

The Globalization of Clinical Trials

Why clinical trials are and should be done globally, including the developing world.

Global pharmaceutical companies including Pfizer are doing increasing number of trials at sites in the developing world, in addition to sites in wealthy countries. In this regard, we are obliged to continue ensuring that the design, oversight, and execution of the studies are fully addressed and meet both legal and ethical standards. At Pfizer, every trial – regardless of where it is conducted – must meet our Company Policies and international standards, including the ICH Guideline for Good Clinical Practice (International Conference on Harmonization 1996) and the principles in the Declaration of Helsinki (2008).

Global Standards

Pfizer, which has run trials in over 60 countries, only places trials in markets where the investigational medicine will be made available, if it is shown to be safe and effective, and only where there is a qualified pool of physician-investigators, sufficient medical infrastructure to support quality research, and a sufficient number of patients who are likely to be interested in participating. Increasingly, this includes countries in the developing world.

Pfizer's research, like that done by other pharmaceutical companies, is done to international standards, regardless of where the trial site is located, usually under global protocols, under the oversight of multiple regulators, and without exploitation. Our Policies and Processes require that informed consent, independent ethics review, post-study care, and the use of placebos conform to established international ethical standards. We don't pay patients to enroll in clinical trials and we don't use placebo-controls, or withhold life-saving drugs, in any study where doing so would harm the participants.

Other standards apply equally to clinical research in both the developed and developing world.

- **Site and Investigator Selection, Training.** Local investigators and research sites' capabilities are carefully reviewed by a study team and can only be included in the trial only if they have sufficient knowledge, expertise and infrastructure to conduct a clinical trial in accordance with Good Clinical Practice. Pfizer provides training in Good Clinical Practice and the study protocol to all investigators and all sites and conducts pre-trial assessments of all sites. We have developed a certification program for our clinical research staff and contractors, with over 1,000 colleagues and contractors now having successfully completed this certification program.
- **Monitoring and Oversight.** To ensure ethical conduct, we establish detailed monitoring plans for each trial and review the data and human subject protection procedures at each site over the course of the trial. Last year, Pfizer conducted over 69,000 monitoring visits of some 14,000 sites around the world. Regulators from the U.S., Europe, and Japan, and elsewhere regularly audit trials and trial sites abroad, to



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ensure that the data is trustworthy. In addition, we establish independent Data Monitoring Committees (DMCs) for trials where mortality or major morbidity is an endpoint. Last year, we had 84 different data safety monitoring committees overseeing Pfizer trials around the world.

- **Informed Consent.** Our informed consent disclosures are based on model documents designed for the study and then adapted to local needs. The disclosure document is reviewed by local ethics committees, and administered by trained investigators and study personnel, fluent in the local language.

All our informed consent disclosures make clear what the risks and benefits to participating are, what alternative medical treatment is available, and whether treatment will be provided after the trial is over. We often provide ongoing access to treatment, where the disease or condition is serious and there are limited options for alternative therapy.

- **Registration, Results Posting & Authorship.** We are publicly registering all of our interventional trials, regardless of where they are conducted. Over 1,000 Pfizer-sponsored trials are listed on <http://clinicaltrials.gov>. We publicly post summary results of all interventional trials following approval, anywhere in the world, as well as for programs where development has been discontinued. Over 800 summaries of Pfizer's trial results are posted so far. See <http://clinicalstudyresults.org>

We encourage publications of the results in peer reviewed journals and enforce the authorship standards, with respect to Pfizer scientists and physician-investigators, established by the International Conference of Medical Journal Editors.

Capacity-Building

To do ethical research in lower resource countries, Sponsors have to find ways to partner with local health authorities to improve medical infrastructure. Industry sponsors routinely work with international and local groups to improve standards, oversight, and training. For example, Pfizer has worked with regulators and administrators in India to improve the ethics committee at a hospital where we do research, with government officials in Suriname to set up the country's first clinical trial ethics council. Last year, Pfizer Korea initiated several training programs on good clinical practice standards with the Ministry for Health, the Korea National Enterprise for Clinical Trials (KoNECT) and clinical trial centers from university hospitals. This training reached over 1,000 investigators and study staff.

- **Emerging Markets.** We partnered with Books of Hope, the World Medical Association, Steve Biko Centre for Bioethics, and the South African Medical Association on a speaking book about research, "*What it Means to Be Part of a Clinical Trial.*" This speaking book has a soundtrack that helps illiterate patients to understand their role, rights and responsibilities when participating in a clinical trial. Several thousand



copies have been distributed to urban medical clinics in South Africa and three other sub-Saharan African countries.

With the Association of Good Clinical Practice in Nigeria, we sponsored 3 day “train-the-trainers” workshops last year to teach research standards to local physician-scientists. In India, Pfizer is developing a series of workshops and symposia in collaboration with the Forum for Ethics Review Committees of India (FERCI).

Pfizer has partnered with Makerere University to build a regional HIV/AIDS treatment, research & training institute in Kampala, Uganda to strengthen regional capacity. The institute has trained 2,400 healthcare professionals from 26 African countries and provides care to about 10,000 patients. Scientists from developing countries, participating in the World Health Organization’s Special Programme for Research in Tropical Diseases (WHO/TDR), have access to Pfizer’s library of medicinal compounds and are trained by Pfizer in drug discovery techniques.

- **International.** In addition to our efforts in specific markets, Pfizer experts provided training to IRB members, provided comments and suggestions to the World Medical Association on the Declaration of Helsinki, presented at the 9th World Congress of Ethics, and participate with groups such as part of the Public Responsibility in Medicine, in advancing knowledge of human subject protection standards. Our training on good clinical practice has been used around the world and is licensed to health authorities, at no cost to them, for their use.

Pfizer’s Global Health Fellow program has sponsored over 171 company scientists, health professionals, and others in working full-time with NGOs in 31 countries, while on paid leave from Pfizer.

Pfizer is the first pharmaceutical company to pursue voluntary accreditation for our early stage testing of new compounds in healthy volunteers.

Ethnic & Population Differences

Ethnic and population differences do have the potential to affect the safety or efficacy of some medicines. However, the fact that treatment naïve patients in the developing world may have differ in that regard from patients in the developed world, are not reasons to limit or discourage global clinical trial programs.

The results of our trials, including ethnic or population differences, will be assessed by multiple, independent, regulators, prior to approval of the drug. Regulators often require minimum numbers of patients from a specific region or with specific ethnic factors, to support a regulatory decision. However, even where they don’t require a specific number of patients from an ethnic or population subgroup, we can address such differences by including multiple ethnic populations in our trials, in accordance with well-established regulatory standards (ICE E5 Guidance on “Ethnic Factors in the Acceptability of Foreign Clinical Data”).



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As scientific knowledge about genetic diversity increases, the need for global clinical trials that involve the developing world will also increase.

Access to medicines

The principle that patients enrolled in clinical trials should have access to any proven therapies identified in the study is one we support. This is a responsibility not just of the Sponsor, but of health systems, to ensure that patients have access to proven therapies. However, we do not and will not conduct trials in countries where we do not intend to commercialize the medicine, should it prove to be safe and effective.

Conclusion

The introduction of international research and Good Clinical Practice standards to the local medical sites in the developing world benefits patients throughout the world. Our goal of developing drugs expeditiously is aligned, with clear public health imperatives.

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