



Breaking the Mould: *MHRA's Draft Paves the Way for Individualised mRNA Therapies*

Scientists have long understood that cancers are as individual as the patients in which they develop and proliferate. We still classify cancers in different groups depending on tissue origin, morphology and other factors, but genomic studies have revealed that on a cellular and molecular level, cancer cells can be very individual within a group. We also know from antibody-based therapies that the patient's immune system can be used to fight cancer cells. Antibody-based therapies have been, and newly developed antibodies will continue to be, successful in the treatment of cancer. But the idea of directly activating the patient's humoral immune response against tumour cells promises a lasting vaccine-like response. Individualising this immune response, tailored to unique (mutated) proteins produced by patients' own cancer cells, opens a new avenue of vaccine-like cancer therapies. Individualised mRNA cancer vaccines may be the answer to the treatment of previously untreatable or unresponsive cancers.

Unfortunately, individualised treatments are not something that drug developers, manufacturers and regulatory authorities are used to dealing with. The MHRA draft guideline on individualised mRNA cancer immunotherapies indicates that regulatory authorities are willing to discuss new ideas and QC-concepts required to industrialise the individualisation of mRNA therapies.

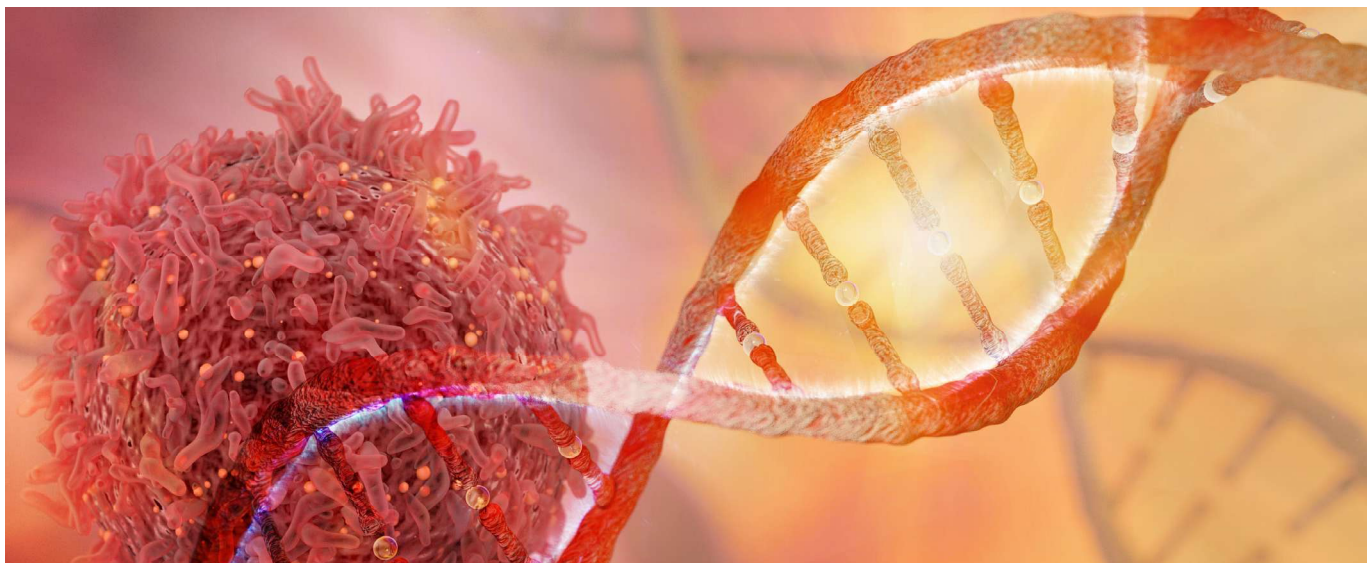
The publication of the MHRA's draft regulatory guidance on individualised mRNA cancer immunotherapies marks more than just a technical milestone in regulatory science. It addresses the fundamental challenges to the way medicines have been conceptualised, manufactured and approved for over a century. Once, the industry relied on the predictability of mass-produced drugs designed, tested and delivered in homogeneous batches. Now, individualised drugs demand a regulatory framework for therapies that are, by definition, unique to every patient. Traditional drug development, however, is built upon scale. A single molecule, discovered and refined, undergoes years of preclinical and clinical testing across populations to establish safety and efficacy before being manufactured at scale. Regulatory oversight centres on batch integrity, ensuring that each vial, tablet or syringe from a given lot is chemically and functionally identical. Quality assurance is grounded in reproducibility over the complete lifecycle of the product. Although individualised therapies break with this paradigm, most elements of the production will still have to be reproducible and traceable to ensure that the quality in terms of identity, purity and quantity is designed into the product and, more crucially, that each single batch is received by the intended patient. A guideline should address these points.

The MHRA draft document challenges the fundamentals of traditional mass-produced medicines and accommodates

the concept of an individualised mRNA cancer vaccine, which is designed against each patient's tumour molecular profile, integrating mutational data into a bespoke RNA construct. No two patients' products are exactly the same, nor are they intended to be. Here, the very definition of a batch is inverted; the patient-specific product is the batch. Whereas the new Ph. Eur. chapters 5.36 mRNA vaccines for human use, 5.39 mRNA substances and 5.40 DNA templates, coming into effect on January 1st 2026, only conceptualise how mRNA vaccines are already designed and manufactured, they do not make reference to how such vaccines may be individualised. The MHRA takes the bold step of taking the specific regulatory requirements of individualised mRNA cancer vaccines head-on, rather than leaving innovators to navigate a regulatory vacuum. The guidance acknowledges that classical comparability, stability and potency testing models cannot simply be retrofitted. Instead, it gestures towards a more flexible, risk-based approach, focusing on the robustness of the platform technology, the reliability of bioinformatic pipelines and the control of manufacturing processes, rather than on product-by-product characterisation.

