

# Advancing regulatory science for innovative medical products

**Summary of a FORUM workshop held on  
3 March 2021**



Medicines & Healthcare  
products  
Regulatory Agency

### **The Medicines and Healthcare products Regulatory Agency**

The Medicines and Healthcare products Regulatory Agency regulates medicines, medical devices and blood components for transfusion in the UK. The Agency is an executive agency, sponsored by the Department of Health and Social Care and includes three expert business centres: the Clinical Practice Research Datalink (CPRD), the National Institute for Biological Standards and Control (NIBSC) and the MHRA regulatory centre (MHRA).

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The Academy of Medical Sciences is the independent body in the UK representing the diversity of medical science. Our mission is to promote medical science and its translation into benefits for society. The Academy's elected Fellows are the UK's leading medical scientists from hospitals, academia, industry and the public service. We work with them to promote excellence, influence policy to improve health and wealth, nurture the next generation of medical researchers, link academia, industry and the NHS, seize international opportunities and encourage dialogue about the medical sciences.

**Opinions expressed in this report do not necessarily represent the views of all participants at the event, the Academy of Medical Sciences, or its Fellows.**

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# Executive summary

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**Scientific and technological progress is creating new challenges for regulation. Regulatory authorities need to respond to the increasing diversity and complexity of medical interventions, which can include medicines, vaccines, prophylactics, medical devices, software and diagnostics, as well as their use in combinations or as platform technologies.**

These authorities include the Medicines and Healthcare products Regulatory Agency (MHRA), which is responsible for evaluating the efficacy, safety and quality of new medical interventions and granting marketing authorisation; the Health Research Authority (HRA), which provides a unified system for the governance and ethical approval of health research; and the National Institute for Health & Care Excellence (NICE) (and corresponding organisations in the devolved administrations<sup>1</sup>), which determines the cost-effectiveness of new interventions and produces guidance on their use.

The primary priority for these regulatory authorities should be ensuring that patients have timely access to safe and effective healthcare products and new, potentially life-saving innovations. Patients understandably expect early access to these innovations and are increasingly calling for greater patient involvement in regulatory decision-making, introducing new opportunities as well as requirements for new methodologies and data sources.

The COVID-19 pandemic has presented a further set of challenges, requiring more flexible and collaborative approaches to accelerate the development, evaluation and licensing of medical interventions in an emergency situation. While it is unlikely that all practices adopted during such a public health emergency will become routine, important lessons can be learned to guide future activities and embed those new approaches and flexibilities that add most value.

Furthermore, the UK's departure from the European Union (EU) is providing an opportunity for UK regulators to explore more flexible and agile approaches to regulation in response to the changing scientific landscape.

In March 2021, a FORUM roundtable jointly hosted by the Academy of Medical Sciences and the MHRA brought together leaders from multiple stakeholder organisations to discuss the drivers of change in regulatory practice and the potential of regulatory science to inform the future direction of travel. The meeting was chaired by Dr June Raine CBE, Chief Executive of the MHRA, and Professor Deborah Ashby OBE FMedSci, Director of the School of Public Health at Imperial College London. Participants identified a range of key themes:

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<sup>1</sup> These are the All Wales Medicines Strategy Group, the Scottish Medicines Consortium and the Department of Health, Northern Ireland.

**Supporting innovative regulation:** Changes to regulatory practice need to be underpinned by rigorous evidence. Regulatory science, the application of scientific methods to assess and improve regulatory processes and inform benefit-risk judgements, has the potential to deliver this evidence. Regulatory science strategies have been developed by agencies such as the US Food and Drug Administration (FDA) and the European Medicines Agency (EMA), and some regulatory science research is already being carried out in the UK. While positive progress has been made, the impact of this research on regulation is yet to be fully evaluated. Key issues to be resolved include the scope of regulatory science and its relationship with the wider field of innovation. There is also a need to identify priority research questions. An overarching principle is that regulatory science research should have the explicit goal of informing effective regulation.

**Engaging and involving researchers:** It was suggested that academic scientists with an interest in translational research typically have limited understanding of product innovation in general and regulatory processes specifically. In the university sector, translational research tends to focus on discovery and early stages of translation rather than later-stage evaluation and implementation. Strengthening the ability of academic researchers to be involved in end-to-end innovation could help build national expertise in translation, regulation and adoption of healthcare products and regulatory science. Informed by a comprehensive needs assessment, modular and multidisciplinary postgraduate training programmes could strengthen UK capacity, potentially as part of wider educational programmes focused on medical innovation.

**Attracting industry:** It was argued that a regulator that is dynamic, pragmatic, flexible, efficient, interactive and driven by public interest will contribute to an attractive environment for investment in clinical research and filing data for regulatory review. Although international regulatory alignment is important, UK regulators are globally influential and have the potential to pioneer new approaches and catalyse international innovation in regulatory practice.

**Utilising data opportunities:** The increasing availability of a wider range of data sources is creating new opportunities to gather timely evidence on safety, efficacy and cost-effectiveness. Trials embedded in routine clinical practice and retrospective health data analysis are providing new ways to collect data to complement traditional clinical trials. Exploiting these opportunities is likely to require further investment in health data science capacity, building on UK strengths in this area.

**Involving patients and the public:** Patient and public involvement (PPI) is now seen as central to regulation as well as medical research, and several regulatory agencies have developed models of good PPI practice. One important role of regulatory science is to explore how patients and the public can best contribute to regulation.

**Collaborating with funders:** Participants suggested that limited funds are currently available for regulatory science research. Dialogue about how sources of funding could contribute to development of the UK's regulatory science base and to identify the most appropriate forms of sustainable support is a priority.

In conclusion, participants suggested that the UK now has the potential to become a global leader in regulatory science, as part of its drive to reshape regulatory practice in response to emerging challenges and opportunities. This could provide an attractive environment for innovative medical research and reinforce the message that the UK is 'open for business' for healthcare product developers.

Many of the key issues facing regulators are well-recognised and the MHRA and others are already carrying out research into them. There is now a need to build on this foundation to identify and prioritise the key regulatory science questions that need to be addressed. Key enablers, such as workforce capacity, technical infrastructure, and sources of funding, should also be identified.

