BIA response to MHRA consultation on gene therapy medicinal products

Overview

The BIA has responded to the MHRA's consultation on proposed updates to the definition of gene therapy medicinal products. The proposed updates aim to modernise the GTMP definitions to reflect current scientific practice due to advances in gene therapies since the original definitions were developed in 2007. The MHRA's proposals are largely aligned with the EU's proposed amendments, with a few differences which are outlined in the consultation document.

The BIA welcomes the MHRA's proposals, which provide greater clarity for developers and will help to maintain the UK's position as a supportive environment for advanced therapy development. In our response, informed by input from BIA members, we:

- Welcomed the MHRA's proposals to align with the key revisions in the EU's updated GTMP definition, with a few differences which aim to provide greater alignment and consistency.
- Highlighted areas where the guidance would benefit from further clarity, including by providing illustrative examples.
- Set out our perspective on the impacts of the changes for developers and the wider life sciences sector involved in the supply chain for advanced therapies.

Consultation questions

1. **Do you think that medicinal products produced from non-biological starting material should also be classified as gene therapy medicinal products (GTMPs), if they meet other proposed criteria of GTMPs as outlined in Appendix 2?**

BIA response – agree

Explanation: We agree that whether a product is made from biological or synthetic starting material should not determine its regulatory classification.

The supplementary guidance should provide additional detail and examples, including regarding quality grade requirements, the applicability of GMP principles, and the need for a GMP certificate when semi-synthetic or synthetic products (such as enzymatic DNA) are used as starting materials in GTMPs/ATMPs. This should explicitly include expectations for synthetic biology-derived inputs and enzymatic nucleic acid production workflows, including control of raw materials, traceability, and comparability between biological and synthetic manufacturing routes.

2. **Do you think that medicinal products containing recombinant or synthetic nucleic acids should be classified as gene therapy medicinal products, only where said nucleic acids undergo transcription or translation?**

BIA response – neither agree nor disagree

Explanation: The proposed change aligns with the scope of the EU definition while adding additional clarity on the inclusion of RNA-based products and non-natural constructs by using the term "nucleic acid sequence" instead of "genetic sequence".

MHRA should consult with industry on supplementary guidance to confirm the scope of this change. This guidance should include examples of products that fall inside and outside this definition. This would avoid unintended reclassification and help developers and industry partners to get classification right from the start, rather than discovering issues later when they are much more difficult and resource-intensive to address.

Areas where additional clarity is needed include:

- Whether this definition includes translation within the delivery vehicle, or only translation when delivered to the target genome. We recommend that it includes

translation within the delivery vehicle, as is the case with engineered microbial therapies.

- Whether the proposed requirement for transcription or translation could exclude in vivo editing products, if administered in nanoparticles that would not require transcription or translation of the editing tools.
- Whether this definition includes medicinal products where additional sequences are integral to the mechanism of action and contribute to the therapeutic effect.
- Further clarity on how the MHRA will approach the regulation of other active substances which sit outside this definition but could benefit from a risk-based approach.

3. **Do you think that medicinal products should be classified as gene therapy medicinal products when their mechanism of action involves deliberate, sequence specific genome editing, regardless of the composition of the active substance?**

BIA response – agree

Explanation: We agree that any product designed to make a targeted, predeterminate edit to a specific location in the genome should be classified as a GTMP, regardless of the composition of the active substance.

We also encourage MHRA to provide practical examples covering emerging non-nucleic acid-based genome editing technologies to ensure consistent interpretation across innovation pathways.

4. **Do you think that medicinal products that modulate gene expression through epigenetic (or epitranscriptomic) mechanisms without altering a nucleic acid sequence should be classified as gene therapy medicinal products?**

BIA response – disagree

Explanation: We disagree with the proposal in this question, and therefore agree with the MHRA proposal to *not* include medicinal products which only affect gene expression though epigenetic mechanisms – without actually changing the nucleic acid sequence – in the GTMP definition.

To provide additional clarity, the MHRA's supplementary guidance should include examples illustrating different scenarios – specifically distinguishing between products that are excluded because their mechanism is purely epigenetic with no transcription or translation activity, and products that may still qualify as GTMPs because their nuclear cargo undergoes transcription or translation even if the ultimate biological effect is epigenetic in nature.

