Medicines & Healthcare products
Regulatory Agency

Response to consultation feedback on *Draft guideline on individualised mRNA cancer immunotherapies*

Contents

Introduction

Individualised mRNA cancer immunotherapies (colloquially referred to as personalised cancer vaccines) are a new type of cancer treatment that use mRNA technology. Unlike conventional cancer therapies, each patient receives a slightly different version of the mRNA therapy which has been matched to their unique tumour fingerprint using deterministic algorithms or artificial intelligence (AI). In this way, the therapy aims to teach the patient's immune system to target and destroy their specific tumour cells.

This novel individualised approach poses unique regulatory challenges, and there is a need for guidance. On the 3rd of February 2025, we sought feedback on our draft guideline on individualised mRNA cancer immunotherapies. This outlined a regulatory pathway to approval, covering regulatory classification, product design and manufacture, evidence of safety and effectiveness, post-approval safety monitoring, and information for patients and the public. Our aim is to facilitate patient access to these novel individualised cancer therapies, while maintaining our stringent standards of safety, quality and efficacy.

We requested feedback from manufacturers, developers, patient organisations, academics and other stakeholders on our regulatory approach. The consultation ran for 8 weeks until the 31st of March 2025. A total of 49 responses were received from 18 individuals,12 pharmaceutical companies/CROs, 7 patient organisations/charities, 5 non-profits membership groups, 3 trade associations, 2 international regulators, 1 academic group and representatives from the NHS. The majority of responses were from UK based individuals/organisations.

We have carefully reviewed and analysed each of the comments received. This feedback will help us, in collaboration with Highly Personalised Medicines Expert Working Group, to publish the final guideline at a later date.

The consultation feedback is summarised below by relevant guideline section, followed by the government response.

Overarching

Summary of feedback

We received overarching consultation feedback on guideline scope and terminology.

There were requests for more clarity on whether the guideline is intended to support regulatory requirements for clinical trial authorisation (CTA) or marketing authorisation (MA) or both. There was a request for the scope to include drug delivery system other than lipid nanoparticles (LNP), and to allow for the inclusion of multiple mRNA molecules in a single LNP.

Some respondents disagreed with the term ‘neoantigen’ since this does not encompass potentially relevant non-mutation-based antigens.

Respondents also flagged inconsistencies across the different sections, for example, the use of the terms ‘chain of custody’ and ‘chain of identity’ for product tracking and traceability.

Government response

We welcome the feedback on scope, terminology and inconsistencies.

The draft guideline was intended primarily to support the data requirements to support marketing authorisation (licensing). However, based on the consultation feedback, we are considering whether to broaden the scope to include the inclusion of additional guidance on requirements for authorisation of clinical trials that investigate individualised mRNA cancer immunotherapies.

The scope of the guideline is individualised mRNA cancer immunotherapies that use lipid nanoparticle (LNP) delivery systems. This type of drug carrier has already been shown to be effective clinically for mRNA vaccines to prevent infectious diseases, and this is the system used by the majority of mRNA cancer immunotherapies to date. As we acquire experience of different drug delivery systems, we may update the guideline accordingly.

The guideline is not intended to exclude multiple mRNA molecules in a single LNP if clinically justified. However, relevant pharmaceutical development data would be required to support the optimisation process of the formulation, confirming consistency of the ratio of each mRNA in the final product. The level of expression or required potency of the different mRNAs may also need to be considered in relation to product safety and efficacy. These aspects will be reflected in the final guideline.

The identified inconsistencies will be reviewed and corrected in the final guideline. We will carefully consider terminology and include a glossary. Importantly, the ‘chain of custody’ and ‘chain of identity’ concepts will be reviewed to ensure consistency and align with the intent to track and trace the individualised product from patient sampling through to patient administration.

Regulatory principles

68% of respondents agreed with the regulatory principles outlined in the draft guideline.