The FORUM roundtable discussions identified a range of issues where further dialogue among a wider group of stakeholders is required to advance plans for a coordinated regulatory science initiative in the UK, including:

- **Defining the scope of UK regulatory science**, such as whether its focus should just be on licensing or also on other aspects of clinical research governance (e.g. ethical approvals, health technology assessment and pharmacovigilance), and its relationship with the wider field of innovation.
- **Identifying key stakeholders**, their roles and how best to ensure collaboration and communication between them.
- **Establishing how patients and the public can best be involved** in further discussions.
- **Identifying mechanisms for taking the regulatory science agenda forward.**
- **Working with funders** to identify the most appropriate mechanisms for supporting regulatory science and developing regulatory science research capacity.

Delegates expressed an enthusiasm to maintain the dialogue while exploring what lessons can be learned from the COVID-19 experience, and to bring in additional stakeholders with the MHRA continuing to play a central strategic and convening role.

# Introduction

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**This is a pivotal moment for regulation in the UK. The increasing number and diversity of medical interventions, and combinations thereof, are presenting challenges to traditional regulatory processes. In addition, the need for rapid responses to the COVID-19 pandemic has led to significant innovation in regulatory practice. Patient expectations for earlier access to innovations, and for involvement in regulatory decision-making, introduce opportunities as well as requirements for new methodologies and data sources. The UK's departure from the EU may also provide scope for more flexible approaches to regulation.**

Benefit-risk assessments and changes to regulatory policy and practice need to be based on robust evidence. Regulatory science has emerged as a multidisciplinary field of academic endeavour that aims to generate the evidence needed to inform the development of regulatory processes and to support robust, timely decision-making.

On 3 March 2021, the Academy of Medical Sciences and the MHRA hosted a roundtable meeting to consider the current regulatory landscape for innovative medical products and explore how advances in regulatory science can enable efficient and effective regulation of current and emerging medical products.

The meeting, chaired by Dr June Raine CBE, Chief Executive of the MHRA, and Professor Deborah Ashby OBE FMedSci, Director of the School of Public Health at Imperial College London, convened stakeholders from across the regulatory landscape, including academic researchers, innovators, industry, funders, regulators, and patient and public representatives to:

- Discuss the current regulatory frameworks for innovative medical products and define what is meant by regulatory science.
- Identify the future priorities for regulatory science in the UK, reflecting on lessons learnt during the COVID-19 pandemic.
- Explore the roles of different stakeholders in working with the regulator to achieve these priorities.

To open the meeting, Professor Sir Kent Woods FMedSci, Emeritus Professor of Therapeutics at the University of Leicester, provided an outline of the UK regulatory landscape and its interactions with regulatory science. Representatives of different stakeholder groups then made brief presentations to lay out the key issues and to stimulate discussion. Sir Mene Pangalos FMedSci, Executive Vice President of Biopharmaceuticals Research and Development at AstraZeneca provided an overview

of what regulatory science means to the field of drug development. Professor Cathie Sudlow OBE, Professor of Neurology and Clinical Epidemiology at the Usher Institute and Director of the British Heart Foundation Data Science Centre, presented on the implications of regulatory science on the fields of big data and artificial intelligence (AI). Professor Dame Sarah Gilbert DBE FMedSci, Saïd Professor of Vaccinology at the Jenner Institute and Nuffield Department of Clinical Medicine, provided an overview of what regulatory science means to the field of vaccine development. Finally, Professor Melanie Calvert, Professor of Outcomes Methodology at the University of Birmingham, presented on recent progress in regulatory science in the UK and elsewhere.

This report provides a summary of the discussions that took place at the meeting. It does not necessarily represent the views of all participants at the event, the Academy of Medical Sciences or its Fellows, or those of the MHRA.

The meeting formed part of the Academy of Medical Sciences' FORUM programme, which was established in 2003 to recognise the role of industry in medical research and to catalyse connections across industry, academia and the NHS. We are grateful for the support provided by the members of this programme and are keen to encourage more organisations to take part. If you would like information on the benefits of becoming a FORUM member, please contact [FORUM@acmedsci.ac.uk](mailto:FORUM@acmedsci.ac.uk).



# Regulatory science

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## What is regulatory science?

The need to ensure that regulation keeps pace with scientific developments has promoted renewed interest in regulatory science. Regulatory science involves the application of multidisciplinary research methods to assess and enhance regulatory activities. Several formal definitions have been developed (see Annex I), including the following adapted from a definition by GA FitzGerald that was specifically raised at the meeting:

*'Regulatory science may be defined as the acquisition and analysis of data sufficient to inform decision making pertinent to the approval and monitoring of safe and effective medical interventions.'*<sup>2</sup>

Although differing in detail, the core principles of all definitions of regulatory science are essentially the same – the use of scientific approaches to optimise regulation. Regulatory science provides rigorous methods to enable regulators to better judge the balance of benefits and risks associated with novel medical interventions. It is distinct from regulatory affairs, which covers the actual practice of regulation and the activities necessary to ensure compliance with regulatory requirements and standards.

The field is young, but regulatory science strategies, with specific research priorities, have been developed by some regulatory authorities, including the FDA and the EMA.<sup>3,4</sup> In the US, four Centers of Excellence in Regulatory Science and Innovation (CERSIs) have been established, focusing on research, scientific exchange and training.<sup>5</sup> Other US academic centres also conduct regulatory science research.

Participants noted that regulatory science is multidisciplinary, sitting at the interface between clinical practice, research (academic and industry-based) and regulation, including its legal frameworks and tools. It is potentially very broad in scope, encompassing any type of study or research activity with the potential to inform regulatory practice and decision-making, including behavioural research.

Furthermore, as well as product approvals, the scope of regulatory science could potentially cover other aspects of the governance of clinical research and decision-making, including ethical approvals, health technology assessment and pharmacovigilance. Regulatory science is therefore of potential interest to other UK bodies, such as the HRA. It could also cover other elements of technology appraisal, such as evidence syntheses and meta-analyses.

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<sup>2</sup> Adapted from FitzGerald GA (2011). *Regulatory science: what it is and why we need it*. Clin Pharmacol Ther **89(2)**, 291-4.