Further clarity on how the MHRA will approach the regulation of other active substances which sit outside this definition but could benefit from a risk-based approach, including antisense oligonucleotides. A separate classification may be needed in future and this could be an opportunity for the UK to adopt a pro-innovation approach and influence how other regulators classify these products.

5. **Do you think that classification of a product as a gene therapy medicinal product should include medicinal products for which the transferred genetic material is not directly responsible for the therapeutic, prophylactic, or diagnostic activity of the product?**

BIA response – agree

Explanation: We support removing the requirement that the transferred genetic material must be directly responsible for the therapeutic, prophylactic, or diagnostic activity of the product in order for it to qualify as a GTMP.

6. **Do you think that medicinal products which exert their action through targeted genomic edits should be classified as gene therapy medicinal products regardless**

of whether these edits occur directly within human cells or in other cells administered to the patient?

BIA response – agree

Explanation: The location where the edits occur should not affect the classification.

Supplementary guidance should include illustrative examples covering modalities including engineered microbial therapies, ex vivo edited cell therapies, and vector-based delivery systems to ensure consistent and predictable classification across development pathways.

7. **Do you think that medicinal products which exert their action through the expression of a recombinant or synthetic nucleic acid should be classified as gene therapy medicinal products regardless of if this activity occurs at the level of a human cell or in other cells administered to the patient?**

BIA response – agree

Explanation: The location where the activity occurs should not affect the classification.

8. **Do you think the UK should consider classifying only those medicinal products which exert their effect through "long lasting" transcription or translation of a recombinant or synthetic nucleic acid as gene therapy medicinal products?**

BIA response – disagree

Explanation: We do not support the introduction of a "long lasting" criterion as a condition for GTMP classification. We recognise the MHRA's concern that the inclusion of a duration-based qualifier may have implications on regulatory status of medicinal products that are currently considered as ATMPs, and therefore agree with the MHRA's proposal to diverge from the proposed EU definition here.

Duration of effect should instead be considered as part of the risk assessment and assessed within a broader, science-based framework including persistence, biodistribution, and reversibility of effect, rather than acting as a binary classification criterion. These factors should be taken into account when determining proportionate post-approval requirements.

9. **In the context of the proposed amendments, to what extent should the Human Medicines Regulations 2012 mirror the proposed EU definition, or be tailored to better reflect the UK innovation landscape?**

BIA response – Alignment with the EU is important as companies operate globally and UK and EU definitions divergence adds cost and time, and results in the UK being deprioritised. Therefore, we welcome MHRA's approach to align with the key revisions in the EU's updated GTMP definition.

However, there are a few parts of the EU definitions which lack clarity and could be interpreted differently, and in these instances we welcome MHRA's proposal to provide additional clarity (as set out in the table in line 448). We also support MHRA's proposal not to include an explicit reference to "long lasting" transcription or translation requirement, as set out in our answer to Q8.

We also encourage MHRA to work towards alignment with FDA and other major regulators over time. Where divergence occurs, it should be accompanied by clear technical guidance to avoid interpretational uncertainty across jurisdictions.

10. **Do you agree or disagree with the proposed changes as outlined in Appendix 2, to the definitions of gene therapy medicinal products?**

BIA response – agree

Explanation: We agree with the proposed changes to the definitions of GTMPs as outlined in appendix 2. As set out in our answers to the previous questions, the proposed changes

help to modernise the GTMP definitions to reflect technological advances, and create broad alignment with EU's planned changes.

MHRA should also consider clarifying that a gene therapy could also function by *deleting* part of a sequence.

11. What implications, benefits, or risks do you foresee the proposed changes to the definitions of gene therapy medicinal products?

Anticipated benefits:

- Developers using synthetic manufacturing routes will have a clear regulatory pathway in the UK. This removes a real barrier that has damaged the attractiveness of the UK as a location for some research projects.
- The risk-based approach will be available to a wider range of products that need it.
- Close alignment with the EU will make it easier to run projects across both markets without duplication

Anticipated risks:

- Some of the products currently regulated under non-ATMP pathways may now fall within the GTMP definition. MHRA should give developers clear information and enough time to adjust their regulatory and manufacturing strategies.
- If the risk-based approach is not applied in a proportionate manner then there is a risk that the changes result in additional costs and longer development timelines for the products which now fall under the scope of GTMPs. It is important that the risk-based approach is provided in a clear and proportionate way which recognises the specific risk-profile of different classes of product.