	Strongly disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
Individuals	2			1	
Organisations	2		3	11	3

Summary of feedback

Respondents agreed that a single marketing authorisation (MA) could be issued for an individualised medicine where a variable component of the active substance is tailored to a unique patient characteristic, for example, a tumour antigen profile. This would be especially important when there is high unmet need. Other aspects should be standardised, including manufacture and analytical control processes, and there should be robust systems to ensure consistency.

Respondents asked if a standard full MA or conditional MA would apply to individualised mRNA cancer immunotherapies, and whether the MHRA's international recognition procedure (IRP) , or collaborative pathways such as Project Orbis or the Access Consortium work-sharing initiative could be used.

We received feedback about the regulatory classification of individualised mRNA cancer immunotherapies. Where derived or manufactured from a living biological system, they are currently classified as Advanced Therapy Medicinal Products (ATMPs), and subclassified as gene therapies, under the under the Human Medicines Regulations 2012 (as amended) (HMRs). Respondents were in favour of retaining ATMP classification as this allows for a risk-based approach, use of existing ATMP-specific good manufacturing practice (GMP) guidelines, and requirements for traceability and follow-up. Respondents favoured the creation of a new subclassification to distinguish individualised mRNA cancer immunotherapies from gene therapies that modify the host genome. This could address negative perceptions about gene therapy and reduce regulatory burden by facilitating the development of more specific guidance. However, there were warnings that too many sub-classifications could lead to an excessive series of standards, and pleas for future-proofing and global alignment.

The ability to leveraging prior knowledge was endorsed, in alignment with current International Council for Harmonisation (ICH) Quality Guidelines Q8 to Q14, where applicable. Nevertheless, there was a request for more clarity on applicable product types and processes, and a request to extend use of prior knowledge to non-clinical and clinical data.

Government response

We welcome the constructive feedback on the regulatory aspects.

The type of MA (conditional or full MA) would be decided case-by-case during the assessment of the MA application. A full MA could be foreseen for individualised mRNA cancer immunotherapies if comprehensive clinical data are available, although it is likely that any full MA would be subject to conditions such as post-authorisation studies (see section 7 of the draft guideline).

We would prefer national MA applications for individualised mRNA cancer immunotherapies due to our interest and expertise in this area. However, we would also consider other collaborative assessment models where this could facilitate early access for UK patients.

The consultation feedback on future changes to the regulatory classification of individualised mRNA cancer immunotherapies will inform any proposals to amend the HMRs, which would be subject to a separate UK Government consultation.

Developers can utilise prior knowledge case-by-case if justified, and pre-agreed with the MHRA. The leveraging of prior knowledge to support the non-clinical data requirements is foreseen; the section on non-clinical aspects states that it is acceptable to cross-refer to studies with other mRNA constructs, if these are shown to be relevant. The leveraging of prior knowledge to support the clinical data requirements is not specific to individualised mRNA cancer immunotherapies (for example, leveraging clinical safety data from products from the same drug class). We recommend that developers seek scientific advice from the MHRA on the non-clinical and clinical data requirements of individualised mRNA cancer immunotherapies.

Product design

54% of respondents agreed with the product design principles outlined in the guidance.

	Strongly disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
Individuals	1				
Organisations	2	3		6	1

Summary of feedback

There were 3 groups of themes to the consultation responses, as summarised below:

Dual regulation of medicinal products and medical devices

- Good Manufacturing Practice (GMP) versus Medical Devices Regulations (UK MDR): There was feedback that product design steps (e.g., sequencing and bioinformatics) should be regulated under GMP, not through medical device regulatory frameworks.

- Regulatory Burden: There were concerns that applying medical devices regulations would impose unnecessary complexity, hinder innovation, and create inequities.

- Framework Clarification: There were calls for clearer guidance on which aspects fall under medicinal product versus medical device regulation, especially for software and diagnostics areas.

- International Alignment: Recommendations to harmonise UK guidance with US Food and Drug Administration (FDA) and European Medicines Agency (EMA) positions to avoid divergence and support global innovation.

- Support for Limited Device Regulation: There was some support for applying medical device regulations only to specific components of the product design process (e.g., in vitro diagnostic (IVD) medical devices used) and not to the entire product design process.

