GENE PEOPLE

the genetic conditions support network

Gene People response to MHRA Clinical Trials Consultation March 2022

Clinical trials are vital to those with genetic conditions. Gene People sent a response to the MHRA consultation on clinical trials on behalf of the rare condition community. It was a highly technical consultation and not all questions were relevant to our community.

Consultation questions

1. *Do you agree that the legislation should include a requirement for the involvement of people with relevant lived experience in the design, management, conduct and dissemination of a trial?*

Yes – The rare disease community have a principle that is 'nothing about us without us' and it is a principle Gene People strongly advocates. Inclusion in all aspects of clinical trials will help to meet the actual real needs of that particular patient and family community rather than the assumed or perceived needs. Rare disease patients and families and their support groups have crucial insights into their disease that it would be difficult or impossible to gather from other sources such as clinicians because they have the lived experience of the condition. These insights can influence the conduct of trials by helping to define end points and in the measurement of changes brought about in their condition by the therapy under development. This also contributes to the eventual determination of cost and clinical effectiveness and to decisions about patient access.

2. *Do you agree that the legislation should include a requirement to register a trial?*

Yes – Gene People would endorse the requirement to register a trial so that research funding – often raised by charities and patient groups – can be spent on items not already under investigation. A full register would also make it easier for patients and families to find trials and participate in those relevant to their condition for which they are eligible.

3. *Do you agree that the legislation should include a requirement to publish a summary of results within 12 months of the end of the trial unless a deferral has been agreed?*

Yes – Gene People believes this would save potential duplication and would faster advance scientific knowledge. Speed of discovery is a key factor for many rare conditions that are often life-changing, life-limiting and devastating.

4. *Do you agree that the legislation should include a requirement to share trial findings with participants? (or explain why this is not appropriate)*

Yes – The rare disease patient community is very supportive of research and development, raising funds to support basic research and participating actively in the design of clinical trials and the recruitment of patients and families. Individuals often take a deep interest in the science around their condition or that of their family member and want to understand the new knowledge relating to that condition. Additionally, sharing findings with participants would close the communication loop, which is good practice.

5. *Do you support a combined MHRA and ethics review, with an initial decision given on the application (i.e. approval or a request for further information) within a maximum timeline of 30 days from validation?*

Yes – Gene People supports means of streamlining processes as these will ultimately help patients gain access to novel treatments in a shorter timeframe.

6. *Do you support a sponsor-driven timeline to respond to any requests for further information (nominally 60 days but with flexible extension)?*

No comment

7. *Do you support a combined MHRA and ethics final decision on a trial of a maximum of 10 days, following receipt of any Requests for Further Information (RFI) responses? The overall time for a final decision would be sponsor driven, depending on their need to take an extended time to respond to an RFI.*

Yes – no further comment

8. *Do you support the ability for the regulators to extend the timeframe for medicinal products or trials where the risks involved may be greater so that independent expert advice can be sought?*

   Yes – this could impact the rare disease community more frequently than patients with more common conditions as treatments for rare conditions are increasingly sophisticated and innovative. However, just because a disease is rare does not mean that patients and families are prepared to accept lower standards for quality, efficacy and safety than is the case for the treatment of common diseases. Because of the small numbers involved, traditional methods for determining these may be inappropriate or impossible and patients would welcome the use of AI models to give greater assurance as to safety to enable participation in trials.

9. *Do you consider it appropriate that a clinical trial approval should lapse after a specified time limit if no participants have been recruited?*

   No – this is not suitable for rare diseases, especially in consideration of ATMP development where the criteria for those eligible to participate in trials are likely to be highly restricted. For some conditions there will be an inherent delay to

recruitment of participants. There are also geographical considerations given the size of some patient populations; please see responses to questions further in the survey. NB this response was put into the comment box above clearly marked as no comments were asked for in relation to this question.

10. *Do you consider that a trial sponsor having sight of Requests for Further Information (RFI) when they are ready, rather than issued when the final part of the assessment is complete would be advantageous?*

Yes

11. *Do you consider that the ability to receive an RFI during the review of a substantial amendment would be beneficial?*

No comment

12. *Do you agree that we introduce the concept of a notification scheme into legislation?*

Yes

13. *Do you consider that the proposed provisions for clinical trial approvals strike the right balance of streamlined, proportionate approval with robust regulatory and ethical oversight?*

Yes – we are keen to expedite access to new treatments for rare diseases and these proposals appear to be contributing to that endeavour whilst maintaining a focus on safety and ethics.

14. *Do you have any views about the membership or constitution of Research Ethics Committees?*

Gene People would strongly advocate for patients to be involved in the REC, either as individuals or patient organisations – with a structured programme of support and attention to conflict of interest. Gene People queries the concept of 'lay' members as those with lived experience of conditions are expert by experience, and frequently have a much higher understanding of factors such as disease burden than those not in the rare disease community. Patients and families with rare conditions have a unique perspective on benefits and risks. Not all benefits are equally valuable, and not all risks are equally acceptable.

We would also ask that contribution is recognised for both individuals and organisations with the payment of an honorarium. Patient support groups, especially for those with ultra-rare conditions, are frequently tiny and lack resource and expertise in the regulatory process. If they are to be able to contribute effectively there will need to be investment in capacity building and the creation of new routes to support their contribution.

15. *Should we introduce legislative requirements to support diversity in clinical trial populations?*

No – Gene People welcomes all attempts to broaden the backgrounds of those who participate in trials as this creates more robust evidence, however, because of the nature of rare conditions we think this should be guidance and not legislation unless clear exemptions are included. There are some rare conditions that are limited in the population affected, e.g. Duchenne affects boys only, and we would not want to see trials fail because of a lack of diversity in the proposal.

