

The background image is a complex digital graphic. It features a central globe composed of a grid of white dots. A hand is shown interacting with this globe, with a finger touching it. Surrounding the globe are several concentric, glowing rings that resemble a futuristic control panel or data interface. The background is dark, with a network of white lines and dots connecting various points, suggesting a global or digital network. There are also some circular icons with human figures inside, possibly representing users or data points. The overall aesthetic is high-tech and innovative.

Advancing Regulatory Science and Innovation in Healthcare

July 2020

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The views expressed in the report are those of the authors and should not be specifically attributed to specific organisations unless explicitly stated.

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Foreword

"Regulation matters. Not only does it ensure that new technologies are safe, but regulation impacts how quickly vital advances reach the market and ensure the sustainability of our innovative businesses and the vitality of our wider economy. For healthcare, this also determines how quickly new products and services can reach the patients and citizens whose health – and indeed lives – may rely upon them. Recognising this, the Government has established the Regulatory Horizons Council to identify the implications of technological innovation with high potential benefit for the UK economy and society, and advise them on critical regulatory reform needed to support its rapid and safe introduction. I am delighted to be appointed as the inaugural Chair of the Regulatory Horizons Council, which will play an important role in ensuring an outcome focused, and flexible regulatory system in the UK. Our aim will be to enable innovation to thrive while protecting citizens and the environment. However, this is not something we can – or wish to – deliver in isolation. Our work critically relies on our interactions with industry, with sector experts, with charity and policy bodies, with academia, and critically with citizens. Regulatory science can harness the capabilities of brilliant minds across multiple vibrant sectors to prioritise, investigate and accelerate new ways to support the technologies which will revolutionise the UK's capabilities. I welcome this report, which I believe will light the runway for regulatory science in healthcare in the coming years."

Cathryn Ross,
Inaugural Chair of the Regulatory Horizons Council

"Our members are responsible for some of the most ground-breaking existing and emerging medicines in the world, bringing huge benefits to millions of patients as well as substantial economic returns to the UK. The pre-clinical research, clinical trials and pharmacovigilance undertaken to support these products not only illuminates important new insights into how these products are performing now, but also how they - and other, related breakthroughs - might deliver benefit in a broader range of conditions. New data and technology mean we can do research in new ways, looking into treatments that previously seemed impossible. We have been clear in our recommendations that the UK continues to operate in a collaborative way with Europe and the wider world to ensure that the UK is a globally relevant and competitive destination for research and development. We also see a key role for innovative regulation to enable medicines development to harness the new technologies and data appropriately. This opens up new areas for the UK's global leadership through regulatory science - something that ABPI has championed for many years. We must work together more collaboratively than ever before to understand previous learning, current challenges and future opportunities. This report represents an important new step on that journey, and we are ready to pick up the baton to begin moving these recommendations into practice."

Sheuli Porkess,
Executive Director Research Medical & Innovation,
Association of the British Pharmaceutical Industry



"Patients are often seen as the grateful beneficiaries of scientific discoveries, new technologies and improved medications - which of course we often are. But that is not all we are or should be. Patients, as well as our wider, diverse communities, can provide unique insights into which specific problems and priorities these discoveries, technologies and medications should be targeted; what kind of evidence validates their effectiveness; and what "value" truly means in terms of our health and treatment outcomes. Trust and transparency are more critical than ever. We want better treatments as quickly as possible, but not at the cost of our safety, privacy or awareness of risk. Laws, regulations and standards play a vital role in enshrining our requirements and innovators' responsibilities. Where these are adapting - which we recognise they must, to respond to the scale and pace of opportunity in healthcare - it is essential that patients have a voice, that they are not only expected to be grateful beneficiaries of what science and technology have to offer, but that they are accepted as true partners in these endeavours who can provide the lived experience and deeply meaningful insights into all aspects of healthcare. This report highlights clear and important ways in which multiple stakeholders can work together to effect positive change, and I am pleased and proud to see proper recognition of the important role patients and citizens must play in moving this agenda forward."