Managing Artificial Intelligence (AI)/Machine Learning (ML) updates and changes

- Distinction Between AI/ML Types: Respondents shared the need for clear regulatory separation between pretrained deterministic models and adaptive, continuously learning models.

- GMP Oversight: Calls for deterministic models used in manufacturing to be managed under existing GMP change control processes with EU GMP Annex 11 provided as an example.

- FDA Frameworks: Multiple stakeholders recommend adopting the US FDA frameworks (e.g. Predetermined Change Control Plans) for managing AI/ML updates.

- Risk Management: There were proposals for tiered risk assessment - low-risk changes could be auto-approved, while high-risk updates could require MHRA oversight.

- Traceability and Versioning: There was feedback on the importance of maintaining clear records for software versions used in patient-specific manufacturing.

- International Harmonisation: There were calls to align with global standards and practices to support innovation and ensure patient safety.

General feedback

- Context of Use (COU): There was a request to define AI/ML applications in neoantigen selection, with examples of deterministic versus non-deterministic models. Respondents suggested that COU should guide regulatory expectations.

- Risk-Based Approach: There were recommendations to align with FDA and EMA by adopting a risk-based regulatory framework tailored to the COU of AI/ML models.

- Sampling and Quality Control: Respondents suggested to generalise patient sampling procedures and improve clarity on tissue quality, blood sample volumes, and sequencing standards.

- Patient Involvement: There were calls for advocacy for integrating patient perspectives into therapy design.

- Technical and Regulatory Challenges: There were concerns raised about software validation, performance monitoring, and regulatory burdens for bioinformatics and sequencing processes.

Government response

The MHRA agrees with many of the responses for quality controls at each stage of the product design process. We will place greater emphasis on quality control measures and will consider additions to the final guideline to elaborate on quality assurance processes between the stages of product design and within certain stages for sample collection, processing & transportation and sequencing.

The MHRA acknowledges interest in regulating product design via the application of GMP of medicines and ATMPs, and supports this approach. The MHRA will give consideration in the final guideline to regulating product design via the application of GMP where the intended purpose is for product manufacturing. This approach is intended to allow the UK to align with international standards and approaches, for example via the application of EU GMP Annex 11 (Computerised Systems), Annex 15 (Qualification and Validation) and the proposed Annex 22 (Artificial Intelligence).

The UK Medical Device Regulations will apply where the intended purpose in the product design stages is not for product manufacturing, and the product solely meets the definition of a medical device or IVD device. An example is where the AI/ML neoantigen selection stage has the intended medical purpose of creating a compendium of neoantigens that would not be used in product manufacture.

The MHRA will consider international regulatory practices in product design oversight.

The MHRA will define a common set of nomenclature to drive clarity in terminology throughout the guidance.

Product manufacturing

71% of respondents agreed with the product manufacturing principles outlined in the guidance.

	Strongly disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
Individuals	1		1	1	
Organisations	1		1	8	1

Summary of feedback

Many of the respondents highlighted the difficulties of batch release for an individualised mRNA cancer immunotherapy. They consistently outlined the need for flexibility in the regulatory expectations for batch release and welcomed those proposed in the draft guidelines. There was agreement that some indications would need a rapid turnaround in manufacture and that real-time release testing is a pragmatic approach to expedite access. The flexibility to perform control testing at drug substance or drug product was also welcomed. The respondents requested further clarification on the use of rapid release methods, particularly for microbial tests, and the use of two-stage batch certification. The need for justification and clinical mitigations in the use of these flexibilities was widely acknowledged. Some of the most detailed responses related to potential out-of-specification (OOS) testing whether pre- or post-administration. The respondents requested guidance on OOS and compassionate use.

