

BioIndustry Association response to MHRA consultation on proposals for legislative changes for clinical trials

March 2022



This consolidated BIA response was developed with input from our Regulatory Affairs Advisory Committee and submitted using the online survey providing our comments in response to questions raised in the MHRA [consultation document](#) on proposals for legislative changes for clinical trials.

The MHRA has consulted on a set of proposals to update the current UK clinical trials legislation, the Medicines for Human Use (Clinical Trials) Regulations 2004, as amended. This will provide the opportunity to design a world-class regulatory environment for clinical trials to support the development of new innovative medicines and ensure that the UK retains and grows its reputation as world leading base for life sciences, in line with the ambitions of the [Life Sciences Vision](#).

The legislative proposals aim to streamline clinical trials approvals, enable innovation, enhance clinical trials transparency, enable greater risk proportionality, promote patient and public involvement in clinical trials, as well as ensure the legislation builds international interoperability to conduct multinational trials.

Background questions

When responding please say if you are a business, individual or representative body. In the case of representative bodies, please provide information on the number and nature of individuals or firms you represent.

Which best applies to you:

- I am responding as an individual
- I am responding on behalf of an organisation**

If you are responding on behalf of an organisation, please tell us the geographical area(s) your organisation covers

- United Kingdom**
- Great Britain
- England
- Northern Ireland
- Scotland
- Wales

Name of organisation

UK BioIndustry Association (BIA)

Main activities of your organisation

The BIA is the trade association for innovative life sciences in the UK. Our goal is to secure the UK's position as a global hub and as the best location for innovative research and commercialisation, enabling our world-leading research base to deliver healthcare solutions that can truly make a difference to people's lives.

Are you

- a patient / carer
 a healthcare professional / trial investigator

Working in:

- Pharma
 Biotech
 Contract Research Organisation
 academia /non-commercial
 a trial funder
 charity
 Other – please specify

The BIA represents over 460 members, including UK-based life science companies, international biopharmaceutical companies and Contract Research Organisations.

Consultation questions

Patient and public involvement

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?

NO

Please provide any further detail to your answer, including how you think this could be best implemented

- BIA agrees that participant involvement and inclusion of lived experience is important. Whilst we are supportive of the involvement of patients/care givers in the design of clinical trials we do not consider it necessary to make this a requirement in legislation. We believe this could be adequately covered in detailed best practice guidance to help sponsors of trials demonstrate how involvement of people with lived experience has been included in trial design, management and conduct.
- The guidance should allow for degrees of public and participant involvement to be applied where appropriate to ensure this does not become an unnecessary burden on trial set up. For example, lived

experience is important for the understanding of rare disease indications, but required to a lesser degree for well characterised disease areas such as oncology. The level of patient engagement should be expected where the need is greatest rather than across all trials, depending on different factors such as degree of unmet medical need.

- Moreover, we would require clarity as to whether we are aiming to gain input from UK only patients, and/or patient groups outside the UK. For multinational trials, there is concern this would increase the time and burden of setting up trials in the UK, which would be contrary to the aims of the UK vision for the future of clinical research delivery and the Life Sciences Vision.

Research transparency

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

YES

Please provide any further detail to your answer

- BIA agrees with the proposed requirement to register trials in publicly accessible databases, which is standard practice for member companies. Registration in a primary clinical trial registry recognised by WHO, e.g., EU Clinical Trials Register (EU-CTR), ISRCTN registry, would enable compliance with the legislative proposal. We noted the partnership of the Health Research Authority (HRA) with ISRCTN whereby from 1 January 2022 clinical trial applications that are submitted via the new Integrated Research Application System (IRAS) will be registered on the ISRCTN registry after trial authorisation. Further clarity is requested about the registration process and data used from the HRA's system, and whether trial sponsors could choose a different registry.
- It is important to include an option to extend the time for registering a phase 1 trial. In addition, members suggested the registration of a minimal set of data for such trials as concerned to having data made public so early in development.