<sup>3</sup> Food and Drug Administration (2011). *Advancing Regulatory Science at FDA: A Strategic Plan*. <https://www.fda.gov/media/81109/download>

<sup>4</sup> European Medicines Agency (2020). *Regulatory Science to 2025*. [https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/ema-regulatory-science-2025-strategic-reflection\\_en.pdf](https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/ema-regulatory-science-2025-strategic-reflection_en.pdf)

<sup>5</sup> Food and Drug Administration. *Centers of Excellence in Regulatory Science and Innovation (CERSIs)*. <https://www.fda.gov/science-research/advancing-regulatory-science/centers-excellence-regulatory-science-and-innovation-cersis>

Regulatory science also covers all forms of medical intervention, including medical devices, software such as medical device apps, and diagnostics. In effect, its scope would cover any tool insofar as it is subject to regulatory oversight.

It was also noted that this broad scope inevitably means that regulatory science is closely associated with innovation more generally. The process of new product development is significantly influenced by the nature of the pathways that must be followed to secure approval. Participants suggested that it is important to view regulation within this wider context, as streamlined regulatory processes will have limited impact on public health if other stages of the innovation pathway, including the adoption of innovation in healthcare, are not also optimized.

## Why is regulatory science needed?

The MHRA is charged with ensuring the safety and quality of medical products marketed in the UK. To fulfil this role, the MHRA must make systematic assessments of the safety, efficacy, and quality of a medical intervention, and use these to judge the balance of benefits and risks. This must occur not only at the time of introduction but throughout the product lifecycle. The Agency must make timely judgements that are in the best interests of patient and public health and communicate its decisions and the evidence underpinning them in accessible form to a wide range of audiences, including product developers, medical practitioners and the general public.

Within the limits of available data and scientific methodologies, the aim of the MHRA is to ensure that patients and the public have access to safe, effective and high-quality medical products. Systematic processes have been put in place to support rigorous evaluation of safety and efficacy that underpins evidence-based decision-making at the time of licensing, and to monitor the benefit-risk balance in clinical use. However, it is important that processes remain proportionate and adaptable to the changing nature of medical innovation in the context of public health needs.

Several key trends are driving the MHRA to consider whether its procedures continue to be fit for purpose, particularly scientific and technological developments that are having a major impact on the type of medical products developed. Drivers of change include:

**Increasing diversity and complexity of products:** Regulation has evolved in relation to the specific characteristics of major classes of healthcare interventions, principally the two main categories; pharmaceuticals and medical devices. However, an increasingly wide range of medical products are now being developed, including complex biomolecules, genetic and cellular therapies, diagnostic platforms, digital health-management products (e.g. apps) and other software. Products are often developed in tandem, such as targeted therapies and companion diagnostics. Traditional methods of regulatory assessment may not necessarily be easy to apply to such innovative new products and applications of medical technology.

**Stratified medicine:** Regulation has traditionally relied heavily on data from large pivotal phase III trials. However, the development of targeted therapeutics is leading to smaller sample sizes and considerable innovation in trial design, as well as the co-development of companion diagnostics. New approaches are needed to assess the safety and efficacy of these types of products, particularly in long-term clinical use.

**Unmet medical needs:** There is high demand for new products to address unmet medical needs, particularly with the growing opportunities for patients' voices to be heard. It is important that, as well as protecting public health, regulators do not create unnecessary disincentives to medical

innovations, or put in place barriers that slow their development. When the value of promising innovative interventions is uncertain, it is vital that decision-relevant evidence is generated and evaluated as rapidly as possible so that regulation, policy and clinical decisions can be based on sound evidence.

**Data opportunities:** While randomised clinical trials remain the mainstay of regulation, these are typically long, expensive and involve only a subset of patient types of varying relevance to the real world of healthcare. Increasingly, effectiveness and safety data can be obtained from alternative sources that complement traditional trial designs, including pragmatic randomised trials within clinical practice settings and by analysis of routinely collected data. Hence, more data, and data from different sources, are potentially available to inform regulatory decision-making.

**Public health imperatives:** A further key driver of change has been the COVID-19 pandemic, which has presented major challenges to healthcare and regulatory systems worldwide and has brought about significant innovations and flexibilities in regulatory practice to support timely and risk-proportionate decision-making. The emergence of a novel respiratory virus with the potential to cause severe disease created enormous demand for effective and safe vaccines, therapeutics, medical devices and *in vitro* diagnostics. Effective vaccines were developed at unprecedented speed, dependent in part on frequent proactive dialogue and interaction between product developers and regulators, and on a flexible, pragmatic and responsive approach to regulatory processes. This led to the rapid approval of vaccines and rollout of vaccination in the UK, without any compromise on the rigour with which products were assessed.

**Novel clinical trial methodologies:** During the pandemic, platform trials were rapidly established to evaluate repurposed and new pharmaceuticals, delivering key information on the effectiveness of treatments and prophylactics to inform clinical decision-making. For example, the RECOVERY trial provided evidence for the effectiveness of dexamethasone and tocilizumab in reducing the risk of death of hospitalised patients. Through close liaison with the MHRA, other clinical research oversight bodies, the NHS and health technology appraisal bodies, high-quality pragmatic randomised trial platforms were organised and delivered data that was relevant to regulatory decision-making at great speed. The MHRA has also had to make rapid assessments of medical devices to provide respiratory support and introduced new approaches for the regulation of diagnostic tests, including Target Product Profiles.<sup>6</sup>

**Maintaining public trust:** While more rapid assessments are desirable, speed should not be achieved at the expense of scientific rigour. Furthermore, as the COVID-19 pandemic has illustrated, regulatory decision-making must maintain public trust. For example, immunisation campaigns could easily be undermined if the public has doubts about the robustness of the regulatory judgements on the safety or efficacy of products or lacks confidence in the regulatory authorities that were approving them. Changes to regulation must therefore be mindful of the need to maintain public trust and be underpinned by strong communication.