There was disagreement in the responses over the requirement for potency assays or functionality tests. Some respondents accepted that an assay would need to be in place to evaluate potency during development while taking into account the limited time for product release. Other respondents queried if *in vivo* assays would be required in order to provide a true measure of clinical response; some proposed that a matrix of physico-chemical tests would be sufficient to infer functionality of the mRNA. It is acknowledged that the regulatory expectations for a potency assay or functionality test would need to take into consideration the individualised nature of the product which presents numerous challenges. The respondents appreciated that the guideline addresses definitions and the establishment of potency assays in the context of individualised mRNA cancer immunotherapy, but the provision of examples would be helpful. They requested further clarification on the expectation for correlation of the potency assay to biological effect and clinical response,

particularly when considering the individualised approach for these products and the related clinical responses.

Several organisations and manufacturers asked about the requirements for traceability and labelling. Some specifically queried if the existing ATMP requirements were appliable to individualised mRNA cancer immunotherapies. There was agreement that the chain of identity/chain of custody principles should be used from tumour sampling through to product administration despite the intervening product design step. But there was confusion over whether the drug product label should say ‘autologous use only’. One organisation recommended the use of ISBT 128 as the global standard for human material identifiers. Several respondents noted that traceability would be important for the rapid recall of product if using a two-stage release process.

Many respondents requested additional information on the regulatory expectations for stability studies. They highlighted that performing stability studies on every patient batch would present technical and logistical challenges, particularly in regard to the amount of samples consumed for such studies. Several responders asked if the approach of using representative batches, as proposed in the guidance on validation, could be applied to stability studies.

The clarification on terminology and proposed definitions in the guidance was widely welcomed. But some confusion remained over certain terms, most notably ‘variable’ and ‘constant’ when referring to elements of the mRNA. The need for a glossary and further explanation of terminology was noted.

Government response

We welcome the many and well-considered comments on the guidance for the manufacturing aspects of individualised mRNA cancer immunotherapy. There were many helpful suggestions that will be incorporated into the final guideline. The most common type of comment related to guidance on batch release testing and the need to clarify the position of the MHRA on several aspects.

The final guideline will include detail on the application of GMP across all stages of manufacturing as needed, and the implications for release by the Qualified Person where appropriate.

Where appropriate and to meet clinical need, decentralised manufacturing could be considered, in line with the Human Medicines (Amendment) (Modular Manufacture and Point of Care) Regulations 2025.

The MHRA does not wish to be prescriptive in regard to specific tests or sets of specifications that a manufacturer must perform for batch release. Instead, the guideline

provides recommendations on what manufacturers should consider in establishing release tests based on critical quality attributes of the product. The use of rapid release, typically microbial methods, may be acceptable where justified on patient or clinical need. This will be included in the final guideline and will be evaluated on a case-by-case basis, when supported by relevant data, and as appropriate. A two-stage quality control testing strategy can be adopted where certain tests could be performed post-administration when it is not clinically possible to be carried out in time for therapy, particularly if there is a clinical urgency for the product to be administered, and where the benefits and risks ratio is positive. This should be clearly justified, and a risk-based approach should be considered. Points in the final guideline on two-stage testing will be expanded to clarify regulatory expectations.

The UK's ATMP legislation has provisions for administration when the product is out-of-specification (OOS) if there is an urgent need. The use of this provision is well established notably with CAR-T medicinal products, and the NHS has guidelines on out-of-specification administration. However, the provisions only mention cell- and tissue- based medicinal products. If administration is not urgent, then regulatory approval could be sought through a batch-specific variation, if re-manufacture is not feasible. Re-manufacture or the use of batch-specific variations should be adequate for individualised mRNA cancer immunotherapies and provisions for OOS testing are not needed. The MHRA will ensure that some consideration of compassionate use is included in the final guideline.

The MHRA supports developments in potency assays that could be important for individualised mRNA cancer immunotherapies. The MHRA believes that developing potency assays specific to each mRNA with its unique neoantigen ensemble will not be possible. However, the principle of requiring an *in vitro* potency assay that is a correlate of the biological effect remains a regulatory expectation as set out in the guideline. The MHRA does not wish to be prescriptive on potency or functionality assays. Innovators are encouraged to seek scientific advice from us when necessary, and once they have established the relevant assays. The guidelines are written to allow space for innovation in this area. An appropriately validated potency assay should be based on a defined biological effect as close as possible to the intended mechanism(s) of action/clinical response of the product. Definitions for the terms potency and functionality will be included in the glossary.

