimise safety concerns to ensure that the overall benefits of a medicine outweigh any risks.

More detailed information on [patient safety](#) is available in the background section of our website.

## Our approach

We strive to ensure patient interest is served through the prompt detection of potential safety issues with our products so that appropriate communication with regulators occurs and, following evaluation, decisions can be made and actions taken.

We are also investing in genetic research to help predict an individual patient's response to a medicine. In the future this will help healthcare providers prescribe safer and more effective medicines, resulting in better health outcomes.

### Our monitoring system

We have dedicated teams of scientists and healthcare professionals across the world who monitor, review, evaluate and communicate safety issues. See [Collecting and reporting safety data](#) in the background section of our website for more information.

Product safety is assessed in clinical trials before a product can be approved for marketing. Sometimes adverse events (potential safety issues) occur after approval when a product is being used by large numbers of patients. We have policies and a governance framework in place to help us detect and act on any adverse events. We report potential safety issues to regulatory authorities on a regular basis. See [drug safety governance framework](#) in the background section of our website.

During 2007, 14,000 managers across GSK completed Adverse Event Reporting as part of our 2007 Management Certification process.

In addition, we added an Adverse Event Reporting button to the front page of *myGSK*, our intranet site, to encourage employees to report any adverse event they may learn about.

Adverse events are recorded on our global safety and clinical trial databases and investigated by our clinical and pharmacovigilance teams. This helps us to assess the balance of risks and benefits associated with a particular product. See [benefit-risk management](#) in the background section of our website.

When appropriate, we respond to safety issues by changing product labelling and communicating with doctors. In most cases these actions are sufficient; in a small number of cases we conduct risk minimisation activities, such as further clinical trials, physician or pharmacy education, or even limited distribution programmes, for example for prescription by specialist doctors only. In certain cases it may also be appropriate to stop clinical trials or to withdraw the medicine from the market. See [collecting and reporting safety data](#) in the background section of our website.

## Our performance

We have continued to improve our patient safety systems, safety databases and monitoring processes. Examples from 2007 include:

- Hired toxicity specialists and established Clinical Toxicities Strategy Panels to provide expert safety input throughout the drug development process
- Developed a clinical trials signal detection tool for review of completed study data, in partnership with Lincoln Technologies. This will enhance our ability to identify and explore safety signals in GSK clinical trials
- Developed and launched a prototype for our Molecular Clinical Safety Programme (MCSP). MCSP is a tool that seeks to better inform decision-making in drug development by integrating chemistry, pre-clinical and human safety information. It enables us to look for patterns across different types of safety information including chemical structures, pre-clinical data and human safety data.

### Working with others

We work with government officials, industry partners and policy-makers in efforts to build an enhanced safety system. For example GSK is working with the European Agency for the Evaluation of Medicinal Products on the European network of Centres of Excellence for Pharmacoepidemiology and Pharmacovigilance project. GSK is a key partner among the US Food and Drug Administration (FDA), other pharmaceutical companies and academia in the US to explore the development of a new system for the detection of adverse events and benefits of medicines using large healthcare system databases.

### Serious Adverse Events Consortium

In 2007 we joined with other pharmaceutical companies, academic institutions and the FDA to launch a new patient safety collaboration – the Serious Adverse Events Consortium. The Consortium aims to improve patient safety through genetic research. Its work will include:

- Researching genetic markers that may help predict who is at risk for serious side effects
- Using genetic research to identify which patients will benefit most from which medicines

## The future

We are continuing to look for ways to strengthen and improve our R&D practices. For example, informed consent to participate in a clinical trial requires more than just a signature on a page. Ensuring that participants have understood the information discussed with them during the informed consent process is a key challenge. We are looking at ways to further strengthen and enhance the informed consent process. We have launched an initiative called Patient Empowered, which aims to make the informed consent process a distinguishing feature of GSK clinical trials. This initiative is intended to benefit both GSK and patients. It will include improvements to the informed consent process, a focus on improving the experience of patients in our clinical trials and encouraging patient feedback to help foster a culture of continuous improvement.

## Responding to questions about *Avandia*

*Avandia* is our leading treatment for type 2 diabetes and has been shown to control blood sugar for longer than the most commonly used oral anti-diabetic medicines. Controlling blood sugar is important to help prevent the serious complications of diabetes. In May 2007, the New England Journal of Medicine (NEJM) published a meta-analysis co-authored by Dr Steven Nissen, a cardiologist of the Cleveland Clinic US, which suggested that *Avandia* may be associated with an increased risk of myocardial infarction and death from cardiovascular causes.

The data that contributed to Dr Nissen's meta-analysis were drawn from published literature and GSK's Clinical Trial Register, a web-based repository for clinical data that is available to the public. GSK maintains the register as part of its commitment to public dissemination of scientific information about its marketed products. Prior to Dr Nissen's publication, GSK had posted in the register a summary of its own meta-analysis of 42 double-blind, controlled clinical trials in patients with type-2 diabetes, with findings directionally similar to Dr Nissen's. GSK had also previously submitted its meta-analysis to FDA and other regulators along with the results from both long-term clinical trials and observational studies using large health claims databases which did not show a similar risk.