Kathy Oliver,
Patient representative and Chair of the
International Brain Tumour Alliance

"Birmingham Health Partners is a strategic alliance between the University of Birmingham, University Hospitals Birmingham and Birmingham Women & Children's Hospital NHS Foundation Trusts with a joint vision to deliver "research that matters". We have established a dynamic environment to encourage a multidisciplinary approach to tackle some of the most pressing healthcare challenges faced by our local population. Birmingham Health Partners' not only generate new discoveries and ideas but also work to make sure innovation is rapidly tested, adopted and implemented into clinical care and that the insights gained feed back into the discovery process. To do this requires a robust but conducive regulatory framework. We will shape such a framework using our collective expertise in the emerging field of regulatory science working across policy, science, clinical practice, industry and most crucially with our patients. This will allow us to make sure that innovation is rapidly and safely translated into benefits for society."

Professor David Adams,
Director of Birmingham Health Partners





Executive Summary

Regulatory science can be defined as “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.” (1)

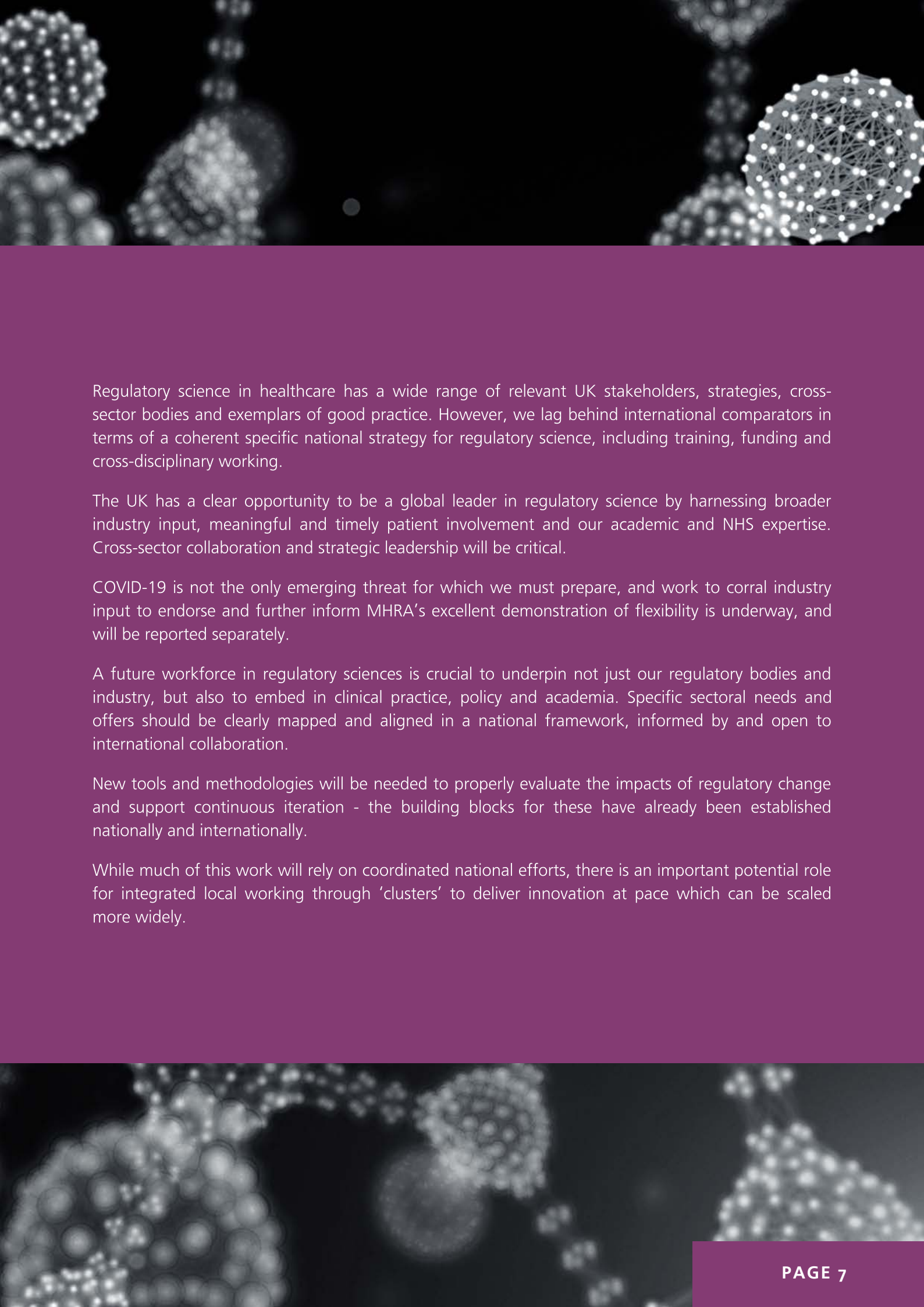
Innovation in regulatory science complements the UK’s Industrial Strategy, enabling accelerated routes to market; increased benefits to public health; greater levels of patient safety; influencing international practice; and promoting investment in the UK.