There are established standards and terminology for cell-based products concerning traceability and labelling. The MHRA agrees with several of the respondents that the principles previously outlined for cell-based products are applicable to individualised mRNA cancer immunotherapies albeit with some alterations. These principles will be outlined in the final guideline. The MHRA will recommend that 'autologous use only' on drug product labels be replaced with 'for named individual only' for individualised mRNA cancer immunotherapies. The suggestion to use ISBT 128 as an established international set of standards for tracing human material is endorsed by the MHRA. The MHRA considers referring to 'principles of' this and other existing guidelines sufficient for this product type.

The extent of the risk to patients from receiving the wrong individualised mRNA cancer immunotherapy is not currently understood. Further experience is required to decide on precise labelling requirements. In the meantime, the MHRA is recommending the principles of existing standards and guidelines on traceability for these products.

The MHRA position on stability for individualised mRNA cancer immunotherapies is that product-specific studies should be performed. Relevant stability batches that represent the expected sequence diversity, with varied lengths (size) and perhaps structures, should be considered to help establish the shelf-life of the drug product. The draft guideline will be altered to emphasise the importance of manufacturers understanding the formulation and its implications for stability through appropriate pharmaceutical development. With an appropriate design space, as per Quality by Design principles, the stability of the final drug product should be understood. The potential degradation pathways should have been characterised to support further individualisation of the drug product, where necessary. There is no requirement for each patient-specific batch to be entered into stability studies. The final guideline will make clear that the pragmatic approach of using representative batches for stability is sufficient. The length of stability studies required is also dependent on the drug product.

In addition to the proposed regulatory definitions for potency and functionality for these products, the MHRA will develop a glossary of terminology specific to these products. This will help with understanding of regulatory expectations.

Non-clinical aspects

70% of respondents agreed with the non-clinical aspects outlined in the guidance.

	Strongly disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
Individuals	1				
Organisations	1		1	6	1

Summary of feedback

Respondents expressed a need for clarity with regards to which parts and principles of existing international regulatory guidance (WHO and ICH) are applicable or relevant to a non-clinical developmental programme for individualised mRNA cancer immunotherapies. There was a request for clearer direction on the appropriate timing of non-clinical studies in relation to the stages of clinical development.

Use of representative or surrogate constructs in place of testing each patient-specific batch was agreed as a principle, noting it is not possible to require testing of each individualised product and yet still offer the patient that treatment in a timely manner. However, this raises a question on how similar product used in patients is to that used in prior testing.

There was a call for further clarity in MHRA's proposal for testing at Stages 1 and 2, with suggestions that the first stage focuses on fixed components, such as lipid nanoparticles and excipients: this should address pharmacokinetics/biodistribution, general toxicity, genotoxicity, immunotoxicity, and reproductive toxicity. The second stage addresses the variable component: the patient-specific mRNA insert. Here, the aim of the MHRA is to promote record-keeping and the scientific justification used to select the particular mRNA for each patient. This could be supported by *in silico* or *in vitro* assessments to evaluate potential efficacy, immunogenicity and off-target effects.

A risk-based approach was addressed and recommended in line with the principles outlined in EudraLex Volume 4, Part IV for Advanced Therapy Medicinal Products (ATMPs). This approach would allow for reduced or waived testing of certain components when justified by prior knowledge and tailoring of testing requirements based on the novelty and risk profile of each product.

Immunological safety remained an important concern, particularly the potential for immune-related adverse events (IRAEs) and long-term immune modulation- issues especially pertinent in cancer immunotherapy. Recommendations included monitoring for systemic immune effects, incorporating immunotoxicity assessments in the first stage of testing, and exploring *in silico* models to predict immune responses.

Another area of focus is biodistribution: there was concern that mRNA and lipid nanoparticles may distribute systemically rather than be confined to tumour sites, raising the risk of off-target transfection and unintended protein expression. It was suggested that this could be assessed in biodistribution studies in animals complemented by *in silico* and *in vitro* assessments. A need for long-term safety evaluation was emphasised.