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

Please provide any further detail to your answer

- It is assumed the end of the trial covers global end of trial.
- As regards summaries of phase 1 trial results we would recommend that these are published at least 24 months after the last visit of the last subject.

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

Please provide any further detail to your answer

- Guidance should be provided on the format and means by which trial findings are expected to be shared with participants. We would suggest publishing a summary of the trial results in the public domain and informing patients of the timeframe when this will be available (and who to contact for discussion) at the time of informed consent. However, the introduction of this requirement should not add unnecessary burdens to sponsors or investigators (e.g., tracking if participants have received/read the information). It would be helpful to understand the need to share information with relatives/nominees of participants because certain trials due to their nature may not have results available after participation or participants may not survive until the trial results are published.

Clinical trial approval processes

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

Please provide any further detail to your answer

- BIA strongly supports this proposal; this would make the UK very competitive in terms of regulatory and ethics committee approval timelines for start-up of phase 2-4 trials.
- We also recommend that the current expedited approvals of phase 1 trials are maintained in the combined review system when the proposed legislative changes are introduced.

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

YES

Please provide any further detail to your answer

- BIA supports the proposed timeline of 60 days (with the possibility of flexible extension) for a sponsor to respond to any requests for information raised which would facilitate the harmonisation of multinational/global trial protocols and better align requests for changes from multiple regulators.

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

Please provide any further detail to your answer

- BIA supports the MHRA/ethics final decision timeline of a maximum of 10 days following receipt of responses to RFIs. In the event of subsequent RFIs after the first RFI responses, further clarity is

requested as to whether the MHRA/REC would be able to clarify any deficiencies in RFI responses within the 10-day period (rather than initiating another round of RFIs).

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

Please provide any further detail to your answer

- Further clarity is requested on the type of products/trials for which the MHRA needs to obtain independent expert advice from the Commission on Human Medicines and its Expert Advisory Groups (EAG). Sponsors should be informed of the timeline extension during the validation period. We would also recommend the ability of trial sponsors to approach the MHRA for advice on prospective EAG review to reduce review timelines for the regulatory and ethics combined review.
- The regulatory and ethics review timelines are currently not the rate limiters to clinical trials. Rate limiters for trials with innovative products or advanced therapies are often the subsequent approvals required from authorities like the Department for Environment, Food & Rural Affairs (DEFRA), the Health and Safety Executive (HSE), the Administration of Radioactive Substances Advisory Committee (ARSAC), and the Human Tissue Authority (HTA). We would strongly recommend enabling a process using IRAS to submit the application for the MHRA/Ethics combined review process, as well as the applications for parallel reviews and combined approvals of all other required authorities.

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

- Changes in medical practice regarding an approved trial can be effectively managed through the process of substantial amendments of trials. Setting a 2-year target timeline from trial approval to recruitment of subjects would disproportionately affect trials that are generally slow to recruit such as those in rare disease indications or those with paediatric participants.
- The need to apply for an extension of the trial approval due after a specified time limit is likely to increase the administrative burden to conduct trials in the UK.

10. Do you agree that the detail currently outlined in schedule 3 would be better in the form of guidance rather than legislation?

YES

Please provide any further detail to your answer

- BIA would support the information currently outlined in schedule 3 to be made available in the form of guidance rather than legislation. This will provide flexibility to update the required documents for applications, while allowing regulators to remain agile and responsive to future policy changes and innovation in research.

11. 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

Please provide any further detail to your answer

- BIA would strongly support a ‘rolling review’ approach to RFIs and sponsor responses. The experience gained from COVID-19 clinical trial applications has demonstrated the benefits direct communication between sponsors and reviewers has in reducing overall RFI response timelines. We agree that this proposal has the potential to improve efficiency of interactions.