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<sup>6</sup> Medicines & Healthcare products Regulatory Agency (2021). *Target Product Profile: antibody tests to help determine if people have recent infection to SARS-CoV-2: Version 2*. <https://www.gov.uk/government/publications/how-tests-and-testing-kits-for-coronavirus-covid-19-work/target-product-profile-antibody-tests-to-help-determine-if-people-have-recent-infection-to-sars-cov-2-version-2>

Some work has already been carried out on the strategic needs for regulatory science in the UK. For example, a 2020 report from the Birmingham Health Partners Centre for Regulatory Science and Innovation recommended actions in four areas:<sup>7</sup>

- **Strategy and leadership:** defining a regulatory science research agenda.
- **Enabling innovation/horizon scanning:** anticipating and addressing emerging issues to create an environment that supports research and development (R&D) and innovation.
- **Implementation and evaluation:** evaluating changes in regulatory practice and promoting continuous learning.
- **Workforce development:** understanding education and training needs for the regulatory science field.

In terms of horizon scanning, this is an important role of the Regulatory Horizons Council,<sup>8</sup> an independent expert committee responsible for providing the UK Government with advice on technological innovations and the need for regulatory reform to ensure their rapid and safe introduction.

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<sup>7</sup> Samuels M, Marston E, Calvert M (2020). *Advancing Regulatory Science and Innovation in Healthcare*. Commissioned on behalf of Birmingham Health Partners Centre for Regulatory Science and Innovation. [https://www.birminghamhealthpartners.co.uk/Advancing%20Regulatory%20Science%20and%20Innovation%20in%20Healthcare.pdf?\\_t=1594305225](https://www.birminghamhealthpartners.co.uk/Advancing%20Regulatory%20Science%20and%20Innovation%20in%20Healthcare.pdf?_t=1594305225)

<sup>8</sup> UK Government. *Regulatory Horizons Council (RHC)*. <https://www.gov.uk/government/groups/regulatory-horizons-council-rhc>

# Challenges and opportunities

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**Following the presentations, speakers and delegates representing different stakeholder communities, including patients and the public, discussed a range of key issues, including the nature of regulatory science and how it should inform regulation in the UK, regulatory priorities for the UK, and the roles of different stakeholders. These presentations and discussions highlighted the following points:**

## **Academic science needs**

It was suggested that academic researchers who generate potentially translatable findings typically have little experience of product innovation in general and regulatory processes specifically. Academic researchers therefore generally have a limited understanding of what regulators require. Beginning the process of translation can be daunting, and there is a need for training, mentoring and support for those embarking on the journey for the first time. The Vax-Hub initiative, for example, aims to create a forum spanning the academic, biotechnology and pharmaceutical sectors to accelerate vaccine discovery, development and manufacture in the UK.<sup>9</sup>

More generally, it was argued that early engagement between regulators and academics can ensure that scientists have a better understanding of regulators' needs and can focus efforts on the generation of the specific types of evidence that regulators require, avoiding wasted efforts. Flexibility is required on both sides, with early dialogue also providing an opportunity for researchers to discuss potential issues and agree scenario-specific approaches with regulators. The new ways of working during the COVID-19 pandemic demonstrated how early and flexible engagement between developers and regulators accelerated generation of evidence that was relevant to regulatory decision-making and expedited the introduction of innovation into clinical practice. It was suggested that more integrated approaches to licensing and health technology assessment would be helpful, to shape data collection strategies that cover both approvals and cost-effectiveness assessments.

Participants noted that education, training and wider capacity development in academia will be critical. As well as building researchers' skills in innovation and knowledge of regulatory processes, there is also a need to develop capacity in regulatory science itself. Centres such as the Birmingham Health Partners Centre for Regulatory Science and Innovation have been created to

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<sup>9</sup> University College London. *Vax Hub*. <https://www.ucl.ac.uk/biochemical-engineering/research/research-and-training-centres/vax-hub>

provide a multidisciplinary environment for regulatory science studies.<sup>10</sup> Regulatory science researchers are likely to be drawn from multiple disciplines, so there will be a requirement for flexible, modular and multidisciplinary postgraduate education strongly rooted in practice, and potentially part of a wider programme covering innovation in the medical domain. A needs assessment and landscaping analysis could help to identify priority areas for capacity building and course development.

It was suggested that, within academia, early stages of translation have been prioritised, and incentives might be needed that focus more attention on later stages of clinical evaluation and implementation of medical innovations, together with outcome evaluation. It was also noted that bodies such as the National Institute for Health Research (NIHR) and structures such as Academic Health Science Networks provide vital support for innovation adoption and have the potential to contribute to accelerated later-stage translation.

Increasing numbers of innovative medical products, including apps and other software, themselves collect and analyse data. Software development is already covered by regulation, but the growing use of artificial intelligence (AI) in medical innovations is raising additional regulatory challenges. Some AI-based digital health tools are qualitatively different from traditional software, given their potential to 'learn'. The SPIRIT-AI and CONSORT-AI initiatives provide guidance on the reporting of clinical trial protocols and trial reports for interventions that include an AI component.<sup>11</sup> New regulatory approaches to benefit-risk assessment throughout the product lifecycle will also be needed. Following the roundtable, the MHRA was awarded a grant from the Department for Business, Energy and Industrial Strategy's 'Regulator's Pioneer Fund' to develop a method to determine whether the logic of an algorithm has changed significantly since it was authorised, and how these changes should be regulated.<sup>12</sup>

## Industry needs

Securing timely regulatory approval is a critical driver of pharmaceutical companies' clinical evaluation strategies. Industry therefore seeks regulation that is interactive, pragmatic, flexible, efficient and driven by public interest. It was argued that these attributes can help to create a national environment that is attractive for clinical research and regulatory filing, thereby ensuring that citizens gain early access to innovative new medicines.

The MHRA's Innovative Licensing and Access Pathway (ILAP), which aims to reduce the time to approval of innovative new medical products by improving the efficiency and flexibility of the regulatory process, has been broadly welcomed by industry since its introduction in January 2021.<sup>13</sup> This new regulatory approach provides scope for early dialogue on plans for regulatory approval, spanning both licensing and health technology assessments for the NICE and Scottish Medicines Consortium (SMC).

Participants noted that small and medium-sized enterprises (SMEs) make important contributions to new product development, particularly early-stage drug development and medical device

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<sup>10</sup> Birmingham Health Partners. *BHP Centre for Regulatory Science and Innovation*.