The selection of neoantigens as a safety challenge was raised. Reference was made to the mismatch between neoantigen and host HLA profiles, with a risk of off-tumour targeting and triggering unintended immune responses. It was proposed that testing strategies should simulate both best- and worst-case scenarios and assess potential cross-reactivity with healthy tissues.

An innovative addition amongst responses was the use of digital twin simulations, i.e. virtual models that replicate parts of the development and safety testing processes, reducing the need for physical testing and expediting regulatory decisions. However, their adoption as a regulatory tool will require further development and validation.

Finally, compliance with Good Laboratory Practice was mentioned for pivotal safety studies, likely done at Stage 1.

Government response

In the final guideline, there will be consideration of which parts of existing guidelines should be applicable to individualised mRNA-based cancer immunotherapies.

The concept of Stages 1 and 2 testing will be explained further. Stage 1 is intended to establish safety and function of fixed components (e.g. LNPs, excipients, mRNA backbone) such that further testing of a specific product is not required; Stage 2 seeks to ensure that the reasons why the specific product was designed and used for each patient is recorded so such data are available for later analyses. No specific tests are expected to be mandated in Stage 2, but the basis for making that product should be detailed and recorded. However, any experimental data generated with the patient-specific product (e.g. *in vitro* activity on patient-derived tissue) should be recorded as this may be useful for retrospective analyses.

The MHRA will monitor developments regarding potential relevance of HLA matching and neoantigen ranking, and may provide further guidance in the future.

Suggestions on use of digital twin simulations are appreciated: this is an emerging concept that seems to have promise, but these may apply more in quality control and process validation than to non-clinical testing.

Clinical aspects

85% of respondents agreed with the clinical aspects outlined in the guidance.

	Strongly disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
Individuals				3	
Organisations	1		1	7	1

Summary of feedback

Much of the consultation feedback on the clinical aspects concerned scope and clinical trial design.

There were requests to provide guidance on all phases of clinical development, including the design of dose-finding, adaptive, platform and basket trials. More guidance on acceptable endpoints was sought.

The inclusion of the dedicated subsection ‘Considerations for randomised placebo-controlled trials’ created the impression that other trial designs were unacceptable. There were also requests to clarify the guidance on study objectives and estimands.

The apparent restriction of scope to the adjuvant cancer setting was questioned.

Recognising that clinical trial populations often lack diversity, there was a request to include guidance on this important aspect.

Respondents asked for more guidance on how to demonstrate that the investigational medicinal product is representative of the commercial product.

Regarding safety evaluation, some respondents did not agree with the recommendation to collect solicited reactogenicity data.

Government response

We welcome the constructive feedback on the clinical aspects.

The aim of this section is to cover considerations that are specific to the clinical development of individualised mRNA cancer immunotherapies. Therefore, we do not propose to include detailed guidance on study design aspects that would also apply to non-individualised cancer therapies, for example, endpoints. Instead, we will refer to existing guidelines on clinical trial design in the cancer setting.

We recognise that the use of 'Considerations for randomised placebo-controlled trials' as a subsection title created the perception that other trial designs are precluded, which is not the case, particularly in exploratory development. We require the same evidence standards as for non-individualised therapies, therefore, for example, a single arm trial may be justifiable in an advanced cancer setting in the context of a conditional marketing authorisation. The purpose of this subsection was intended to be to address considerations for trial design arising from the manufacturing time needed for individualised therapies, but this purpose was obscured by the choice of subsection title and focus on placebo-controlled trials. We propose to replace the subsection on considerations for randomised placebo-controlled trials with a more general subsection on considerations for trial design arising from the manufacturing time needed for individualised therapies.

The purpose of the guidance on study objectives and estimands is to encourage thought about the study objectives in the presence of issues which arise because therapy is individualised. For example, with delayed manufacturing, different objectives are possible based on considering all patients or all treated patients. We will consider edits to the text to clarify the different hypotheses and populations arising from the delay in treatment availability.

