European Federation of Pharmaceutical Industries and Associations

EFPIA Position

Clinical trial standards in developing and emerging countries in the context of the proposed EU Regulation on clinical trials on medicinal products for human use

30 October 2012

Introduction

Clinical trials are an essential part of medical research. No new medicine can be approved without its safety and efficacy first being proven in several clinical trials. While in the past the majority of clinical trials have been conducted in Western European and North America recent years have seen an increase in the number of trials conducted in developing or emerging countries. This is mainly due to the following facts:

- Countries (e.g. China, India, Russia, Taiwan, Ethiopia) request the inclusion of local data as part of the marketing authorisation application for new medicines;
- Countries increasingly request clinical data on existing drugs' efficacy and safety regarding their patient populations;
- Availability of relevant patient populations for specific diseases (for example malaria, hepatitis C, lung cancer, diabetes);
- Some countries provide a more competitive environment for clinical trials, subject to the condition that there is sufficiently developed clinical infrastructures and appropriate regulatory and ethical expertise.

EFPIA members' principles and commitments

Regardless of where a trial is conducted, EFPIA member companies abide by the principle that "the rights, safety, and well-being of the trial subjects are the most important considerations [in clinical trials] and should prevail over interests of science and society[1]."

EFPIA member companies, by conducting all their trials according to similar **internationally agreed scientific and ethical standards[2]**, in addition to local legislation, **apply the regulatory and ethical standards in place in the EU and the US.** In doing so, they play a significant role in improving local standards and supporting the development of similarly high standards in national legislation around the world.

Given their global presence, EFPIA member companies are acutely aware of the **complexity** of running clinical trials in developing or emerging countries with differing cultural, social, economic, medical and regulatory needs, while adhering to universal ethical standards.

EFPIA member companies have worked with regulators and government bodies to further ensure the safety and well-being of people taking part in trials in developing countries by improving ethical and quality standards and their application in practice, ensuring relevance of trials to the needs of the local population, improving monitoring and control etc. These efforts have resulted in a series of international principles[3], stronger regulatory measures and greater and more transparent commitment to research ethics.

In particular clinical trials sponsored by EFPIA member companies in developing countries:

[1] International Conference on Harmonisation – Good Clinical Practice guideline E6, paragraph 2.3.
[2] Such as the International Ethical Guidelines for Biomedical Research Involving Human Subjects issued by the Council for International Organizations of Medical Sciences (CIOMS 2002); the International Conference on Harmonisation Good Clinical Practices (ICH-GCP) Guidelines; Declaration of Helsinki and declarations by member companies are available on their websites.
[3] See point 2 above

- Address diseases and test innovative medicines and vaccines that are **relevant for the local population** with an intention to pursue local marketing authorisation.
- Pay specific attention to the **potential vulnerability of patients and communities**, in particular to ensure that the principles of individual **informed consent** are fully respected.

Conducting clinical trials in developing or emerging countries, with the appropriate regulatory and ethical review capacities, not only **brings benefits to participants** (potential alleviation of a condition) but also contributes to **capacity building of the local medical community** (data generation, experience with the latest medical advances), and of **health systems** (investment in infrastructure), during and after the trial.

EU legislation and safeguards to ensure safety of clinical trial participants

From 2005 to 2010 over 73% of participants whose data was used as part of clinical trial applications relating to a centralised marketing authorisation from the EMA were from the EU/EEA/ETA and North America. Participants, for the same studies, also came from Africa (2.76%), Middle East/Asia/Pacific (8.7%) and Central/South America (8.5%)[4].

The European Union (EU) does not have the legal power to regulate clinical trials outside of its border. However, the current EU legislation governing clinical trials[5] introduced the '***equivalence rule'***. This means that any trial used for a marketing authorisation in the EU must meet equivalent principles and standards expected of a trial taking place in the EU. Regulatory authorities in the EU also have the power to inspect any suspected infringements, and can exclude such data from an application for a marketing authorisation in Europe.

The European Medicines Agency (EMA) is currently developing EU regulatory authorities' capacity for oversight of trials outside the EU, including the ability to sanction any infringements of ethical principles. As part of this strategy, the EMA, and several national EU regulatory agencies are also developing their capacity to share their expertise internationally[6].

Proposal for a Regulation on Clinical Trials

The proposal for Regulation on Clinical Trials[7] builds on the '*equivalence rule*'.

- **Article 25** (concerning data submitted in the application dossier) requires that trials taking place outside of the EU must respect key principles enshrined in the legislation regarding subject rights, safety and reliability and robustness of data generated. Otherwise this data cannot be used as part of the marketing authorisation process for a licence within the EU.
- **Article 76** (concerning "Union controls and Union inspections") introduces a new responsibility for the European Commission. The Commission will be able to control and conduct inspections to verify whether regulatory systems applicable to clinical trials conducted outside the EU comply with good clinical practice and standards set within the EU.

EPFIA supports the equivalence rule established by the EU and welcomes the new provisions proposed in the Regulation which aim to further ensure that regulatory frameworks and ethical standards in developing and emerging countries provide the appropriate high level of protection to patients.

[4] Reflection paper on ethical and GCP aspects of clinical trials of medicinal products for human use conducted outside of the EU/EEA and submitted in marketing authorisation applications to the EU Regulatory Authorities, EMA, 2012:
[5] European Clinical Trials Directive 2001/20/EC and European Directive 2003/63/EC Annex 1 amending Directive 2001/20/EC
[6] Such as FP7 project European & Developing Countries Clinical Trials Partnership, and the WHO Collaborating Centres for Bioethics.
[7] Proposal for a Regulation of the European Parliament and of the Council on Clinical Trials on Medicinal Products for Human Use, and repealing Directive 2001/20/EC

Partnering to ensure appropriate scientific and ethical standards in developing countries

As well as supporting the provisions outlined above, EFPIA supports capacity building initiatives aimed at ensuring proper scientific and ethical standards for clinical trials in developing countries. In particular, EFPIA members partnered with the European and Developing Countries Clinical Trials Partnership (EDCTP) for a better use of local capacities and improving the way clinical trials are conducted. The EDCTP is now working to launch its second phase.

EFPIA welcomes the recent consultation process to develop and strengthen further EDCTP activities in developing countries. In collaboration with the European Commission and the EDCTP, EFPIA is working to ensure a renewed and stronger industry commitment and cooperation from 2013 within this partnership in order to further develop local undertaking of clinical trials.