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

YES

Please provide any further detail to your answer

- BIA would support this proposal. This would reduce the instances where rejections are issued when deficiencies can be responded to through an RFI step prior to conclusion of the MHRA/REC review.

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

YES

If yes, do you agree that the subset of trials outlined would be appropriate to be eligible for a notification scheme?

YES

Please provide any further detail to your answer

- The proposed notification scheme for low-intervention trials will reduce the burden for global and local regulatory submission teams. The concept aligns with that of low-intervention trial in the EU Clinical Trials Regulation. However, these trials are subject to the same assessment process as any other clinical trial, but with adapted dossier requirements.
- The examples outlined are helpful in defining the types of trials that could be eligible for a notification scheme. It would be interesting to understand though if any gap analysis has been undertaken to understand why the uptake currently is so low and if the proposed introduction of the concept into legislation will address this gap.

14. 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

Please provide any further detail to your answer

- The proposals outlined for low-interventional trials are pragmatic and proportionate. This will help to create the right research environment for these types of trials in the UK.
- Consideration should be given to certain trials that would be low-interventional in the UK but meet the EU definition for similar trials. Industry will need assurance that data collected from trials in the UK is not treated any differently for the purposes of a marketing authorisation application based on multinational trials run in the UK and EU.

Research Ethics Review

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

- BIA would support the adoption of unified guidance for all RECs in the UK if schedule 2 of the current legislation were to be removed. The HRA guidance need to ensure consistency while allowing for greater agility in decision making. Membership should include appropriate medical and clinical development expertise.

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

NO

Please provide any further detail to your answer

- BIA strongly supports increasing diversity in clinical trial populations. However, we do not consider it is necessary to introduce this concept into legislation for it to become routinely embedded in clinical research. We would propose to have best practice guidance documentation, while avoiding any reference to quotas or specific measures that could be construed as coercive or applying undue pressure to currently under-represented groups or individuals to participate in clinical trials.
- The detail for different participant groups (e.g., women at different stages of pregnancy, age groups, ethnic groups) and disease/indication specific scientific guidelines would be necessary to help sponsors demonstrate participation from a diverse and representative patient population.
- Regulators should also engage with representative patient groups on guidance development, and proposals in this area will need to be sufficiently broad to accommodate future developments e.g., current draft ICH proposal on inclusion of pregnant women in clinical trials.

Informed consent in cluster trials

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

YES

Please provide any further detail to your answer

- BIA agrees that legislation should enable flexibility on consent provisions assuming participants are informed, and confidentiality is protected.

- Guidance would be required to provide clarity where such flexibilities can be applied, and the characteristics of trials that qualify.

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

YES

Please provide any further detail to your answer

- BIA agrees that it would be appropriate to streamline the requirements to seek consent from participants for low-interventional cluster trials comparing existing treatments. It would be useful to understand the need for consent in certain trials where participants would only be treated according to approved, standard of care regimens (i.e., no interventional elements such as deviating from standard treatment or use of placebo).

Safety reporting

19. 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.

YES

Please provide any further detail to your answer

- BIA supports the removal of the requirement for individual SUSARs to be reported to all investigators. This is a positive development, which will help reduce the administrative burden on sponsors and investigators.
- We would support the removal of this requirement for all trials, including SUSARs for rare disease studies.

20. 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.

YES

Please provide any further detail to your answer

- BIA agrees with the proposed removal of this requirement. This is a duplicative and unnecessary process. This would reduce the administrative burden on sponsors with a clear single point of accountability with the MHRA established.

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

YES

Please provide any further detail to your answer

- BIA is supportive of the proposal to report SUSARs in an aggregate manner; this aligns with other regulatory authorities' initiatives such as the FDA. It would be helpful to clarify 'where justified and approved'; without clarity member companies risk running parallel processes for notification of SUSARs to the MHRA (individual vs aggregated). The engagement of an Independent Data Monitoring Committee (IDMC) to allow for aggregated reporting may increase complexity for studies where individual SUSAR reporting is preferential.
- We would require guidance, including illustrative examples, on the timing of submission of these reports, the format (either in a Development Safety Update Report or IDMC review) and information about the types of trials where this would be considered justified to ensure that aggregate reporting is appropriate for oversight of emerging safety signals.

