

EMA plans to increase inspections of clinical trials conducted in third countries

The European Medicines Agency plans to strengthen its oversight of clinical trials, especially those conducted in third countries, to ensure that they comply with good clinical practice and ethical standards¹. The agency's new approach, which has been outlined in a strategy paper, would result in increased GCP and routine inspections before, during and after the submission of a marketing authorisation application.

The strategy paper, the EMA said, was produced in light of "growing concern both among regulators and in public debate about how well these trials are conducted from an ethical and scientific/organisational standpoint (including GCP compliance) and about the available framework for the supervision of these trials".

There has been an increase in the number of patients being recruited into clinical trials in countries outside the "traditional" Western European and North American research areas, the agency says. The EMA's own data on the geographic origins of patients included in pivotal trials for drugs submitted for evaluation through the centralised procedure between 2005 and 2008 show that about a quarter were recruited in countries in Latin America, Asia, the Commonwealth of Independent States (ie Azerbaijan, Armenia, Belarus, Georgia, Kazakhstan, Kyrgyzstan, Moldova, Russia, Tajikistan, Turkmenistan, Uzbekistan and Ukraine) and Africa².

The issue of clinical trials conducted in these countries arose last year, for example, when two advocacy groups in the Netherlands - the Centre for Research on Multinational Companies (SOMO) and the Wemos Foundation - issued a report alleging that medicines that have been tested unethically in low- and middle-income countries were being marketed in the European Union³. Also last year, questions were raised about the booming clinical trials industry in India after reports of 49 infant deaths at a leading government health research institute⁴.

Wemos project co-ordinator (medicines) Annelies den Boer welcomed the strategy paper, saying it was a positive development⁵. "Since 2006, we have been expressing our concern about drugs increasingly being tested on people in developing countries, and we have been asking for thorough ethical checks before granting market authorisation. This strategy paper states that [the] EMA will actually perform these checks," she said.

Wemos is particularly interested in the practical application of ethical standards and said there was a need for political support both at European and at member state level to implement the proposed steps. "We hope that the latest version of the Declaration of Helsinki will be the guiding principle [for ethical standards] and that [the] EMA will consult with experts from the developing countries where the trials are being carried out, because they have an important contribution to make," Ms den Boer added.

EMA's three-year plan

The EMA says that its work programmes for 2008 and 2009 set out a number of actions relating to clinical trials

performed outside the European Economic Area. Among other things, they require the agency to verify, when evaluating marketing authorisation applications, that trials conducted in third countries meet the required standards. They also call for greater transparency in the verification process.

The EMA's new strategy will develop and expand these actions through an itemised three-year action plan that will focus on third-country trials but will have relevance to other clinical trials forming part of marketing authorisation applications.

The proposed activities would cover all areas of the EMA's responsibilities affecting clinical trials, starting with the early phase activities, such as:

- recommendations for the development of new medicinal products and conduct of clinical trials;
- orphan designation;
- protocol assistance and scientific advice;
- paediatric investigation plans; and
- the presubmission phase.

They would continue through marketing authorisation application assessment (both initial submission and variations or line extensions); postauthorisation clinical trials; and inspections before, during or after marketing authorisation applications.

The planning and development of the new action areas would involve work such as:

- clarifying the practical application of ethical standards for clinical trials;
- considering issues driving the recruitment of subjects in third countries;
- reviewing actions of noncompliance and establishing a policy; and
- ensuring links with other initiatives taken by EEA member states in this area.

The practical application of the strategy would mean providing further training for, and increasing the awareness of, EMA officials and drug sponsors; improving European Public Assessment Reports; and contributing towards capacity building of developing countries in co-operation with EU member states and European Commission initiatives.

References

1. EMA strategy paper, Issued 5 December 2008, Posted on website 12 February 2009, www.emea.europa.eu/Inspections/docs/22806708en.pdf
2. Interstate Statistical Committee of the Commonwealth of Independent States website, accessed 23 February 2009, <http://cisstat.com/eng/cis.htm>
3. The Regulatory Affairs Journal - Pharma, 2008, 19(4), 249-251
4. The Regulatory Affairs Journal - Pharma, 2008, 19(10), 697-698
5. Personal communication, Wemos Foundation, 23 February 2009