16. *Do you agree that legislation should enable flexibility on consent provisions where the trial is considered to have lower risk?*

No comment

17. *Do you agree that it would be appropriate for cluster trials comparing existing treatments to use a simplified means of seeking agreement from participants?*

No comment

18. *Do you agree to remove the requirement for individual SUSARs to be reported to all investigators? They will still be informed via Investigator's Brochure updates.*

No comment

19. *Do you agree with removing the requirement to report SUSARs and annual safety reports to RECs? Noting that MHRA will still receive these and liaise with the REC as necessary.*

No comment

20. *Do you agree that, where justified and approved by the regulatory authority, SUSARs can be reported in an aggregate manner?*

No comment

21. *Do you agree with the proposal to remove the requirement to include listings of serious adverse events and serious adverse reactions in annual safety reports and instead include an appropriate discussion of signals/risks associated with the use of the medicinal product as well as proposed mitigation actions?*

No – Gene People would like SUSARS included in the annual safety reports but contextualised so patients, families and clinicians can form an evidence-based judgement on their implications.

22. *Do you agree with the proposal to extend the written notification for Urgent Safety Measures from no later than 3 days from when the measure was taken, to no later than 7 days?*

Yes – as long as there is no change to the process that will impact patient safety. This seems an administrative task to confirm something already notified.

23. Do you agree that the proposed safety reporting requirements will reduce burden on researchers but maintain necessary levels of safety oversight?

No comment

24. We are proposing changing the current legislation to incorporate more elements on risk proportionality. Our desire is that this will facilitate a culture of trial conduct that is proportionate and 'fit for purpose' for both researchers and regulators. Do you agree with this approach?

No - Clinical trials for rare disease therapies frequently recruit across national boundaries. This is possible because of regulatory harmonization. If the UK departs from arrangements currently in place to the extent that international recruitment becomes more difficult or impossible then trials will not be located in the UK, and UK patients and other stakeholders will be denied the opportunity to benefit. This will result in otherwise avoidable harms to patients, loss of leadership for the academic and clinical community and economic harm as companies relocate their business.

25. Do you agree that service providers of electronic systems that may impact on participant safety or reliability of results should also be required to follow the principles of GCP?

Yes – all aspects of a trial should meet the same standards to increase patient trust and stimulate participation and retention in trials.

26. *Do you agree that the current GCP principles require updating to incorporate risk proportionality?*

No comment

27. What GCP principles do you consider are important to include or remove and why?

No comment

28. Do you agree that regulators should be permitted to take into account information on serious and ongoing non-compliance that would impact participant safety they hold when considering an application for a new study?

Yes – Gene People does not want patient safety compromised and knowledge of previous in non-compliance forms a significant piece of information to mitigate those risks. However, Gene People suggests that evidence of rectifying the non-compliance be presented alongside the information relating to the non-compliance as organisations could and should be encouraged to learn from past mistakes.

29. Do you agree it would be appropriate to enable regulatory action to be taken against specific part of a trial rather than the trial as a whole?

Yes

30. Do you agree that we should introduce the term 'non-investigational medicinal product' into legislation to provide assurance on the quality and safety of these products?

No – due to the size of patient populations for rare conditions trials are frequently pan-European if not global in recruitment. We do not want there to be any unalignment with other regulatory regimes that might cause confusion or create additional burden to companies that, in turn, might dissuade them from using the UK as a trial site as this would lead to UK patients facing delayed access to innovative treatments.

31. Do you agree that where a medicine is labelled according to its marketing authorisation (and is used in its approved packaging) that specific clinical trial labelling may not be required?

No comment

32. Do you agree that it is appropriate for radio pharmaceuticals used in a trial to be able to be exempted from the need to hold a Manufacturers Authorisation for IMPs?

No comment

33. Do you have any comments or concerns with the proposed updates to the definitions outlined?

Gene People welcomes greater alignment with international practice.

34. Which healthcare professionals do you consider should be able to act as an Investigator in a trial?

No comment

35. Do you consider that the legislation should state that any appropriately trained and qualified member of the investigator's team can seek consent?

Yes – Gene People welcomes this move as it will remove a barrier to the speed of accessing trials.

Q: *Do you consider it appropriate that data collection following MHRA approval for use of an unlicensed medicine can be considered as non-interventional where the collection is according to the 'approved' use? Yes/No Please provide any further detail to your answer*

Yes

36. Do you agree that the proposed changes introduce improvements to streamline processes and to remove unnecessary burdens to trial sponsors?

No opinion as the range of proposals and our responses to them are varied.

37. Are there other aspects of the Clinical Trials legislation that you believe have not been considered but need to be? For example, is there something you think should be addressed now or should be considered for future legislative changes?

There are significant numbers of rare disease therapies under development which fall into the ATMP category. The revised regulatory framework for clinical trials must accommodate this development if gene and stem cell therapy trials are to be undertaken in the UK. Furthermore, horizon scanning indicates that more novel methodologies, for example genome editing, are in the pipeline so the regulatory framework needs to be future proofed if these are to be tested in the UK and rare disease patients' participation is to be enabled.

38. We do not consider that our proposals risk impacting people differently with reference to their protected characteristics or where they live in NI. Do you agree?

Yes - We agree with your view with the caveat that those in Northern Ireland and other communities not connected to the mainland would need additional support to participate in clinical trials as there would be significant burden of travel for these communities. It is also important to consider the provision of materials in non-English languages in order to promote recruitment.

Impact Assessment

1. *Are there potential costs or financial implications of the proposals outlined that you think we need to especially consider? Can you provide any evidence or comment that would help us develop the cost benefit analysis on the proposed changes?*

No comment