CONSULTATION ON THE EUROPEAN COMMISSION'S PROPOSAL FOR A CLINICAL TRIALS REGULATION

Response sheet

Instructions

Please send your responses electronically to clinical.trials@mhra.gsi.gov.uk using the table below. If you reply in writing, please also use this table. Responses should be sent by 31 December 2012.

Respondent details

Please provide your details as requested below.

- Please provide your name and (if relevant) the organisation or body you represent:

Dr A D Dwarakanath FRCP Edin Secretary Royal College of Physicians of Edinburgh

- Please tick this box if you want the information that you provide to remain confidential: ☐
- Please tick this box if you or the body you represent are in the NHS or public sector: ☐
- If you represent a private sector company, please indicate the number of employees in the company by ticking the relevant box below:

9 or less ☐ 10-49 ☐ 50-249 ☐ 250 or more ☐

Nr.	Question	Response
1	**Do you have views on the scope of the Regulation?**	We believe the scope of the proposed Regulation is appropriate. The regulation of trials of medications prescribed within their licensed indication has been unduly onerous. There certainly needs to be harmonisation in Europe as countries have all implemented the Clinical Trials Directive differently.
2	**Do you agree with the introduction of low-interventional studies?**	Yes. However, we believe the term "low-interventional" is inappropriate (and not good English!) as these studies may involve really valuable interventions. The level of risk to trial subjects is relatively low as all will receive active treatment with a medicine of proven efficacy and safety. These are therefore "low-risk" rather than "low-interventional" studies. That a different level of regulation is appropriate for such studies is clearly sensible and will encourage such studies, many of which are likely to be investigator-driven and thus "academic" rather than "commercial".
3	**Do you have views on any of the proposed definitions in Chapter 1 (Article 2) of the proposal?**	The definitions seem reasonable, but how helpful they will prove to be remains to be seen – they are very high level concepts which would probably require more detailed definition within an individual trial protocol. They do, however, ensure that high level discussion takes place using common terminology, which is helpful. We can foresee some difficulties, as a low risk trial in one country may not be seen as such in another country where the medicine is unlicensed.
4	**Do you agree that a single authorisation and a single decision (for both regulatory and ethics approval) through an EU portal will be of benefit to researchers? If so, how will this benefit you?**	We are strongly in favour of a single authorisation and a single decision process. This will be beneficial to study sponsors in avoiding the need to submit multiple versions of the same basic protocol in different forms and languages, and also in achieving a single approval without (or with minimal) country-specific requirements. The concept of "tacit approval" will also be valuable in minimising unnecessarily bureaucratic approaches to assessment. However we do foresee significant problems with this, as what is ethical in one EU state is not necessarily ethical or practical in another. For example in a country with poorly developed health care, most interventions are not only ethical but very welcome as otherwise inferior care may be provided. In countries with a free NHS, the ethics of research are not so clear cut. Licensing is another issue. Take the simple example of colchicine, which is licensed in some but not all EU countries for gout. In Denmark it is not used, so a trial in Denmark may not be considered low risk. There are very many other examples of inter-country differences

Nr.	Question	Response
5	**Do you agree that the proposed multi-state application and authorisation process reduces the burden on researchers? If so, how and would you be able to quantify this reduction?**	We do agree that the proposed multi-state application and authorisation process will reduce the burden on researchers. However it would be difficult to quantify this and we are not sure that efforts to do so will be feasible or worthwhile – it seems unlikely that failure to quantify the reduced burden would undermine the proposed regulation change.
6	**Keeping in mind that the proposal introduces a single decision (including regulatory and ethics approval) - would an extension of the timelines beyond the Commission's proposal (maximum 65 days) impact significantly on the conduct of clinical trials? And what timeline would be acceptable for this single decision?**	We believe that an extension of the timeline would not impact significantly on the conduct of clinical trials and 90 days would be reasonable if it was a single clear system underpinned by the concept of tacit approval. There may be merit in having an option to seek more rapid review in the event of a particular health emergency (e.g. to test a novel anti-viral agent before an impending flu pandemic) and also perhaps "low risk" trials could be approved within a shorter period such as 30 days
7	**What opportunities do you see to introduce more risk-adapted elements?**	Risk in the clinical trial setting needs to be balanced by potential or actual health benefits from participation in the trial, including (but not limited to) the risks of the new medicine itself. If "personalised medicines" are to give their predicted targeted benefits, then the acceptable level of risk is likely to be higher than for a more conventional therapy – however the actual level of risk (and even the nature of risk with newer types of medicine) may be very uncertain. Those reviewing and assessing proposed trials will need to handle even greater levels of uncertainty than in the past, but not to do so would deprive patients of possibly very useful medicines. It could be argued that trials of treatment strategies and trials using medicines that are so old that they have no patent protection require only "light touch" regulation. If we are to find new uses for older medications then we must make it easy to do this.
8	**Have you ever experienced difficulties obtaining insurance for a clinical trial?**	Yes. Some of our Fellows have found it very difficult or impossible to obtain insurance for a clinical trial.
9	**Do you recognise the Commission's suggested rise in costs of insurance?**	Yes. Sponsors will not perform a trial without insurance. Pharmaceutical companies have to self-insure. Investigators want to be absolved of product liability and protocol liability.

Nr.	Question	Response
		Insurance will not go away with no-fault compensation schemes. Insurance is here to stay and it will only get more expensive.
10	**Do you see benefits in a Government run scheme? If so, please explain what you think the benefits would be?**	A government run insurance scheme would probably only cover medicines that had no patent protection. So if a pharmaceutical company refused to cover the insurance for its product tested outwith its licence then they could effectively stop the trial. Once the liabilities are examined I expect that the insurer would have to be the EU. We have difficulty foreseeing our government taking on potentially unlimited liability. If they do then this would be very good for clinical research.
11	**Do you think that there are opportunities to include more specific requirements for GCP, or is the regulation specific enough?**	We think the regulation is specific enough as presently formulated.
12	**Have you identified any potential risks or improvements to the quality of clinical trials based on the proposed Regulation?**	We do not think that the proposed changes represent any appreciable increase in the level of risk associated with clinical trials. The reduction in the regulatory burden will be particularly welcome to academic investigators and may lead to important “low-risk” trials being undertaken which would not have been performed under the existing regulations. Overall we think that the proposed changes represent a substantial and welcome improvement for investigators and clinical trial subjects
13	**Are there any features that you think should be included in the proposal that would make the EU a more attractive place for the conduct of clinical trials?**	We believe that removal of the excessive burden imposed by the previous regulations will, of itself, make the EU a much more attractive option for clinical trials. It will be trial costs and availability of investigators and subjects that will ultimately drive decisions on the placement of clinical trials. We do not see anything in the revised regulations that is likely to prove excessively burdensome and therefore a major disincentive to a trial proceeding within the EU.
14	**Are there any other elements of the proposal that you would like to comment on?**	No