ESC responds to EU Clinical trials directive revisions

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In anticipation of the consideration of the draft report by the European Parliament Environment, Public Health and Food Safety (ENVI) Committee expected early next week, a position paper by the European Society of Cardiology (ESC) welcomes the "spirit" of the European Commission's proposed revision of the text of the European Clinical Trials Directive (EUCTD), as an important contribution to "simplifying, clarifying and streamlining" rules for conducting clinical trials across Europe.

The position paper, coordinated by the ESC European Affairs Committee, comes as the European Commission proposal is being considered by The European Parliament and The Council of the European Union. The ESC's main calls include the suggestion for the role of Reporting Member States to be extended to cover "aspects of an intrinsic ethical or national/local nature". Greater representation of women, different age groups and ethnic minorities in trials, the ESC stress, would further enhance the cardiovascular (CV) research environment across Europe.

"We firmly believe that to properly tackle CV disease (CVD), which is the number one killer in Europe, there's an urgent need to make it easier for scientists to undertake clinical studies and have come up with some additional suggestions to further simplify the research environment," says Professor Frans Van de Werf, chairman of the ESC European Affairs Committee.

The ESC, he adds, has been particularly concerned by the adverse impact the 2001 EUCTD has had on non-industry trials (undertaken by academics, foundations, hospitals or research networks), which account for approximately 40% of clinical trials in the EU. "If it's made easier for academics to set up trials it should help us answer some really fundamental questions for people with CVD that aren't being addressed by Pharma," says Professor Van de Werf, from the Catholic University of Leuven in Belgium. Questions, like for example the optimum dose of aspirin in patients with diabetes, he says, have not been studied by industry because many drugs are off-patent. "We hope revisions will stem the decline in the number of investigator-led clinical trials that have occurred in the last few years and prevent patients from missing out on life saving advances," he says.

It also needs to be acknowledged, he stresses, that clinical research has implications going beyond science to the economic wealth of Europe. "The reality is that a robust clinical trials environment provides a lot of jobs for doctors, nurses, administrators and statisticians," says Van de Werf.

In the position paper the ESC welcomes:

1-The co-sponsor concept. One of the main obstacles generated by the 2001 EUCTD, believes the ESC, was the concept of a "unique sponsor", which required one institution to take legal responsibility for the initiation and management of the trial. The consequence was the huge organizational burden placed on individual investigators, companies, institutions or organisations, whose multiple responsibilities included pharmacovigilance, adverse event reporting, archiving, good clinical practice, drug packaging, site visits, etc.

The newly introduced concept of "co-sponsorship" is in recognition of the fact that clinical trials are increasingly initiated by loose networks of

scientists or scientific institutions within one member state or across several member states. It delivers the major advance of allowing any or all of the tasks and responsibilities to be delegated from the sponsor to co-sponsors. "The bottom line here is that one investigator will no longer be required to carry out the lion share of the work, a factor that has put so many investigators off getting involved in trials," says Van de Werf.

Furthermore, the possibility of having co-sponsors located in third countries (i.e. those outside the EU) who can deal with local legal aspects of the trial should facilitate global recruitment to EU studies. The requirement to take care of the legal aspects of trials has deterred many European sponsors from undertaking collaborations with investigators in places like the US, Australia and Asia. Such revisions, hope the ESC, should also facilitate enrolment of patients from multiple countries into clinical trials to the benefit of the development of personalized medicine. "Research in this field requires large geographical territories to be able to enrol a sufficient number of patients," write the authors of the ESC position paper.

2-The creation of a single EU portal to submit applications, and EU databases. One of the main objections to the 2001 directive has been that the sponsors of multinational trials are required to submit applications to conduct clinical studies in each member state concerned, creating a huge administrative burden. To address this, the Commission has suggested that an EU portal be created where sponsors can file an application for conducting a clinical trial. "Such a solution will simplify the administrative work of academic researchers and investigator led research projects, notably for large-scale multi-national trials," write the ESC authors.

3-One reporting member state. For aspects covered in Part I of the assessment report (covering aspects such as the therapeutic and public health benefits) the revisions propose that one reporting member state

would be appointed as the main contact point for the sponsor, coordinating the response of all the member states involved. "This system will avoid lengthy approvals in multi-country trials," says Van de Werf.

According to the ESC, the same system – (i.e. one reporting Member State) – should be extended to aspects covered by Part II of the report (dealing with aspects of an ethical or local nature, such as recruitment). The European Commission has stated their intention to continue the practice of independent assessments by individual Member States here. "If the sponsor needs to receive a report from each member state on Part II, instead of via the reporting member state, the advances achieved from one reporting state in Part I may be cancelled out," says Van de Werf.

4-The ESC also appreciates efforts made by the European Commission to define strict timelines for submissions, assessments and decisions on clinical trials, as well as recognition that informed consent is not needed for the conduct of trials in emergency situations (such as when patients have suffered a myocardial infarction), and that clinical studies that do not involve "interventions" (and therefore do not pose significant risks to subjects) can be excluded from the legislation.

Further recommendations from the ESC include:

1.-Clinical trial populations reflecting the diversity of real life populations. The ESC feels that it is important that clinical trials enrol a significant proportion of women, young, and elderly subjects, as well as people from ethnic minorities, with clinical trials systemically analyzing results for these different groups. "In the specific case of gender, differences in the clinical presentation of some diseases (such as CVD) have been demonstrated and some therapeutic options may not be equally effective and safe in men and women," write the ESC authors.

2-Clinical trials involving CV imaging being encouraged. While the rapid development of CV imaging techniques has provided new tools for diagnosis and treatment of patients with CVD, limited clinical research has been undertaken comparing outcomes for the different modalities. "Although imaging techniques, such as MRI and angiograms, are widely used for patients with chest pains we're aware that few studies have been undertaken comparing their effectiveness. We therefore want to underline the importance of initiating trials to provide a scientific rationale for imaging" explains Van de Werf.

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