22. 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?

YES

Please provide any further detail to your answer

- BIA supports this proposal. Providing a discussion of the signals/risks together with the proposed mitigation actions will lead to a harmonised approach which reduces the potential for individual investigators to interpret the findings and develop their own mitigation action.
- A flexible approach would be welcome, not requiring member companies to produce a separate DSUR for the MHRA. These listings may be required in reports to other regulatory authorities.

23. 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

Please provide any further detail to your answer

- The resulting alignment with the EU Clinical Trials Regulation and harmonisation of timelines for reporting Urgent Safety Measures is welcome.

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

YES

Please provide any further detail to your answer

- BIA agrees that the proposed safety reporting requirements will reduce unnecessary burden and harmonise approaches to interpreting signals and mitigating any ensuing risks. The proposal will help streamline the amount of information being sent to keep it relevant during submission of Annual Safety Reports or Development Safety Update Reports.

Good Clinical Practice

25. 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?

YES

Please provide any further detail to your answer

- BIA supports the concept of risk proportionality as outlined in the consultation document. The areas where risk proportionality may be applied require further clarity to ensure that the proposed reduction of burden does not inadvertently affect quality of data or compromise patient safety.
- The proposed requirement for a proportionate Trial Master File is welcome and help reduce the focus on extensive filing. However, it may be challenging for companies conducting multinational/global trials to have a country specific approach that is different from the global standard for TMF filing.

26. 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

Please provide any further detail to your answer

- BIA agrees with the proposal. We support the need for providers of electronic systems to follow the principles of GCP, particularly when the use of such systems has the potential to directly impact the safety of participants in clinical trials or the quality of data resulting from trials.
- Moreover, the rate of evolution of electronic systems is rapid and the potential benefits that they can bring to the conduct of trials should be enabled by taking a risk proportionate approach to GCP compliance. The legislation should not become a barrier to adoption of electronic systems for use in clinical trials.

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

NO

Please provide any further detail to your answer

- BIA member companies stressed the need for convergence with the ICH GCP for conducting clinical trials and not developing a set of ‘UK GCP’ principles.

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

- There are not any specific GCP principles that require removing, other than the level of documentation/retention schedule which could be updated.

Sanctions and corrective measures

29. 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

Please provide any further detail to your answer

- BIA is supportive of this approach. Clarity is requested on the types of non-compliance that may result in action from the regulators to ensure this is not seen as a deterrent to potential sponsors. Relatively minor transgressions by a sponsor should not have an impact on review of subsequent clinical trial applications.
- A robust and rapid appeal process against grounds for non-acceptance should be in place.

30. 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

Please provide any further detail to your answer

- BIA agrees with this proposal enabling regulatory action against a specific part of a trial without the entire trial being stopped. This approach would be beneficial for trials with multiple arms where only parts of the trial can be halted based on regulatory/clinical need.
- It would be helpful to provide clear guidance and examples where such regulatory action can be expected.

Manufacturing and assembly

31. 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

Please provide any further detail to your answer

- The concept of a ‘non-investigational medicinal product’ (non-IMP) has existed in clinical trial terminology for many years and there is guidance setting out how a medicine is considered as non-IMP in the context of a trial.
- We will see little benefit with the introduction of this term into legislation If guidance maintains current concept for future clinical trial applications.

32. 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?

YES

Please provide any further detail to your answer

- BIA supports this proposal to introduce risk-proportionate requirements in UK legislation, but the legislation should not preclude some form of IMP labelling if needed for operational purposes.
- Currently a minimal label is required for trials where medicines are to be used according to the marketing authorisation. This enables identification of sponsor/CRO/investigator with a trial reference code to identify the site/investigator and participants. This also aids in differentiating stock intended for clinical trials vs that in place at a site for normal use and enables drug accountability.

