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Dear Sir or Madam

We would like to contribute the following comments on the European Commission Review of the Clinical Trials Directive. In the first section we have commented on the Key Issues set out in the NHS European Office's consultation paper and we then address other issues that have arisen at our organisations, following the implementation of the UK Clinical Trials Regulations.

1. Streamlining of clinical trial assessment procedures

In order to better streamline trial assessment and approvals, we would support a full harmonisation model, with one body awarding CTAs valid across the whole EU. This would help reduce any variances between NCAs and also ensure a greater level of consistency in trial assessments. In particular, whether a product is classified as an IMP should not vary between NCAs.

Greater co-operation between Ethics Committees, and further clarification on NCAs and ECs roles would also be useful. If authorisation requests were submitted to a 'one stop shop', it would avoid the increased paperwork of submitting information to all bodies and the delay in waiting for the information to be processed by each individual office.

2. Inconsistent implementation of the Directive

We agree that there is an element of over-classification of substantial amendments by Sponsors as they do not wish to be non-compliant. Reducing the number of amendments that require approval would also reduce paperwork, resources and administrative delays (in particular gaining the local NHS approvals).

Any measures to reduce variation in interpretation of the Regulations with regards to SUSAR reporting and follow-up and amendments would be beneficial to multinational trials.

3. Framework not always adapted to practical requirements

It is accurate to state that academic sponsors have difficulty taking responsibility for trials in other countries, mainly due to the increased cost of the resources required to do this. However, it is also the case that they are increasingly reluctant to act as Sponsor for UK trials, given the regulatory risks that this entails. A review of the implementation guidelines could improve the issue but an exclusion of academic Sponsors from the Directive would not help the issues faced by academic Sponsors of multinational trials, if each country were to set its own rules and results were not able to be used to support a marketing authorisation.

4. Special types of clinical trials

Amendments to the Directive that facilitate emergency and paediatric trials would be beneficial in ensuring that these types of trials do take place. Sponsors are keen to ensure that regulations are not being breached but different interpretations may have emerged in different countries. Academic Sponsors have less confidence that they can oversee the trial to the required standard if they are not able to obtain direct advice from the NCA. Greater guidance on these types of trials would ensure greater compliance with the regulations and more assurance that any additional risks were being managed effectively.

5. Ensuring compliance with GCP in 3rd countries

It is understood that GCP in 3rd countries may not meet the same standards as in the EU, making academic sponsorship difficult to oversee. Greater scrutiny of trial results submitted as part of marketing authorisations and supporting third countries where regulation of clinical trials is currently weak would help ensure GCP is enforced.

6. Other Issues

6.1 Classification of proposed studies

The regulatory framework surrounding the management of CTIMPS is necessarily strict and our organisations appreciate fully why this should be so. However, the classification of trials quite often throws up some quite surprising results. Some examples are:-

- Simple studies examining samples (single blood samples) for one-off analyses to study the effect of a particular drug on a particular patient cohort. These laboratory based studies have no patient follow-up visits, indeed the initial contact with the patient is the only contact. These studies are not clinical trials, but are often classified as such by the MHRA, in line with the Directive.
- Studies including food products (e.g. red wine, chocolate, beetroot juice, cabbage extract, and vitamins) mainly used as dieting supplements are frequently classified as CTIMPS, when this may not always be the case. These types of product can be purchased at numerous outlets throughout the UK by anybody and yet, in the context of a clinical trial, must be QP released in addition to adhering to the very strict regime of standard operating procedures that institutions must have in place, if such studies are to comply with the Directive.

Clearly tight regulation is required to ensure clinical trials are conducted in accordance with GCP. However, serious questions must be raised about how studies are classified as clinical trials and the type of products that are subject to regulation. Does it really make sense that the process of gathering evidence to support a view that regular use of a freely available foodstuff (chocolate or beetroot) not part of a core treatment regime, should be subject to the same level of control as that of a clinical trial of a new chemical entity?

6.2 Implementation of the Directive in the UK - MHRA Inspections

Many of the problems that we face with regards to sponsoring or hosting clinical trials in our organisations, that are now widespread in the Academic community, stem from the UK's own regulatory regime and in particular the approach to inspection that the MHRA have adopted. Both of our organisations have undergone GCP inspection. These visits proved to be burdensome. As Sponsors of research our organisations expected a full and thorough review, but found that the focus of the inspection and the production of findings by the inspectors, to be conflict driven, negative in perspective and unhelpful to both the investigators who lead our research and the administrators that seek to maintain quality standards. In addition, a large part of the inspection focused on administrative process and not on the safety aspects associated with the use of experimental medicinal products. The point here is that our experience of working with other academic and healthcare organisations throughout the European Union shows that although subject to the same Directive, these organisations are not subject to the same, extreme level of control that UK establishments are subject to. This makes it difficult for UK Sponsors to maintain a consistent level of quality management across multinational trials, as many European Union partners cannot equate the levels of control we in the UK are required to adopt, to that of their local regulatory bodies.

If you require any more information, or clarification of any of the points raised, please do not hesitate to contact me.

Yours Sincerely

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