<https://www.birminghamhealthpartners.co.uk/programmes/bhp-centre-for-regulatory-science-innovation/>

<sup>11</sup> SPIRIT-AI & CONSORT-AI. <https://www.clinical-trials.ai/>

<sup>12</sup> Department for Business, Energy & Industrial Strategy (2021). *Projects selected for the Regulators' Pioneer Fund*. <https://www.gov.uk/government/publications/projects-selected-for-the-regulators-pioneer-fund/projects-selected-for-the-regulators-pioneer-fund>

<sup>13</sup> Medicines and Healthcare products Regulatory Agency (2021). *Innovative Licensing and Access Pathway*. <https://www.gov.uk/government/publications/innovative-licensing-and-access-pathway-ilap-for-medicines>

innovation. SMEs often have less in-house regulatory affairs expertise than large pharmaceutical companies and would benefit more from closer engagement with regulators. The NICE–MHRA scientific advice initiative, for example, has been particularly helpful to SMEs.<sup>14</sup>

## Regulatory needs

Given the importance of regulation to the health of the public, it was felt that regulation and regulatory science should be seen by scientists and clinicians as attractive areas in which to develop public health careers. It was also seen as important that scientists are engaged in the end-to-end process of innovation, from discovery to implementation, to encourage research that has a greater likelihood of achieving impact. Greater familiarity with regulatory processes in academia would also encourage greater involvement in regulatory science.

It was suggested that the UK's departure from the EU provides an opportunity to be more agile and innovative in the approach to regulation. However, international regulatory alignment is also important, with different regulatory requirements in different jurisdictions adding to industry costs and lengthening development timelines. Project Orbis, an FDA oncology initiative, was cited as an example where international cooperation between regulatory authorities (including the MHRA) has helped to streamline and harmonise regulatory procedures.<sup>15</sup> Greater sharing of data between regulatory agencies was also suggested as a way to reduce the burden on product developers.

It was argued that, as a globally influential body, the UK regulator now has a chance to be a world leader and to catalyse changes in practice worldwide. The MHRA recently joined the Access Consortium, a coalition that includes the national regulatory authorities of Australia, Canada, Singapore and Switzerland, providing a further route through which it could influence global practice.<sup>16</sup>

## Data opportunities

The lifecycle of medical products has traditionally involved pre-licensing and post-licensing phases, marking the transition from a carefully controlled development phase to the real-world use of the product. With the introduction of conditional licensing in certain areas of medical need, this distinction has been blurred. Conditional licensing relies on phase IV post-licensing data collection alongside routine clinical use, illustrating that there are alternative or complementary approaches to the traditional pivotal phase III trial. More generally, the 'learning health system' concept captures the idea that health systems have the potential to acquire evidence to guide more refined use of medical innovations, enabling more flexible approaches to regulation.

During the COVID-19 pandemic, the RECOVERY trial was established as a platform able to carry out pragmatic randomised studies of COVID-19 treatments. It was embedded in routine care and the trial design was kept simple, enabling all acute secondary care health facilities in the UK to participate. It has generated robust evidence on the effectiveness of repurposed treatments such as dexamethasone and tocilizumab (as well as on the lack of effectiveness of therapeutics such as

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<sup>14</sup> NICE. *NICE-MHRA scientific advice*. <https://www.nice.org.uk/about/what-we-do/life-sciences/scientific-advice/nice-mhra-scientific-advice>

<sup>15</sup> U.S. Food & Drug Administration. *Project Orbis: Strengthening International Collaboration for Oncology Product Reviews, Faster Patient Access to Innovative Therapies*. <https://www.fda.gov/news-events/fda-voices/project-orbis-strengthening-international-collaboration-oncology-product-reviews-faster-patient>

<sup>16</sup> Medicines and Healthcare products Regulatory Agency (2020). *Access Consortium*. <https://www.gov.uk/guidance/access-consortium>



hydroxychloroquine). Factorial trial designs are now allowing the evaluation of multiple interventions simultaneously.

It was suggested that the rapid launch of the RECOVERY trial had been aided by early engagement with regulators, ongoing dialogue during protocol development, and rapid but rigorous reviews. The mechanisms established also enabled clinical practice recommendations to be made very rapidly once data analysis had been completed. Although not all new regulatory ways of working adopted in response to the COVID-19 pandemic will be sustainable for routine regulatory operations, there are opportunities to review the past two years and to identify lessons learned and new practices that can be embedded.

Participants pointed out that the UK has several features that could facilitate a more flexible approach to data collection for regulatory purposes, for all kinds of medical innovation, including medical devices as well as pharmaceuticals. These include the nationwide NHS, NIHR infrastructure to promote enrolment in research, Health Data Research UK (HDR-UK), which is uniting the UK's health data to enable discoveries that improve people's lives, and a strong academic presence in data science.<sup>17</sup> It was argued that an explicit strategy was required to mobilise the UK's data resources to support regulatory decision-making.

It was suggested that opportunities exist for practice-embedded trials, analogous to RECOVERY, with data collection through electronic health records. Retrospective analysis of real-world evidence is also possible, including innovative data linkages, although participants acknowledged that bias due to confounding is an important issue to be addressed in non-randomised studies.

Challenges identified included the technical difficulties of data linkage, the need for investment in infrastructure to deliver such studies, and over-protective attitudes of data custodians, which can sometimes be an obstacle to data sharing. The acceptability to regulators of routine data recorded in electronic health records as outcome measures may also need to be addressed.