The intention was not to restrict the scope to the adjuvant cancer setting and we will ensure that the updated guidance could be applied to clinical developments in other cancer settings.

Alongside the Health Research Authority (HRA), we have developed draft guidance for developing and submitting an inclusion and diversity plan for clinical research. This joint HRA and MHRA draft guidance is applicable to all interventional clinical trials and clinical investigations, regardless of product type. We will consider whether the joint HRA and MHRA draft guidance needs to be updated in light of the consultation feedback on the draft guideline on individualised mRNA cancer immunotherapies.

We will consider additional guidance on how to demonstrate that the investigational medicinal product is representative of the commercial product, for inclusion in the product manufacture section of the final guideline.

It is agreed that reactogenicity events do not need to be solicited and could be collected using Common Terminology Criteria for Adverse Events. The guidance will be updated accordingly.

Post-authorisation aspects

70% of respondents agreed with the post-authorisation aspects outlined in the guidance.

	Strongly disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
Individuals					1
Organisations	1	1	1	5	1

Summary of feedback

The majority of comments on Section 7 of the draft guidance related to post-authorisation safety studies (PASS). Comments were raised both in favour and opposing the need for a PASS for these products. A number of comments raised that it is not clear in the guidance if registry studies would be an appropriate study design for a PASS. Comments were raised requesting further detail on possible methodologies and data sources for a PASS. Comments noted that post authorisation monitoring of effectiveness of the product was not mentioned in Section 7.

The importance of considering patient experience when designing aspects of safety monitoring were highlighted in several comments. This included considering the use of patient reported outcomes in a PASS and communicating the results of studies to patients. Patient consent was also highlighted.

Comments were raised in relation to signal management processes, including the use of genomic data in signal detection and the feasibility of signal management processes considering individual neoantigens.

A small number of comments referred to risk minimisation measures, both in support and in disagreement with potential need for additional risk minimisation measures.

Two comments highlighted that although the text refers to use in adjuvant setting, the products are also being developed for use in other settings. Two comments highlighted that the analysis which selects the neoantigens are not always AI/ML but can be deterministic.

Comments were raised which are covered by other guidance documents referred to within Section 7, or which are covered within Section 8 of the guidance.

Government response

We consider that a PASS would be necessary for these products until there is further understanding of the long-term safety of these products. The final guideline will clarify in relation to the methodology for a PASS, that various study designs including a registry may be appropriate. We will consider if further detail can be included in the final guideline in relation to examples of possible data sources. Reference to effectiveness will be included in the final guideline.

We acknowledge the helpful comments on patient experience. The final guideline will further discuss signal management processes.

Minor edits will be made in the final guideline to ensure clarity, including on risk minimisation measures, deterministic algorithms and development for non-adjuvant settings. A cross reference to Section 8 will be included in the final guideline.

Information for patients, healthcare professionals and the public

77% of respondents agreed with the MHRA's expectations of manufacturers/developers around the information to be provided by them for patients, healthcare professionals and the public.

	Strongly disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
Individuals	2	1		4	3
Organisations	1		1	7	3

Summary of feedback

The survey questions centred on the information that should be provided to support patients when deciding whether to be treated with an individualised mRNA cancer immunotherapy. The questions covered the type, format and timing of the information. Feedback was received from a wide range of organisations including industry, international regulators, professional bodies, public sector organisations and cancer charities.

Respondents said that the information should be relevant, meaningful and tailored to the patient. The difference between individualised and non-individualised immunotherapy should be explained, and terminology should be consistent. Patients should understand how this medicine compares to other relevant treatment options. Information should include how the medicine is made and how long that takes; the ingredients; how the medicine is given, when and how often; what type of cancer it is used for and how it works. Religious and ethical aspects should be considered.

The results from clinical trials should be presented in a simplified and transparent way, allowing patients to understand efficacy in terms of cure or remission rates, symptom control, or additional survival time. The numbers of patients from ethnic minority backgrounds who participated in the clinical trial should be provided. The side effects and risks should be clearly explained, including any action to be taken by the patient on experiencing any such events.

