Rebuilding the EU clinical trials framework

The European Commission has recently adopted a proposal to overhaul the *EU Clinical Trials Directive (2001/20/EC)*, a law that has improved the protection of trial subjects but has been heavily criticised for being cumbersome and costly for sponsors. The Commission unveiled its draft Clinical Trials Regulation on 17 July 2012 and says it will lead to swifter approvals of multinational trials as well as reduced administrative costs of about €270 million annually.[1] It is also hoped that the changes will help to revive flagging investment in EU research.

Many of the system's shortcomings stem from divergent national implementation of the directive. To avoid this in the future, the Commission is introducing a regulation that will apply 'to the letter' in all 27 EU member states. It is also harmonising the submission and assessment procedures, and simplifying other requirements.

Authorisation

The proposal would do away with the existing process under which trial sponsors have to submit applications to each member state where they intend to carry out a trial. Instead, both commercial and non-commercial sponsors (eg academia) would file a harmonised authorisation dossier on both scientific and ethical aspects via a free electronic EU portal. Although the type of documentation required in the dossier would be standardised, certain "aspects of an intrinsic ethical or national/local nature" such as informed consent would be specific to the concerned member state.

Many stakeholders had called for all non-patient related documentation in the submission dossier to be in English, but there are no language requirements in the proposal. This "could potentially cause problems because of the need for translations", European Forum for Good Clinical Practice chair Ingrid Klingmann told *MedNous*.

However, she praised the proposed two-part assessment process, saying it was "an elegant way to leave the authorisation up to member states". Under Part I, a 'reporting member state' would take the lead in assessing the scientific and benefit-risk data (eg protocol, investigator's brochure, quality data on the investigational medicinal product [IMP]), with input from the other member states involved. This would be risk-proportionate. Low-intervention trials for already authorised products would be subject to expedited timelines, but those for trials involving advanced therapy medicinal products would take longer than the normal 25-day period.

An 'acceptable' Part I conclusion by the reporting member state would apply to the other concerned member states, unless they chose to opt out of the process. This 'qualified opt out' would only be possible in limited circumstances.

For Part II, each concerned member state would assess the national, ethical and local aspects of the trial (eg recruitment arrangements, informed consent, proof of insurance). The two assessments would be carried out in parallel and reviewers would have to adhere to strict timelines. Each member state would have the final word and would notify the sponsor of their decision via the portal. The Part I conclusion would stand as the final decision if member states fail to issue their decisions within the given timelines.

The proposal also streamlines the safety reporting rules. For example, suspected unexpected serious adverse reactions (SUSARs) would be reported directly by the sponsor to the European database EudraVigilance and annual safety reports would not be required for already authorised IMPs used within their approved indication.

A new risk-based approach towards insurance/indemnity should also relieve some pressure. Under the proposal, it would not be necessary to provide a specific damage compensation for the trial if it poses negligible additional risk to subjects compared with treatment in normal clinical practice. Dr Klingmann said this would be particularly beneficial for academia.

One of the main complaints about the existing system has been the differing remits of ethics committees across the EU. Stakeholders including the European Federation of Pharmaceutical Industries and Associations (Efpia) had called for a "demarcation of tasks between the assessment authorities and the ethics committees" but the proposal does not introduce any such provisions.[2]

Industry had also sought a link between the authorisation procedure and scientific advice, but the Commission explained that it could not do this because "the authorisation of a medicinal product and the authorisation of a clinical trial follow different aims".

Reactions positive

Reactions to the proposal have been positive but guarded. Efpia said that it was an important first step and the European Association for Bioindustries (EuropaBio) welcomed the proposal but still wants to see a single pan-EU assessment leading to a pan-EU outcome.[3,4] Dr Klingmann said that the proposed authorisation process was a bit complex but that overall the Commission had "really listened to stakeholders".

The proposal now goes to the European Parliament and the Council of Ministers for debate. It is expected to come into effect towards the end of 2016.

References:

1. European Commission, 'Adoption of the proposal for a Clinical Trials Regulation', 17 July 2012, http://ec.europa.eu/health/human-use/clinical-trials/index_en.htm#rlctd.

2. Assessment of the Functioning of the "Clinical Trials Directive" 2001/20/EC: Efpia Response to Public Consultation Paper ENTR/F/2/SF D(2009) 32674, http://ec.europa.eu/health/files/clinicaltrials/docs/responses_2001-20/efpia_1.pdf.

3. Efpia press release, 17 July 2012, www.efpia.eu.

4. EuropaBio press release, 17 July 2012, www.europabio.org.

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