## Public and patient involvement perspectives

It was emphasised that public and patient involvement (PPI) is now seen as an essential aspect of regulation as well as medical research. This is reflected in recent work by the EMA and MHRA to establish how PPI can be integrated into regulatory activities.<sup>18,19,20</sup> The MHRA recently concluded a consultation that invited views on its new proposed Patient Involvement Strategy, which the Academy responded to.<sup>21,22</sup>

At an individual project level, PPI can make important contributions to the design of studies, leading to research that better answers scientific questions. PPI can also ensure that regulatory

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<sup>17</sup> Health Data Research UK. <https://www.hdruk.ac.uk>

<sup>18</sup> European Medicines Agency. Partners & networks. <https://www.ema.europa.eu/en/partners-networks/patients-consumers>

<sup>19</sup> Medicines and Healthcare products Regulatory Agency (2021). *Patient involvement strategy 2021-25*. [https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment\\_data/file/1022370/Patient\\_involvement\\_strategy.pdf](https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1022370/Patient_involvement_strategy.pdf)

<sup>20</sup> Medicines and Healthcare products Regulatory Agency (2021). *MHRA pilots patient involvement in new applications*. <https://www.gov.uk/government/news/mhra-pilots-patient-involvement-in-new-applications>

<sup>21</sup> Medicines and Healthcare products Regulatory Agency (2021). *MHRA Patient Involvement Strategy consultation*. <https://www.gov.uk/government/consultations/mhra-patient-involvement-strategy-consultation>

<sup>22</sup> Academy of Medical Sciences (2021). *Academy of Medical Sciences' response to the open consultation on the MHRA's Proposed Patient and Public Involvement Strategy*. <https://acmedsci.ac.uk/file-download/82234121>



activities take account of patient perspectives, especially on acceptable risk as well as meaningful benefits, which may not necessarily be the same as those of clinicians or other stakeholders.

Among the PPI questions that participants suggested could be addressed are how best to engage patient and public representatives in regulatory decision-making, how to ensure that the voices of hard-to-reach or disadvantaged communities are heard, and the contribution of patient-reported outcome measures (PROMs) to regulatory decision-making.

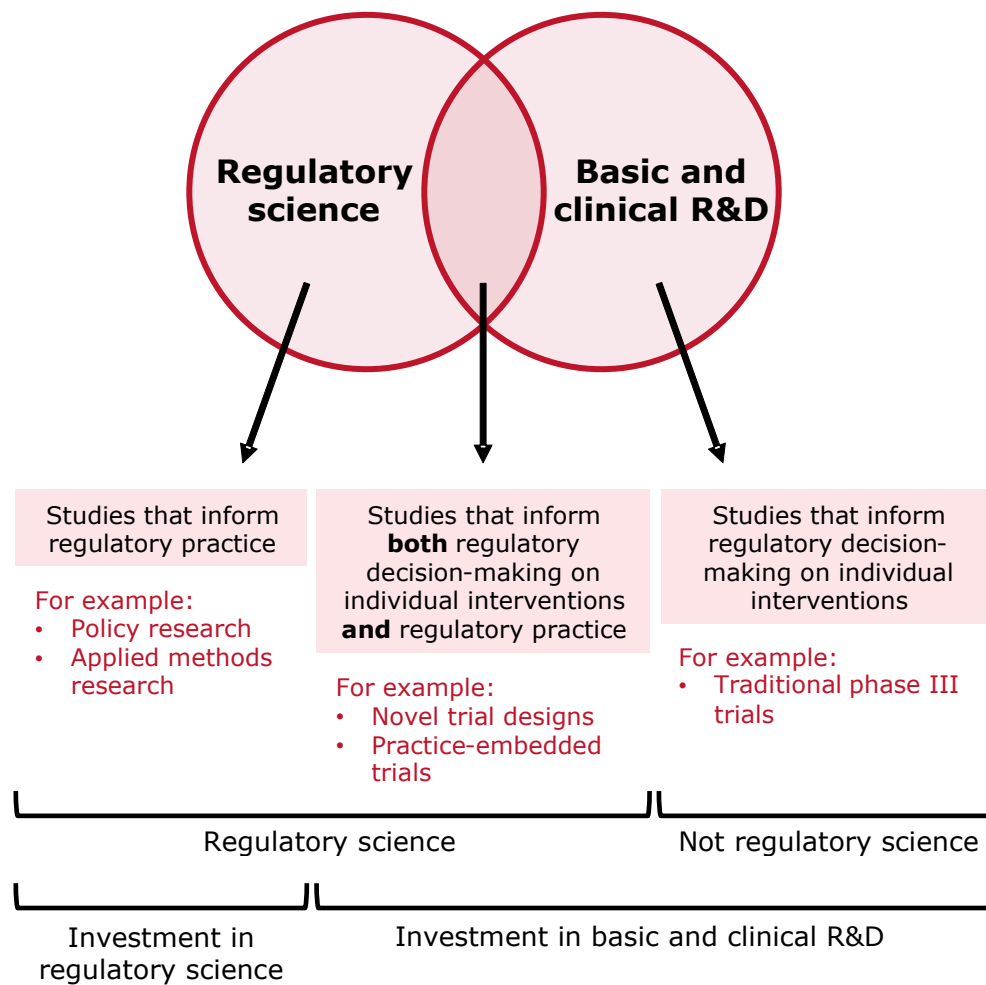
## Role of funders

The MHRA conducts regulatory science research internally. However, there are no specific sources of funding for regulatory science research in the UK. The NIHR and MRC provide limited amounts of support for research that could fall under the umbrella of regulatory science, such as applied methods research. It was suggested that funders are keen to see more regulatory science research proposals and recognise the potential of partnerships with bodies such as the MHRA and those that conduct health technology assessments (e.g. NICE).

Reaching an agreement on the priority research questions in regulatory science could catalyse greater funder interest. Given its multidisciplinary nature, sustainable funding schemes could be organised through partnerships spanning multiple funders. It would be important to consider the most appropriate forms of support, such as a network of centres of excellence (akin to the US CERSI model<sup>23</sup>), consortia or virtual centres, or dedicated fellowships (training and capacity development in regulatory science specifically and innovation more generally will be an important priority). Clarity is needed on the scope of regulatory science research and its relationship to basic or clinical R&D with the potential to influence regulation. Figure 1 illustrates how regulatory science could be defined, with examples relating to regulatory science for clinical trials.

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<sup>23</sup> Food and Drug Administration. *Centers of Excellence in Regulatory Science and Innovation (CERSIs)*. <https://www.fda.gov/science-research/advancing-regulatory-science/centers-excellence-regulatory-science-and-innovation-cersis>



**Figure 1. The scope of regulatory science.** In addition to being used as a term to describe research that informs regulatory practice, regulatory science may also encompass studies that inform both regulatory decision-making on individual decisions *and* regulatory practice. Clarity on this definition is required, as this will have implications on how funding for regulatory science is allocated. As discussed elsewhere in this report, 'regulatory practice' refers not only to product licensing and decision-making, but also other aspects of clinical research governance (e.g. ethical approvals, health technology assessment and pharmacovigilance).