12. Are there specific categories of products which, in your view, should be explicitly excluded from the revised definitions of a gene therapy medicinal product, and what scientific or regulatory rationale supports their exclusion?

BIA response – We support the explicit exclusion of vaccines for infectious disease.

13. Please provide examples of products that were previously not classified as gene therapy medicinal products (GTMP) but would now fall under the revised criteria (as proposed in Appendix 2) of a GTMP?

BIA response –

- Therapies based on synthetic DNA.
- Engineered microbial therapeutics should be included under the expanded definition of GTMPs. However, this specific category of products should receive a stratified and proportionate risk-based approach, due to the fact that these products, which are localised, transient, and do not integrate into the host genome, have a materially different risk profile proportionate to their potential for long-term genetic or biological effects.

14. With reference to 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, we have assessed that the proposals set out in Appendix 2 do not risk impacting people differently with reference to their protected characteristics, or in regard to the Rural Needs Act (Northern Ireland) 2016. Do you agree or disagree with this statement?

BIA response – agree

15. **We assume the main organisations impacted will be developers. We would welcome your view on if you agree or disagree with this, and how many developers you would expect to be affected by these changes. Please share any evidence to support your view.**

BIA response – Developers will be the primary organisations impacted; however, the impact extends beyond developers to the broader life sciences ecosystem.

MHRA's impact assessment should also recognise the wider industry involved in the supply chain for advanced therapies who will also be impacted by the changes, including providers involved in vector production, and cell culture and purification platforms. These stakeholders, many of whom are in the BIA membership, are integral to enabling compliant, scalable, and reproducible manufacturing of GTMPs and will be directly affected by changes in classification and associated regulatory requirements.

16. **We assume that there will be no additional costs to business arising from these proposals. Do you agree or disagree? If you consider that there will be costs, please describe these and share any evidence to support your view.**

BIA position – We disagree that there will be no additional costs to business arising from these proposals.

The changes are likely to generate some transitional costs for businesses due, including from reclassification assessments, revalidation of processes and analytical methods, and potential updates to regulatory strategy and quality systems. MHRA should also ensure its ATMP classification service is sufficiently resourced to meet this additional demand. Products already in clinical development may require dossier amendments, and the MHRA should establish formal transition provisions for these products.

There may also be some ongoing costs, as our members have reported that GTMP classification can result in a longer development timeline and higher resource requirement. Some members reported that they had experienced a higher regulatory bar for

demonstrating safety for GTMPs leading to additional studies and additional product control requirements.

These costs should be mitigated by:

- Proportionate application of the risk-based approach, recognising the different risk profiles of products newly failing within the GTMP definition
- Timely publication of supplementary guidance
- Ensuring the MHRA's ATMP classification service is adequately resourced to meet increased demand
- Putting in place clear transitional provisions including formal transition provisions for products already in clinical development, and a minimum implementation timeline of 12 months from publication of final guidance

17. We expect that there will be a direct benefit for developers, and that the ultimate benefit of these changes will be improved health outcomes for patients. Do you agree or disagree, and please share any evidence to support your view, including on what these improved health outcomes might be.

BIA response – We agree that the additional clarity on regulatory pathways and extension of the risk-based approach has the potential to benefit developers of novel therapies. As set out in previous answers, the risk-based approach should be applied in a clear and proportional way to different classes of products to avoid higher costs and longer development timelines.

The potential for improved health outcomes for patients will also depend on other parts of the healthcare system, including clinical trials, reimbursement, and adoption policies, all of which contribute to these therapies reaching patients in the NHS.

About the BIA

The BioIndustry Association (BIA) is the voice of the innovative life sciences and biotech industry, enabling and connecting the UK ecosystem so that businesses can start, grow and deliver world-changing innovation.

We have over 600 members spanning human health and non-health biotech, including start-ups, scale-ups and established global companies. Our membership also encompasses the full UK ecosystem, including non-commercial research institutions and service providers.