33. 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

Please provide any further detail to your answer

- An exemption from the need to hold a Manufacturers Authorisation may be a concern if the GMP standards are not being met. We would rather recommend an abbreviated Manufacturers Authorisation or special license that would enable a balance of speed as well as compliance with GMP standards expected in clinical trials.

Definitions and other terminologies

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

- BIA generally supports the proposed updates to the definitions outlined in the consultation document to update UK terminology and promote international harmonisation of definitions.
- It would be helpful to provide clarity around the expected responsibilities and roles of sponsors vs. co-sponsors/joint sponsors vs. legal representatives, including guidance where co-sponsors are established in the US or EU, and whether a legal representative would be needed.

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

- The use of the term ‘authorised health professional’ is a good guiding principle. We would recommend that any healthcare professionals are allowed to act as investigators if they can demonstrate that they are suitably qualified and have the necessary experience in the management of patients with the condition under investigation, as required in the clinical trial protocol. The legislation should give greater flexibility so that specialised healthcare professionals (i.e., other than qualified physicians for instance) can be involved.

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

YES

37. 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

Please provide any further detail to your answer

- We would support the proposal to enable long term follow-up of participants in trials to be considered as non-interventional if such follow-up does not deviate from the standard of care management of these participants. This would provide a very pragmatic position to encourage the conduct of advanced therapy trials that typically require extended periods of safety/efficacy follow-up.

Conclusion

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

YES

Please provide any further detail to your answer

- BIA agrees that there are some very promising changes being proposed to be included in the clinical trials legislation.
- We would encourage further integration of CTA processes and including other regulators and regulatory processes (see response below).

39. 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?

- Innovative medicines and advanced therapies are often subject to subsequent approvals required from authorities such as the Department for Environment, Food & Rural Affairs (DEFRA), the Health and Safety Executive (HSE), the Administration of Radioactive Substances Advisory Committee (ARSAC) and the Human Tissue Authority (HTA). We would strongly encourage greater streamlining of these reviews with the combined MHRA/Ethics review process to create a 'one-stop' approval process. This would be a great step forward to making the UK a global destination to conduct clinical trials and market new innovative medicines.
- Aligning the regulatory process for clinical trials alongside other points of engagement with the MHRA e.g., scientific advice, Innovation Passport.
- Timelines need to be globally competitive to ensure R&D investment in the UK.
- The legislation needs to ensure international interoperability to conduct multinational trials since many sponsors conducting a trial in the UK would also be conducting the trial in EU countries and elsewhere.

Impact Assessment

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

- Fees associated to renewal of clinical trials proposed as part of the legislative changes would be a potential financial and administrative barrier to the conduct of trials in the UK.
- A centralised Ethics Committee system should be considered in the UK to streamline the review process from a cost and efficiency perspective.

Equality and Rural Screening – Northern Ireland

In Northern Ireland new policies must be screened under [Section 75 of the Northern Ireland Act 1998](#), which places a statutory duty on public authorities, to mainstream equality in all its functions – so that equality of opportunity and good relations are central to policy making and service delivery. In addition new or revised policies must be rural proofed in line with the [Rural Needs Act \(NI\) 2016](#) which requires public authorities to have due regard to rural needs.

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 welcome any further views on this point.

We seek clarification on packaging and whether specific clinical trial labelling would be required at NI sites compared to GB sites.

Do you think the proposals could impact people differently with reference to their [or could impact either positively or adversely on any of the] protected characteristics covered by the Public Sector Equality Duty set out in section 149 of the Equality Act 2010 or by section 75 of the Northern Ireland Act 1998? If so, please provide details.

NO

Do you have any evidence that we should consider in the development of an equality assessment?

No further comments

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