# Conclusions and next steps

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It is commonly stated that 'regulation should follow science'. How medical interventions are regulated must take account of new knowledge, data sources and methodologies and the development of innovative medical products. What has worked in the past may not be appropriate for the future and may create obstacles that delay the adoption of interventions, a particularly important concern for those innovative products that address unmet medical needs. While certain principles must remain at the heart of benefit-risk decision-making – such as an abiding concern for patients and the public interest – how these are applied in practice must be responsive to the changing landscape of medical science.

Furthermore, there are other key factors driving change. The continuing rise of digital technologies and data science are opening up new opportunities for evidence generation. With the UK's departure from the EU, there is more scope to explore innovative approaches to regulation. And the response to the COVID-19 pandemic has driven innovation and the use of more flexible approaches that hold important lessons for future practice.

Regulation therefore faces a multitude of challenges and opportunities. It is essential that the response to these challenges and opportunities is itself driven by the best available evidence. Regulatory science has the potential to deliver this evidence, as well as validate new methodologies and data sources.

The participants agreed that all stakeholders, including patients and the public, now need to come together to plan a way forward. All stakeholders share the same ultimate goal – delivering measurable public health benefit – and participants agreed that regulatory science focused on an agreed set of priority issues has the potential to accelerate progress towards this goal.

Given its central position in the UK regulatory landscape and its privileged access to data, it is essential that the MHRA is at the heart of any process to identify priority research questions. However, other stakeholders, including other bodies involved in the oversight of clinical research and in health technology assessment, may also have specific research needs. There are also opportunities to learn from the research priorities established by other countries and regions, as many of the emerging challenges are common across all jurisdictions.

The MHRA's current priority areas (see Box) provide a potential foundation for establishing future priorities for regulatory science research in the UK.<sup>24</sup>

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<sup>24</sup> Medicines and Healthcare products Regulatory Agency (2021). *Medicines and Healthcare products Regulatory Agency Delivery Plan 2021-2023*. <https://www.gov.uk/government/publications/the-medicines-and-healthcare-products-regulatory-agency-delivery-plan-2021-2023/medicines-and-healthcare-products-regulatory-agency-delivery-plan-2021-2023>

### **MHRA priority research areas**

1. **Regulatory science in key licensing areas**  
The role of the patient in decision-making; women's health; drug repurposing; orphan medicines; biosimilars, among others
2. **Genomics and diagnostics**  
Precision medicine; companion diagnostics; infectious disease diagnostics; exploring a Yellow Card Biobank
3. **Data science**  
Synthetic data for artificial intelligence algorithms; data-enabled clinical trials; real-world evidence in clinical trials; near real-time pharmacovigilance
4. **Advanced therapies**  
Stem cell supply (UK Stem Cell Bank); 'What's in the tube'; innovative regulation; point of care manufacture
5. **A prioritised laboratory science portfolio for biological standardisation and control**  
Biological standardisation; smart control testing of biologicals
6. **Supporting emergency response to disease**  
Pandemic preparedness (current and next); emerging pathogens

A key overarching principle is that all research should be policy-relevant – having the potential to inform UK regulatory policy or practice.

Further dialogue is now required to clarify key issues and to further establish the foundation for the future of the UK's regulatory science landscape:

- **Defining the scope of UK regulatory science**, such as whether its focus should just be on licensing or also on other aspects of clinical research governance/oversight, and its relationship with the wider field of innovation.
- **Identifying key stakeholders**, their roles and how best to engage them.
- **Establishing how patients and the public can best be engaged** in further discussions.
- **Identifying mechanisms for taking the regulatory science agenda forward.**
- **Working with funders** to identify the most appropriate mechanisms for supporting regulatory science and developing regulatory science research capacity.

Roundtable participants expressed an enthusiasm to maintain dialogue and further explore what lessons can be learned from the COVID-19 experience, and to bring in additional stakeholders with the MHRA continuing to play a central convening role.

# Annex I: Definitions of regulatory science

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There are several current definitions for regulatory science in healthcare, as summarised below:

"Regulatory Science is the science of developing new tools, standards, and approaches to assess the safety, efficacy, quality, and performance of all FDA-regulated products."

— US Food and Drug Administration<sup>(2)</sup>

"Regulatory Science can be described as a range of scientific disciplines that are applied to the quality, safety and efficacy assessment of medicinal products that inform regulatory decision-making throughout the lifecycle of a medicine. It encompasses basic and applied medicinal science and social sciences and contributes to the development of regulatory standards and tools."

— European Medicines Agency (3)

"The acquisition and analysis of data sufficient to inform decision making pertinent to the approval of safe and effective therapeutics, devices and cosmetics and ensuring the safety and nutritional value of the food supply."

— Garret FitzGerald,  
University of Pennsylvania School of Medicine (4)

"The science of developing methods to quantitatively and / or qualitatively analyse and understand the causal relations and mechanisms of the substances and the phenomena around us, and measuring their positive and negative effects. Their efficacy and safety are appropriately predicted, evaluated and judged using the methods developed and the results obtained in the [regulatory science], contributing to public health."

— The Pharmaceutical Society of Japan<sup>(5)</sup>

"The application of the biological medical and sociological sciences to enhance the development and regulation of medicines and devices in order to meet the appropriate standards of quality, safety and efficacy"

— Stuart Faulkner  
Centre for the Advancement of Sustainable Medical Innovation (CASMI) (1)

"Regulatory science is the scientific and technical foundations upon which regulations are based in various industries – particularly those involving health or safety. Regulatory bodies employing such principles in the US include for example the FDA for food and medical products, the EPA for the environment, and OSHA for work safety. Regulatory science is contrasted with regulatory affairs and regulatory law, which refer to the administrative or legal aspects of regulation, in that the former is focused on the regulations' scientific underpinnings and concerns – rather than the regulations' promulgation, implementation, compliance, or enforcement."