The UK’s capability to adapt its regulatory frameworks in healthcare is under pressure - the pace of emerging technologies and the current COVID-19 pandemic makes this a global issue, but leaving the European Union adds a significant, specific national need for change, carrying opportunity and risk that must both be carefully managed. Regulatory science will be crucial to this endeavour.

Life sciences is critical to the UK’s economy, but faces unprecedented challenges in both near-term business viability and long-term sector sustainability due to regulatory uncertainty. Significant effort and funds have been spent preparing for new EU frameworks, and divergence brings challenges around complexity, competence and capacity, as well as the UK’s current status as a ‘tier 1’ site for new medicines. Our representative industry bodies give us a strong framework of insight and ongoing engagement which can be harnessed to mitigate these risks.

We must be highly selective in where we choose to diverge rather than remaining aligned in terms of regulation, based on clear clinical and academic strengths to inform regulatory innovation, and identified industry opportunity either to leapfrog global competitors or to create a national test bed enabling shared global progress.





Regulatory science in healthcare has a wide range of relevant UK stakeholders, strategies, cross-sector bodies and exemplars of good practice. However, we lag behind international comparators in terms of a coherent specific national strategy for regulatory science, including training, funding and cross-disciplinary working.

The UK has a clear opportunity to be a global leader in regulatory science by harnessing broader industry input, meaningful and timely patient involvement and our academic and NHS expertise. Cross-sector collaboration and strategic leadership will be critical.

COVID-19 is not the only emerging threat for which we must prepare, and work to corral industry input to endorse and further inform MHRA's excellent demonstration of flexibility is underway, and will be reported separately.

A future workforce in regulatory sciences is crucial to underpin not just our regulatory bodies and industry, but also to embed in clinical practice, policy and academia. Specific sectoral needs and offers should be clearly mapped and aligned in a national framework, informed by and open to international collaboration.

New tools and methodologies will be needed to properly evaluate the impacts of regulatory change and support continuous iteration - the building blocks for these have already been established nationally and internationally.

While much of this work will rely on coordinated national efforts, there is an important potential role for integrated local working through 'clusters' to deliver innovation at pace which can be scaled more widely.

