motor neurone disease association

RESPONSE TO THE CONSULTATION ON THE CLINICAL TRIALS DIRECTIVE

1.1. Single submission with separate assessment

Consultation item no. 1: Do you agree with this appraisal? Please comment.
In our response to the 2010 consultation, we recommended a single assessment by a body at Community level as the best option. A single submission would be a necessary part of this, and in as far as it goes we would therefore support its introduction.

We would however like to have more detail regarding what information would be handled by the portal: crucially, would it distribute authorisation requests to all necessary ethics committees? Ethics approval and R&D offices are both major sources of costs and delays for clinical trials, and we called for a 'one-stop shop' for ethics committee submissions in our response to the 2010 consultation: we recommend that the new portal provide this function.

Consultation item no. 2: Do you agree with this appraisal? Please comment.
Yes. We called for a single assessment precisely because separate assessments in each member state are problematic. That said, the option of separate assessments in different member states should remain available if the option of multiple sponsors is pursued (consultation item 15), so that each sponsor could make an application in the appropriate member state. This would allow a greater range of organisations to become sponsors, such as charities and NGOs who are not currently willing to do so as it would entail taking responsibility for a trial in other member states.

1.2. Single submission with subsequent central assessment

Consultation item no. 3: Do you agree with this appraisal? Please comment.
Reluctantly, we feel we must agree with this: there is significant potential for problems with the central assessing body to be as bad as the problems they would be trying to solve, for instance if it were to become a bottle-neck that delays trials.

1.3. Single submission with a subsequent 'coordinated assessment procedure'

Consultation item no. 4: Is the above catalogue complete?
Consultation item no. 5: Do you agree to include the aspects under a), and only these aspects, in the scope of the CAP?
The above catalogue appears to be complete to us.

Regarding the proposal for a 'coordinated assessment procedure' itself, we note that the proposals do address the concern we raised in the prior consultation about giving individual member states responsibility for making Europe-wide decisions about trials. The restriction of this role to the functions outlined in (a) attempts to address this concern, but limits the benefits of streamlining the process to the extent that the value of the proposal must be questioned. Too much will still have to be decided by each individual member state.

In particular we regret the lack of proposals to address the bureaucratic burdens arising from ethics approval processes, unless the new single submission process will involve sending all the necessary information to appropriate ethics committees (as per our answer to 1.1).

1.3.2 Disagreement with the assessment report

Consultation item no. 6: Which of these approaches is preferable? Please give your reasons.

Allowing a member state an opt-out on the grounds of risk to public health or safety seems to us to make little sense: the whole point of this process is to reach a decision on the safety of a trial. This decision should be sufficiently robust that other member states should not have grounds to challenge it; this route might, however, provide a pretext for member states to disrupt or exercise influence over a trial for reasons that are not to do with safety.

Equally, if there are significant disagreements about a finely-balanced call on safety, resolving them by simple majority voting is likely to be highly unsatisfactory to the minority.

We therefore support an appeal mechanism to another body: this should resolve disputes when they arise, without creating a significant risk of unnecessary disruption to a trial.

1.3.3 Mandatory / optional use

Consultation item no. 7: Which of these three approaches is preferable?

We would support the CAP being made mandatory for all multinational clinical trials: making it mandatory for all trials would be overkill, as the problems it is intended to address to not affect single state trials, and making it optional would most likely leave trial sponsors uncertain over whether to use it or not, and many would be likely to treat it as mandatory anyway as a result.

1.3.4 Tacit approval and timelines

Consultation item no. 8: Do you think such a pre-assessment is workable in practice? Please comment.

We believe that pre-assessment could be workable in practice. To give a specific example, we are currently funding a trial of lithium carbonate in people with MND, which is the sort of trial that the new 'type A' designation seems intended to include: although as a single state trial, this particular trial might not have benefited from this proposal.

2.1 Limiting the scope of the Clinical Trials Directive

Consultation item no. 9: Do you agree with this appraisal? Please comment.
In principle it might well be better to have harmonised and proportionate requirements: however given the difficulty of this challenge (which the current version of the directive plainly fails) it should not be assumed that this will be practically possible. Improving the rules should be investigated in further detail, but options for limiting the scope of the directive should be developed at the same time, and limiting the directive's scope should not be discounted as an option at this stage. It may be that both options can be usefully pursued: limiting the directive's scope could make harmonisation much easier.

We must also note that we are pleased to see the acknowledgement of the disproportionate burdens placed on trials relating to lower prevalence conditions.

2.1.2. Excluding clinical trials by 'academic/non-commercial sponsors

Consultation item no. 10: Do you agree with this appraisal? Please comment.
We agree with this appraisal: exempting certain categories of sponsor from the directive would encourage perverse behaviour among sponsors who might seek to achieve this exemption artificially, for instance by using a non-commercial organisation as a 'front' for commercial trials.

2.2. More precise and risk-adapted rules for the content of the application dossier and for safety reporting

Consultation item no. 11: Do you agree with this appraisal? Please comment.
Consultation item no. 12: Are there other key aspects on which more detailed rules are needed?
We would like to see more details of these proposals. While application and safety reporting processes can be very burdensome, the proposal essentially adds more guidance and regulation to what is there already: without seeing that, it is hard to know whether it will be effective or not.

Reporting requirements for substantial amendments are particularly onerous: the new guidance would need to simplify these radically in order to be effective.

2.3. Clarifying the definition of 'investigational medicinal product' and establishing rules for 'auxiliary medicinal products'

Consultation item no. 13: Do you agree with this appraisal? Please comment.
As with the previous items, this proposal introduces more definitions and complexity; this will be effective only if the definitions align precisely with the needs of clinical trials.

2.4 Insurance / Indemnification

Consultation item no. 14: Which policy option is favourable in view of legal and practical obstacles? What other options could be considered?
Of the two options, we favour the removal of the requirement for lower risk trials. Obliging member states to indemnify against risk would introduce a new layer of national variation: in practice, some member states will adopt the proposal without any difficulty, but others may do so in a way that creates obstacles for trials.

2.5 Single sponsor

Consultation item no. 15: Do you agree with this appraisal? Please comment.
We accept that more effective harmonisation of rules across member states is likely to reduce the problems of having a single sponsor, but we recommend that the option of allowing multiple sponsorships be investigated further.

Joint or multiple sponsorships might allow the problems arising from diverse rules to be more effectively managed in each member state. In some trials there is a strong case for having multiple sponsors: if there are multiple funders, each financing activity in its own member state, having responsibility attributed to each funder would make a lot of sense. In particular, it could allow charities and NGOs to take on sponsorship responsibility, which currently many are unwilling to do, as it would entail taking responsibility for actions in other member states as well as their own. We would therefore like to see both options explored further, and neither discounted at this stage.

ABOUT MND AND THE MND ASSOCIATION

Few conditions are as devastating as motor neurone disease (MND). It is rapidly progressive in the majority of cases, and is always fatal. Patients will, in varying sequences and combinations, lose the ability to speak, swallow and use their limbs; the most common cause of death is respiratory failure. Most commonly the individual will remain mentally alert as they become trapped within a failing body, although some suffer from dementia or cognitive change. There are around 5,000 people living with MND in the UK. Half of people with the disease die within 14 months of diagnosis. There is no effective curative treatment.

The MND Association is the only national organisation supporting people affected by MND in England, Wales and Northern Ireland, with approximately 90 volunteer led branches and 3,000 volunteers. The MND Association's vision is of a World Free of MND. Until that time we will do everything we can to enable everyone with MND to

receive the best care, achieve the highest quality of life possible and to die with dignity.

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