Critics may rightly question whether regulatory science can keep pace with technological ambition. What happens when accelerated manufacturing timelines, sometimes mere days from biopsy to vaccine, collide with the need for meaningful quality oversight? The MHRA's consultation process is crucial, but the eventual guidance must strike a balance, enabling innovation without eroding the safeguards that patients and clinicians rely on. Therefore, this guidance is hopefully conceived as a living document that should be amended when technology outpaces current thinking; no one can predict the future. This should especially be reflected when individualised mRNA therapies leave the vaccine space and move into other indications like infectious disease, rare disorders, or autoimmune conditions. This forward-thinking guidance document, positioning the MHRA as a regulatory pioneer, could attract developers and clinical trials to the UK, enhancing its scientific leadership in the field. Contrary to libertarian thinking, measured regulatory oversight can be the ground to grow innovation and foster entrepreneurial success, especially in the medical field. Clearly, the early implementation of the FDA as a strong agency drafting regulations with patient safety as their foundation and an open mind to science and innovation to foster the development of new lifesaving drugs, has been key to the success of the US-pharma landscape. The draft guideline for individualised mRNA cancer vaccines proposed by the MHRA has a very similar spirit, regulate but invite new thinking and innovation.

However, the UK needs to remain aware that it does not regulate in isolation. To be a leader in this field, the MHRA should align with the EMA and the FDA. Divergent frameworks risk creating regulatory silos, complicating multinational development and slowing patient benefit. The MHRA's boldness,



therefore, must be matched with diplomacy. Anyone developing individual cancer therapies is well informed to look at related guidelines proposed by other authorities, like the FDA and EMA. The FDA's draft guidance for Analytical Procedures for mRNA Vaccine Quality has been a first out there to propose sets of detailed analytical methods designed to evaluate the quality of mRNA vaccines throughout all production steps. EMA has followed with a very similar approach, having divided their quality expectations into three chapters (5.36 mRNA vaccines for human use, 5.39 mRNA substances and 5.40 DNA templates), reflective of the three main production steps required for mRNA manufacturing. Although these documents do not reference individualised mRNA therapies, they have a stronger CMC focus and fix a shared vocabulary and baseline for release testing, impurities, potency and critical process parameters. If regulation is a two-storied house, the MHRA draft lives upstairs (clinical and regulatory pathway), while the new EMA chapters and the FDA draft guideline form the foundation (CMC and quality standards). All of these documents have shared scientific and technical understanding of mRNA-based therapies and should be read together for a successful mRNA development program.

But the greatest challenge for the success of these potentially lifesaving drugs is not rooted in regulatory oversight. It lies in the restoration of trust in science, scientists and scientific and pharmaceutical institutions. Legislators need to understand the scientific process and that in science, there is no black and white, and that answers to questions may change over time as more data emerges and the knowledge base grows. Scientists need to realise that this is difficult to understand for people outside of the scientific community, who are increasingly told that things can just be either black or white. Patients, patient groups and legislators need to be informed about potential benefits and risks (side effects) in a clear and unbiased language, outlining what we know and don't know. And this is where this MHRA guideline may also have a part to play, taking the individualised mRNA therapies out of the corner of the Advanced Therapy Medicinal Products and away from gene and cell therapies, where concepts are difficult to grasp and therefore daunting for patients and their families. Giving individualised mRNA therapies their own label separately from ATMPs will make it far easier to communicate to all stakeholders

what mRNA vaccines are. What does individualisation in this context mean? What diagnostics and information are required to achieve individualisation? And lastly, the potential benefits as well as risks or side effects of mRNA cancer vaccines.

None of this guarantees that personalised cancer vaccines will fulfil their promise. Science is still wrestling with immune escape, tumour heterogeneity and the sobering reality that not all predicted neoantigens (tumour-specific proteins) drive durable responses. But the regulatory and quality scaffolding is finally catching up. Of course, regulatory authorities can play it safe and wait until the first individualised products are brought to submission and then, based on what they have been presented, start drafting a regulatory framework. Or, they can communicate to developers that they understand that individualisation of therapies is very different to how standard medicines are produced, controlled, distributed and regulated; they see the challenges faced and this is how they want those to be addressed. The MHRA draft guideline signals to companies trying to make individualised mRNA cancer therapies a reality that if you are able to industrialise personalisation, your submission will be evaluated by an agency that has competence and a clear vision to enable a fair process.



Dr. Steven Watt

After studying molecular biology at Bielefeld University and graduating with a PhD in genetics and molecular biology in 2005, Dr. Steven Watt was granted a position as an assistant professor at the department of proteome and metabolome research at Bielefeld University, where he was in charge of a mass spectrometry service unit. In 2008, he changed to industry working, as an instructor and consultant for accurate-mass high-resolution mass spectrometry applications in pharma. In 2010, he joined A&M STABTEST Labor für Analytik und Stabilitätsprüfung to establish a Business Development unit. During his time at A&M, Steven also established the cell-based bioassay operations. He currently holds the position of Managing Director / CBDO.