Recommendations

Strategic Leadership and Coordinated Support



- A specific national healthcare/life sciences strategic advisory committee should be established to provide dynamic oversight to complement the UK's new Regulatory Horizon Council, enabling multidisciplinary and cross-sector input to advance UK healthcare regulation and promote innovation informed by regulatory science. Dynamic oversight should be provided in accordance with principles specified by the Wellcome Trust blueprint (inclusive, anticipatory, innovative and proportionate).
- The MHRA should work with stakeholders - including the devolved administrations in Scotland, Wales and Northern Ireland - to develop a UK strategy for regulatory science to create a roadmap for national efforts, to maximise the speed of UK medicines regulation and health technology evaluation.
- Major UK funding bodies - including UK Research and Innovation, the National Institute for Health Research and members of the Association of Medical Research Charities - should identify potential funding mechanisms for regulatory science which could deliver major benefits aligned to their respective remits and communities.

Enabling Innovation



- Given challenging timelines around the Brexit transition period, multi-stakeholder work is needed to understand and prioritise specific technological or methodological areas in which the UK's capability for regulatory innovation could enable a global leadership position, delivering major economic and healthcare benefits. The UK should maintain high levels of regulatory compatibility and fully understand the threats and opportunities posed by any divergence.
- Emerging technologies should be identified through horizon scanning and where uncertainties arise about how to regulate certain emerging technologies, we need joint working processes enabling regulatory bodies and industry to flag where evidence and innovation is required in regulatory science to justify research and development investments.
- Innovation in regulatory science is needed to underpin an R&D environment that mitigates "high-risk" areas of investment with significant promise – for example antimicrobial resistance or new medications for pregnancy-related conditions.
- Specific consideration should be given to supporting regulatory science aligned to the Accelerated Access Collaborative, establishing how the uptake of innovation within the NHS can be better enabled, and how local good practice can help drive wider national behaviours.

Implementation and Evaluation

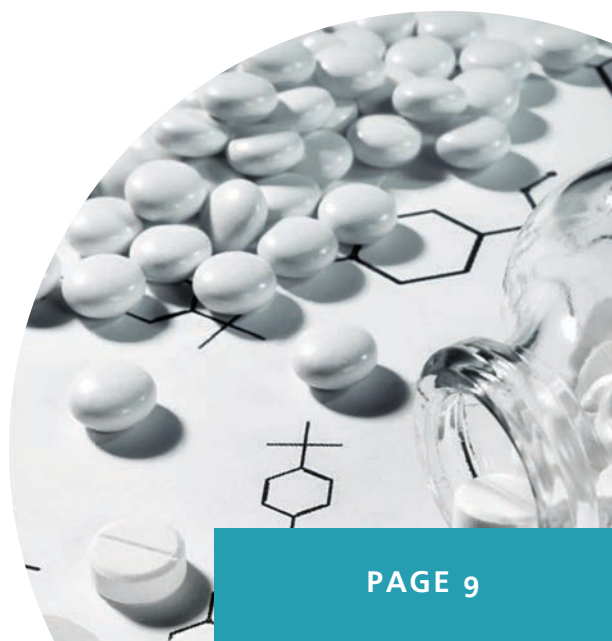


- We need to establish coordinated national and international approaches for promotion of new guidance, including development of implementation tools and resources and training and establishing how regulators, industry bodies, funders, healthcare providers and other agencies can act in concert to accelerate implementation.
- An evaluation framework with agreed metrics should be developed to assess the impact of regulatory innovation and implementation.
- International stakeholders must work collaboratively to understand the benefits and challenges of changes in regulation, such as those arising from COVID-19, and how this could be applied to other settings.

Workforce Development



- A scoping exercise should be undertaken to more fully understand specific training needs across various stakeholder groups to support regulatory science innovation and improve uptake/use of innovative technologies and medicines
- The UK should seek to establish clear career pathways in regulatory science, via internships, fellowships or PhDs involving academia, industry, NHS, patient partners and regulatory bodies as key collaborators, mentors and beneficiaries



Glossary

AAC

Accelerated Access Collaborative: brings together industry, government, regulators, patients and the NHS to remove barriers and accelerate the introduction of ground-breaking new treatments and diagnostics which can transform care

ABHI

Association of British HealthTech Industries. This is the trade association represents medical device technology manufacturers and distributors in the UK