Several respondents said that there should be adequate information on the associated workup, monitoring and follow-up, including tests, procedures and assessments. Related to this, the impact on daily life should be explained, for example, hospital stays and outpatient visits, travel, any need for an accompanying carer, and lifestyle adjustments.

Considering that the therapy is individualised using patient data, including genetic data from patient samples, there were requests for more information on ownership of, storage of, access to and use of patient samples and data.

Many respondents provided feedback on the format of information to support patient decision-making. A range of formats should be made available, including printed and digital, with use of plain language and avoidance of jargon. The information should be culturally appropriate, and made accessible through translations, large print, braille and use of audio or video. Visual aids such as diagrams, illustrations and animations should be considered when communicating complex information. Key information should be highlighted using boxed text and summaries, supported by additional detail through hyperlinks or frequently asked questions.

Some respondents emphasised the importance of face-to-face interactions and ongoing communication with healthcare professionals. The information needs of healthcare professionals, cancer navigators, carers, relatives and patient advocates should also be considered.

Feedback was received regarding the timing of information giving. Respondents said that information about individualised mRNA cancer immunotherapies should be provided as early as possible, ideally at the time of diagnosis, to facilitate consent for tissue sampling, and allow sufficient time for consideration and discussion. A sequenced approach was recommended to allow adequate time to process complex information during what may be a difficult time for patients and relatives. Respondents also highlighted the importance of sufficient time for discussion between patients and healthcare professionals, shared decision-making, and opportunities to clarify or ask further questions.

Respondents recommended that information developers should work with third sector organisations with relevant skills, and that information should be co-designed with patient experts and piloted by representative users. References to existing guidelines on the development of information to support patient decision making will be included in the final guideline. In addition, patients should be signposted to relevant and trusted sites such as the NHS and third sector organisations, and the information should be consistent across these sites.

Government response

We welcome the consultation feedback on the information to support patients when deciding whether to be treated with an individualised mRNA cancer immunotherapy medicine.

Every medicine pack in the UK includes a patient information leaflet (PIL). This will apply to individualised mRNA cancer immunotherapies once authorised. In addition, the PILs of all licensed medicines are available from the MHRA Products site. During any marketing authorisation (licensing) application, the MHRA works with the applicant to ensure that the authorised PIL contains the essential information which a patient needs to enable them to use the medicine safety and gain the most benefit. PILs must also be tested for readability by target patient groups.

Much of the information highlighted by the respondents will be included in the PIL. This includes a description of what the medicine is and what it is used for, warnings and precautions, how it is given, possible side effects, and ingredients. However, we acknowledge that some types of information highlighted during the consultation will not be conveyed within the current format of the PIL, for example, information about how the patient's genetic information is used to design the individualised therapy, or summaries of clinical trial evidence. Furthermore, based on the consultation feedback, the PIL is not necessarily the best format.

The new clinical trials regulations come into force on 28 April 2026. These include new requirements for research transparency in UK clinical trials of medicines, such as providing a lay summary of the results to trial participants and publishing a results summary within 12 months of the end of the trial.

We will update the guideline to reflect the consultation feedback on the type, format and timing of the information, with a focus on aspects specific to individualised mRNA cancer immunotherapies. We will also make it clear that the responsibility for developing information resources does not rest solely with developers or marketing authorisation applicants.

Informed by the updated guideline, the MHRA will work with relevant public sector organisations, patient groups, advocates and carers to support patients, carers, healthcare professionals and the wider public to have early access to good quality information about individualised mRNA cancer immunotherapies. This is important to inform individual benefit risk discussions between patients and their healthcare professional, ensure safe and effective use, and reduce the likelihood of misinformation.

Conclusion and next steps

Our aim is to facilitate patient access to individualised mRNA cancer immunotherapies, while maintaining our stringent standards of safety, quality and efficacy. This consultation has provided very valuable feedback on our draft guideline for developers of these novel cancer therapies. We will publish our final guideline in the coming months. In the future, we may amend the final guideline to reflect regulatory experience.