FUEHRING Stefan (ENTR)

From: ENTR /F/2 PHARMACEUTICALS
Sent: mardi 8 septembre 2009 17:29
To: FUEHRING Stefan (ENTR)
Cc: SALVADOR ROLDAN Rocio (ENTR)
Subject: FW: EU Consultation on Clinical Trials deadline 8th September

A/21467

From: Nicola Parrott [mailto:Nicola.Parrott@uhb.nhs.uk]
Sent: Tuesday, September 08, 2009 5:25 PM
To: ENTR /F/2 PHARMACEUTICALS
Cc: James ND (Birmingham University Staff); Sam Chittenden; James ND (Birmingham University Staff); Bion JF (Birmingham University Staff); Nicola Parrott; David Rosser
Subject: FW: EU Consultation on Clinical Trials deadline 8th September

To Whom it may concern,

I would like to forward the following comments on behalf of University Hospital Birmingham Foundation Trust:

General Comments

- While it is felt that the first EU Directive was in some ways useful, it also ramped up the trials paperwork. This was as much down to the UK interpretation of it both at government and university/charity levels as about what it actually said – people tend to operate on the precautionary principle and increase bureaucracy just in case compliance was not enough.
- Locally we do have a tendency to exercise excessive caution particularly were there is a question mark around capacity to give informed consent. This can often lead to inequalities in access to take part in clinical trials. We persistantly find ourselves in the position were a patient is suitable for inclusion but we shy away from approaching them due to communication, capacity or cultural issues.The latest set of amendments should have addressed this issue but have not done much to improve investigators options in this area. One of the distinguishing features of research hospitals is the US is the way they market early stage clinical trials . We persistantly find ourselves in the position were a patient is suitable for inclusion but we shy away from approaching them due to communication, capacity or cultural issues.
- One of the main problems with the first Clinical Trials Directive was that the insistence on prior written consent by a legal representative on behalf of a patient without capacity (any patient with severe incapacitating acute illness such as someone in ICU). This had a considerable impact on all emergency research in the UK, effectively bring it to a halt for 2 years. After campaigning that this be addressed by the Department of Health, and after a considerable period of time, a legal form for deferred consent was approved for use in the UK. For greater harmonisation of practice the EU directive should now be revised so that it permits countries to apply deferred consent for emergency

research, in effect ‘legalising’ what many countries (including Austria, Belgium, Denmark, France, Germany, The Netherlands and Norway) have already done.

Referenced Comments:

- 1.2- Scope, As with Directive 2001/20/EC, A number of categories of interventional trials are to remain outside of the scope of the directive. Key examples include Holistic therapies such as Acupuncture and Hypnotism, Implantable devices and in-vitro diagnostic. Whilst these are controlled by separate earlier directives/instruments for the purpose of consistency it would be helpful if these studies were considered under the same umbrella as all of our trials of IMPs
- 2.1.2- Applicable delays for Authorisation- It would be useful to have clarity on whether objections to translational aspects of research should delay the general issuing of favourable opinion. Consistent application of rules regarding conditional favourable opinion could benefit from being more explicit.
- 2.2-Covering Letter- States "Moreover, the covering letter should highlight if the trial involves a first administration of a new active substance to humans." It would be helpful to clarify the process for transition of favourable opinion to Phase II and Phase III studies. It is equally important that this information is given and for efficiencies sake it might already be the intention of the investigator to move directly to later phase studies and so conditional approval for this progression may be considered at this point.
- 2.4 Application Form- Would it be possible to consider amending wording to include the initial drafting of an application being made by a designated representative, as is often the case, under the proviso that the application is approved and signed by the investigator/sponsor in question
- 2.5 Protocol- Whilst the document refers to deviations from standard care after the study being mentioned in the protocol it does not mention this in the context of highlighting what the assumption of best supportive care is for the patient population in general. Whilst there is not always an established norm, where there is it would be very beneficial for trials teams to understand this from the outset.
- 2.6 Investigators Brochure It would be highly beneficial to trials staff to include a compulsory safety datasheet/risk assessment in this document as the standard of information of this sort that is provided in this document can often be insufficient. Whilst this is implied in the detail of this section guidance could be more explicit in this regard
- 3.3 The notion of "substantial" (Amendments) Does expanding the audience of trials related information constitute a substantial amendment? i.e. website content or general information available through clinical areas or information center. This is not clear in current guidance and recruitment would benefit from trials teams being able to make information more widely available to patient, clinicians and the public so they are generally more informed of the options that may be available.
- 3.6 Timelines- It would be helpful to include a requirement for sponsors to make sites aware of applications for amendments being made at the time of submission. Similarly once an amendment is approved sponsors should have a short period of time (say 2-5 working days) in which they must make participating sites aware of this decision and its implications. Whilst most sponsors do not often fall down in this area (Urgent changes are almost always

well communicated), those that do can cause significant disruption and expose participating sites to considerable risk in the event of regulatory review.

- 3.9-3.9 Suspension and Non-compliance- In the event of this occurring what would the process for appeal be for sponsors/participants and what arrangements should be made to make current study participants aware of this event?
- 4.4 Follow Up- States "If a new event occurs after the termination of the trial that is likely to change the risk/benefit analysis of the trial and could still have an impact on the trial participants, the sponsor should notify the national competent authority and Ethics Committee of the Member State concerned and provide a proposed course of action." Could this be further qualified to include a requirement for the sponsor to inform all current and historic participating sites at the same time, to ensure the safety of study participants.

That's all I have please let me know if there are any comments you disagree with or if you feel anything has been omitted.

Kind Regards

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