ABPI

Association of the British Pharmaceutical Industry. This is the trade association represents the manufacturers of prescription only medicines in the UK

AHSN

Academic Health Science Networks are membership organisations within the NHS in England. They were created in May 2013 with the aim of bringing together health services, and academic and industry members

AI

Artificial Intelligence

AMRC

Association of Medical Research Charities

BEIS

Department for Business, Energy and Industrial Strategy

BHP

Birmingham Health Partners: a strategic alliance between University Hospitals Birmingham NHS Foundation Trust, University of Birmingham and Birmingham Children's Hospital NHS Foundation Trust bringing together clinical, scientific and academic excellence across an integrated medical and life sciences campus

BIA

UK BioIndustry Association. A trade association for innovative life science companies

BIVDA

British In-vitro Diagnostics Association

CASMI

Centre for the Advancement of Sustainable Medical Innovation

CE Mark

Indicates that the manufacturer of a medical device complies with the relevant European Union Directive on safety, quality and performance

CERSI

Centres of Excellence in Regulatory Science and Innovation: collaborations between FDA and academic institutions to advance regulatory science through innovative research, training, and scientific exchanges

CONSORT

Consolidated Standards of Reporting Trials

CORS

Copenhagen Centre for Regulatory Science

CPRD

Clinical Practice Research Datalink is a real-world research service supporting retrospective and prospective public health and clinical studies. CPRD is jointly sponsored by the Medicines and Healthcare products Regulatory Agency and the National Institute for Health Research, as part of the Department of Health and Social Care

CQC

Care Quality Commission is an executive non-departmental public body of the Department of Health and Social Care of the United Kingdom

CRSI

Centre for Regulatory Science and Innovation, led by Birmingham Health Partners

CSA STARS

Coordination and Support Action on Strengthening Training of Academia in Regulatory Science: an EU funded initiative

EAMS

Early Access to Medicines Scheme

EFPIA

European Federation of Pharmaceutical Industries Associations. European equivalent of the ABPI

EMA

European Medicines Agency

ENPV

Expected net present value is a capital budgeting technique which adjusts for uncertainty by calculating net present values under different scenarios and probability-weighting them to get the most likely NPV

EU

European Union

FDA

Food and Drug Administration. The MHRA/Food Standards Agency equivalent in the United States

HRA

Health Research Authority

ICH

International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use. Brings together the regulatory authorities and pharmaceutical industry to discuss scientific and technical aspects of pharmaceuticals and develop ICH guidelines

IMI

Innovative Medicines Initiative is a public-private partnership aiming to speed up the development of better and safer medicines for patients

ISO

International Organization for Standardization

Glossary

IVD

In-Vitro Diagnostics

IVDR

In-Vitro Diagnostics Regulation

LSIS

Life Sciences Industrial Strategy

MDR

Medical Device Regulation

MEB

Medicines Evaluation Board. Assesses and guards the efficacy, safety, and quality of both human and veterinary medicinal products. The MEB is the primary source of information on new medicinal products, new applications, and current risk information in the Netherlands

MHRA

Medicines and Healthcare products Regulatory Agency

MRC

Medical Research Council

NHS

National Health Service

NHSX

NHSX brings teams from the Department of Health and Social Care, NHS England and NHS Improvement together into one unit to drive digital transformation and lead policy, implementation and change

NIBSC

The National Institute for Biological Standards and Control is a global leader in the field of biological standardisation. It is a centre of the UK Medicines and Healthcare Products Regulatory Agency

NICE

National Institute for Health and Care Excellence, a non-departmental public body responsible for providing national guidance and advice to improve health and social care

NIHR

National Institute for Health Research

NPV

Net Present Value: a series of cash flows occurring at different times

OECD

Organisation for Economic Co-operation and Development is an intergovernmental economic organisation with 36 member countries, founded in 1961 to stimulate economic progress and world trade