The New England Journal publication resulted in extensive coverage in the media, and the FDA convened an Advisory Committee meeting in July to review cardiovascular ischaemic/thrombotic risks of the thiazolidinedione drug class, with a focus on *Avandia*. The Committee of experts examined data from multiple sources and concluded that the available data suggested some ischemic risk with *Avandia*, but declined to formally comment on the comparative risk of *Avandia* to other oral anti-diabetic medicines, or in specific sub-populations. The Committee agreed to recommend continued marketing of *Avandia*, with labelling changes addressing the question of cardiovascular ischemic risk.

In November 2007, the FDA approved updated prescribing information for *Avandia*, including new text in the existing boxed warning to add the FDA's conclusion that, while an FDA meta-analysis of generally short-term studies – mostly against placebo – showed an association between *Avandia* and an increase in myocardial ischemic events, that risk was not confirmed or excluded in three long-term clinical trials comparing *Avandia* against both placebo and other oral anti-diabetes medicines. This new text concludes by stating that '[i]n their entirety, the available data on the risk of myocardial ischemia are inconclusive.' Updated prescribing recommendations, and detail about the data underlying the overall conclusion on the question of cardiac ischaemic risk, are now provided in the revised prescribing information for *Avandia*. In its related press release, the FDA stated that 'At this time, (the) FDA has concluded that there isn't enough evidence to indicate that the risks of heart attacks or death are different between *Avandia* and some other oral type 2 diabetes treatments.'

All medicines, *Avandia* included, carry risks as well as benefits. Because type 2 diabetes is chronic, relentlessly progressive and a life-threatening disease, and physicians often need to prescribe two or three medicines to help their patients maintain their blood sugar levels, having an array of treatment options is important. *Avandia* – the most widely studied oral anti-diabetic medicine for the treatment of type 2 diabetes, with over 100 clinical trials and experience in over 52,000 patients – helps to meet that need. GSK believes it is important that *Avandia* is available to support effective treatment of type 2 diabetes.




---

**GSK is opening an R&D facility in China. Will this affect your research standards? Is it a cost reduction exercise?**

We are opening a new R&D facility in China which will focus on R&D into neurodegenerative disorders such as Parkinson's disease, multiple sclerosis and Alzheimer's.

The new centre will enable us to increase focus and depth in important disease areas and to benefit from accessing the vast talent pool and knowledge in life sciences in China, while continuing to strengthen our global R&D capabilities. The costs of conducting research in China are relatively lower than those in other markets. However, lower costs are not the reason behind the decision to set up this new facility.

Our R&D in China will be conducted to GSK's global quality and ethical standards – all our R&D policies and monitoring procedures will apply to our operations in China. Significant above-country resource, as well as local resource in China is being committed to ensure that the establishment of our facilities and their subsequent operation complies with both Chinese requirements and GSK's global standards.

**What is GSK's response to accusations that research results for *Seroxat* were covered up?**

The BBC Panorama programme, 'Secrets of The Drugs Trials' that aired on 29th January 2007 made allegations that GSK acted improperly in regards to *Seroxat* (known as *Paxil* in the US).

We utterly reject any suggestion that we have improperly withheld drug trial information. Results from trials of *Seroxat* were documented and submitted to regulators in accordance with regulatory requirements. Results were also presented publicly, published in scientific journals and are available on GSK's website.

You can read our full response to the BBC Panorama programme on *Seroxat* on our website. <http://www.gsk.com/ControllerServlet?appId=4&pageId=402&newsId=960>

**Why doesn't GSK publish the results of trials that don't result in marketed medicines – surely these could help to advance scientific understanding too?**

This is an evolving area and this year we reviewed our policy. Our Clinical Trial Register includes results summaries from GSK-sponsored trials of marketed medicines. In addition, to inform the scientific and medical community of important research we register results summaries of trials that do not result in marketed medicines, in the following circumstances:

- GSK-sponsored Phase III clinical trials of investigational medicines that are no longer being developed for any indication by GSK or any third party
  - GSK-sponsored Phase II clinical trials of investigational medicines when the research programme has been terminated due to a safety issue associated with the mechanism of action.
- 

### Links

In this report:

- [About GSK](#)
- [Contribution to health](#)
- [Ethical conduct](#)
- [Public policy](#)

On our website:

- [GSK Code of Conduct](#)
- [Our position on stem cell research](#)
- [Our position on clinical trials in the developing world](#)
- [Our Clinical Trial Register](#)
- [More information on patient safety](#)
- Our response to the [BBC Panorama programme on \*Seroxat\*](#)

Other resources:

- The Association for the Assessment and Accreditation of Laboratory Animal Care International
- [ClinicalTrials.gov](#)