— Wikipedia (6)

# Annex II: Agenda

Wednesday 3 March 2021, 14:00-16:30

|             |  |
|-------------|--|
| 13.45-14.00 | <b>Participants join meeting</b>   |
| 14.00-14.10 | <b>Welcome and introduction</b><br><i>Chair: Professor Deborah Ashby OBE FMedSci</i>   |
| 14.10-14.50 | <b>Regulatory science: perspectives from across the sector</b><br>A series of presentations from stakeholders across the UK regulatory science landscape, outlining what 'regulatory science' means for their disciplines, and current priorities and gaps.<br><br><i>Scheduled speakers:</i> <ul style="list-style-type: none"> <li>• Professor Sir Kent Woods FMedSci, Emeritus Professor of Therapeutics, University of Leicester</li> <li>• Sir Mene Pangalos FMedSci, Executive Vice President of Biopharmaceuticals Research and Development, AstraZeneca</li> <li>• Professor Cathie Sudlow OBE, Professor of Neurology and Clinical Epidemiology, Usher Institute and Director of the British Heart Foundation Data Science Centre</li> <li>• Professor Dame Sarah Gilbert DBE FMedSci, Saïd Professorship of Vaccinology, Jenner Institute &amp; Nuffield Department of Clinical Medicine</li> <li>• Professor Melanie Calvert, Professor of Outcomes Methodology, University of Birmingham</li> </ul><br><i>Chair: Professor Deborah Ashby OBE FMedSci</i> |
| 14.50-15.15 | <b>What is regulatory science and how should it inform regulation in the UK?</b><br>An opportunity for participants to reflect on the perspectives from across the sector and discuss how regulatory science should inform regulation in the UK. Issues to discuss include: <ul style="list-style-type: none"> <li>• How do we collectively define 'regulatory science'?</li> <li>• How should regulatory science inform regulation in the UK?</li> </ul><br><i>Chair: Professor Deborah Ashby OBE FMedSci</i>   |
| 15.15-15.20 | <b>Break</b>   |
| 15.20-15.50 | <b>What are the regulatory science priorities for the UK in the global landscape?</b><br>Discussion to explore the UK's priorities for regulatory science in a global context. Issues to discuss include: <ul style="list-style-type: none"> <li>• What have we learnt from the COVID-19 pandemic?</li> <li>• How do priorities for UK regulatory science align/differ to those of the FDA/EMA?</li> </ul><br><i>Chair: Dr June Raine CBE, Chief Executive, MHRA</i>   |

|             |  |
|-------------|--|
| 15.50-16.20 | <p><b>What are the roles of different stakeholders in the regulatory science landscape?</b></p> <p>Attendees are asked to consider the roles of different stakeholder groups in the regulatory science landscape and how they interact with regulators. Issues to discuss include:</p> <ul style="list-style-type: none"><li>• What are the roles of different stakeholders across the life sciences sectors?</li><li>• What needs to happen going forward to enhance the UK's regulatory science landscape?</li></ul> <p><i>Chair: Dr June Raine CBE, Chief Executive, MHRA</i></p> |
| 16.20-16.30 | <p><b>Summary of key points raised and next steps</b></p> <p><i>Chair: Dr June Raine CBE, Chief Executive, MHRA</i></p>  |
| 16.30       | <b>Close of meeting</b>  |

# Annex III: Participants

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## Co-chairs

**Professor Deborah Ashby OBE FMedSci** (co-Chair), Director of the School of Public Health, Imperial College London

**Dr June Raine CBE** (co-Chair), Chief Executive, MHRA

## Speakers

**Professor Melanie Calvert**, Professor of Outcomes Methodology, University of Birmingham

**Professor Dame Sarah Gilbert DBE FMedSci**, Saïd Professorship of Vaccinology, Jenner Institute & Nuffield Department of Clinical Medicine

**Sir Mene Pangalos FMedSci**, Executive Vice President of Biopharmaceuticals Research and Development, AstraZeneca

**Professor Cathie Sudlow OBE**, Professor of Neurology and Clinical Epidemiology, University of Edinburgh and Director of the British Heart Foundation Data Science Centre

**Professor Sir Kent Woods FMedSci**, Emeritus Professor of Therapeutics, University of Leicester

## Attendees

**Professor Dawn Craig**, Professor of Practice in Evidence Synthesis, Newcastle University

**Professor Alastair Denniston**, Director, INSIGHT, the Health Data Research Hub for Eye Health

**Professor Andrew Farmer**, Director, NIHR Health Technology Assessment Programme

**Professor Ben Forbes**, Head of Institute of Pharmaceutical Science, King's College London

**Dr David Jefferys**, Senior Vice President, Global Regulatory Healthcare Policy and Corporate Affairs, Eisai Europe

**Professor Sir Martin Landray FMedSci**, Professor of Medicine and Epidemiology, University of Oxford

**Dr Ruth McKernan CBE FMedSci**, Chair, BioIndustry Association

**Professor Andrew Morris CBE FRSE FMedSci**, Director, Health Data Research UK

**Professor Sir Munir Pirmohamed FMedSci**, David Weatherall Chair of Medicine, University of Liverpool and NHS Chair of Pharmacogenetics

**Professor Duncan Richards**, Climax Professor of Clinical Therapeutics, University of Oxford

**Dr Christian Schneider**, Chief Scientific Officer, MHRA

**Professor Sir John Tooke FMedSci**, Executive Chair, Academic Health Solutions

**Professor Matt Westmore**, Chief Executive, HRA

**Sophie Wintrich**, Chief Executive, MDS UK Patient Support Group

**Dr Louise Wood CBE**, Director of Science, Research and Evidence, Department of Health and Social Care, Deputy CEO, NIHR

## Staff and secretariat

**Hayley Carr**, Policy Intern, Academy of Medical Sciences

**Dr Claire Cope**, Head of Policy, Academy of Medical Sciences

**Ian Jones** (event science writer), Director, Jinja Publishing Ltd

**Louise Loughlin**, Head of Science Strategy, MHRA



**George Phillips**, Policy Officer, Academy of Medical Sciences

**Dr James Squires**, FORUM Policy Manager, Academy of Medical Sciences

**Angel Yiangou**, Policy Manager, Academy of Medical Sciences

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