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RE: Revision of the 'Clinical Trials Directive' 2001/20/EC
Comments on the European Commission concept paper submitted for public consultation

The Association of Medical Research Charities (AMRC) is a membership organisation of the leading medical and health research charities in the UK. In 2010-2011, AMRC's 126 member charities invested over £1 billion in medical and health research in the UK and a further £100 million to international research. This investment contributes to the UK's strength in biomedical science, bringing huge economic benefits. All our members are focused on benefiting patients and share a commitment to funding the highest quality research. Many have a strong patient group allied to them.

Our members fund a considerable number of clinical trials. In 2009-10 over 3000 clinical studies were conducted in the NHS; 37 per cent were funded by AMRC member charities[1].

Charities value the opportunity to support clinical trials, a clear benefit for their supporters. For example, there is currently only one treatment for the underlying cause of motor neurone disease (MND) which has only a modest effect on survival. Research is underway worldwide to develop new and effective treatments. To those with MND – many of which support the research charity, the MND Association – the opportunity to support and be involved with these trials is very important.[2]

We welcome the aim of the Clinical Trials Directive to provide a standardised framework for clinical trials conducted throughout the European Union and improve patient safety. However it is widely acknowledged that this goal is not currently being met and revisions are needed.

Value for money is a vital factor in charity investment decisions. Charities must ensure their funds and donations are wisely invested to best achieve their public benefit goals, in the case of medical research charities, investing in the development of preventions, treatments and cures on behalf of their supporters.

Charities find the complexity of assessment, including unnecessary duplication, and lack of a proportionate approach to regulation escalate the financial resources required. This presents a considerable barrier to funding trials:

> **Case study – Arthritis Research UK**
> In 2004, Arthritis Research UK funded a study looking at the effect of Vitamin D on older people with knee osteoarthritis. Vitamin D was classed as an investigational medicinal product under the EUCTD, and so researchers had to pay an additional £70,000 to have the vitamin 'repacked'. At the same time, the vitamin could be bought across the EU from online health stores, where it was deemed safe for anyone to buy and use. The requirements in the directive increased the cost of the research with no benefit to the safety of patients. The current revision of the EUCTD does not do enough to encourage regulatory authorities to take a risk-based approach, preventing similar cases in the future.

Below are our comments on the identified consultation items. In responding to these proposals, we have worked closely with fellow funders of medical research in the UK and this response should be considered alongside our joint statement on the revisions which you will receive separately**.**

[1] NIHR figures
[2] See http://www.mndassociation.org/research/research_explained/treatment_trials/ [accessed 12 May 2011]

Single submission with separate assessment
The development of a single submission process would greatly reduce the administrative work required of the sponsors. But requiring each member state to separately assess the information according to their interpretation of the Directive would result in difficulties arising from differing interpretations. Further work would be needed to harmonise the assessment process across Member States to overcome this.

Single submission with subsequent central assessment
We agree that central assessment by a scientific committee would not be feasible.

Single submission with a subsequent 'coordinated assessment procedure'
We are supportive of the principle behind this proposal to establish a 'coordinated assessment procedure' (CAP), led by a 'reporting member state' and allowing input from all member states.

We agree with the proposal that this assessment should have limited scope, excluding ethical and local issues which fall within the remit of member states. It is important that those aspects remaining within the remit of member states do not duplicate assessment, sharing best practice will aid harmonisation of these processes as closely as feasible.

We do retain some concerns over the proposed scope. Trial subjects or their representatives should be involved in the assessment of their acceptable level of risk as this may differ from the perception of academics and clinicians.

Further clarification of how the coordinated assessment procedure might operate is needed.

Disagreement with the assessment report
We are concerned that any proposal to address disagreements with the assessment made under the 'coordinated assessment procedure' should not introduce additional bureaucracy. It should include a mechanism for any lessons to be learnt to inform future operation.

We support the proposal allowing an individual member state to 'opt out' if necessary.

Mandatory/optional use
We believe that the 'coordinated assessment procedure' is not necessary for clinical trials occurring in one Member State so should not be mandatory for all clinical trials.

We support the long-term goal that all multinational trials should use the coordinated assessment procedure, however flexibility may be needed as we work towards this goal.

Tacit approval and timelines
We agree that care should be taken not to introduce steps and procedures to CAP that extend the assessment process – the length of authorisation timelines for research has a significant impact on Europe's competitiveness in medical research.

We support the proposal to identify 'type-A trials' eligible for a shortened assessment process. However we are concerned over the definition of such trials, particularly the interpretation of "*the interventions in the trial do not pose more than insignificant additional risk to the safety of the trial subject compared to normal clinical practice...*" This will need further discussion.

Better adaptation to practical requirements and a more harmonised, risk-adapted approach to the procedural aspects of clinical trials

Limiting the scope of the Clinical Trials Directive
We welcome steps to clarify the scope of the Clinical Trials Directive to aid harmonisation of interpretation across member states. It is a priority to develop, pilot and implement a proportional approach. In the longer term, there may be value in looking at ways to harmonise regulatory approaches to trials outside the scope of the Directive but we do not consider this to be desirable in this phase of revision.

Excluding clinical trials by 'academic/non-commercial sponsors' from the scope of the Clinical Trials Directive
We agree that the Directive should apply to all sponsors of clinical trials – academic/non-commercial and commercial. Consistency of approach is important to avoid disincentivising valuable collaborations between commercial and non-commercial research funders.

However measures to increase proportionality and harmonisation in application of the Directive must ensure that the bureaucratic burden does not remain a barrier to academic/non-commercial sponsors.

More precise and risk-adapted rules for the content of the application dossier and for safety reporting
We would strongly support a proportionate approach to clinical trial approval and monitoring, implementing a risk-based approach, with clear guidelines and an appropriate assessment system.

Such an approach will be complex and should be piloted and evaluated before its implementation. A standardised system is vital so measures should be taken to ensure successful implementation at the level of Member States.

Clarifying the definition of 'investigational medicinal product' and establishing rules for 'auxiliary medicinal products'
We support the clarification of the definition of 'investigational medicinal product' and establishing rules for 'auxiliary medicinal products'.

We would like further detail of the proportionate regulatory regime proposed for the newly defined 'auxiliary medicinal products'.

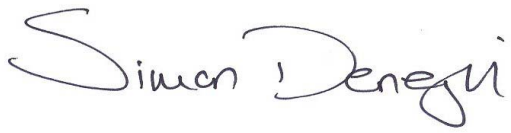
Insurance/indemnisation
In principle we welcome a more proportional risk-based approach. However more information and clarity is needed to comment on these proposals.

Single sponsor
We are concerned that the proposal to maintain the concept of a single sponsor rather than allowing a concept of 'multiple sponsorship' will limit the potential to conduct trials between Member States where it may be difficult to identify a single sponsor. Having more than one sponsor for a multiple-country study is a pragmatic solution as long as responsibility and delegation is clear.

Emergency clinical trials
We support these proposals to ensure emergency clinical trials can take place when appropriate, balancing the protection of individuals and a facilitative environment for research.

Ensuring compliance with good clinical practices in clinical trials performed in third countries
We support the development of an approach which avoids introducing excessive burdens on clinical trials in third countries but supports the maintenance of high standards and prioritises patient safety.

Yours sincerely,



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