ORISE

Oak Ridge Institute for Science and Education: The ORISE Research Participation Program at the FDA is an educational and training program designed to provide college students, recent graduates, and university faculty opportunities to connect with the unique resources of the FDA

PARADIGM

Patients Active in Research and Dialogues for an Improved Generation of Medicines. A public-private partnership co-led by the European Patients' Forum (EPF) and the European Federation of Pharmaceutical Industries and Associations (EFPIA). PARADIGM's mission is "to provide a unique framework that enables structured, effective, meaningful, ethical, innovative, and sustainable patient engagement and demonstrate the 'return on the engagement' for all players"

PDUFA VI

Prescription Drug User Fee Act was first created by US Congress in 1992 and authorizes FDA to collect fees from companies that produce certain human drug and biological products. PDUFA VI strengthens efforts to incorporate patient perspectives into the drug development and review process

PROs

Patient Reported Outcomes

PROTECT

Pharmacoepidemiological Research on Outcomes of Therapeutics by a European ConsortTium: this partnership comprises 34 public and private partners supported by IMI joint undertaking with funding from the European Commission and in-kind contribution from EFPIA

PROTEUS

Patient-Reported Outcomes Tools: Engaging Users & Stakeholders. The PROTEUS Consortium promotes tools and resources to optimize the use of patient-reported outcomes (PROs) in clinical trials to ensure that patients, clinicians, and other decision-makers can make the best decisions about treatment options.

R&D

Research and Development

RSNN

Regulatory Science Network Netherlands is a network of experts from industry, academia, government bodies, and the broader regulatory science field

RWE

Real World Evidence

SISAQOL

Setting International Standards in Analyzing Patient-Reported Outcomes and Quality of Life Endpoints Data

SME

Small and medium-sized enterprise

SPIRIT

Standard Protocol Items: Recommendations for Interventional Trials

STP

Sustainability and transformation partnership. These are areas covering all of England, where local NHS organisations and councils drew up shared proposals to improve health and care in the areas they serve

UKRI

United Kingdom Research and Innovation

WHO

World Health Organisation

Section 1:

The current
context for
regulatory
science



1.1 What Do We Mean By 'Regulatory Science' in Healthcare?

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⁽²⁾

"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⁽⁵⁾

"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)

In order for the area to move forward coherently within the UK, it would be helpful to agree on a shared definition between stakeholders. We suggest that the CASMI definition is sufficiently broad and inclusive as a starting point for further iteration and agreement, for a range of reasons which are explored in more detail throughout this report.

1.2 What Do We Mean By 'Regulatory Innovation'?

“Reforms should help ensure that regulations in all spheres of activity are fully responsive to changes in the economic, social and technical conditions surrounding them. The regulatory process must take into account the effects of regulation on innovation as well as the implications of technical change for the rationale and design of regulation. The regulation/innovation interface is mutual and dynamic; an understanding of this interface is crucial to regulatory reform efforts.”

- Regulatory Reform and Innovation, OECD

Nesta, an innovation foundation, undertook several years of consultation to produce a framework they termed ‘anticipatory regulation’(7), noting that “underlying challenges require new regulatory practices and stances, not just (or always) new regulatory initiatives or bodies.”

In response to Nesta’s work, the scope for proposals under the Government’s Regulators’ Pioneer Fund (8) recommended three particular examples of innovative approaches:

- Advisory approaches, such as the Medicines and Healthcare products Regulatory Agency’s Innovation Office
- Adaptive approaches, such as the Financial Conduct Authority’s Regulatory Sandbox
- Anticipatory approaches, such as the Human Fertilisation and Embryology Authority’s Horizon Scanning Panel

INCLUSIVE AND COLLABORATIVE;

In engaging the public and diverse stakeholders where new technologies and how they are deployed raise ethical issues, and in leveraging the capabilities of businesses, cities and civil society to secure policy goals.

FUTURE-FACING;

In developing resilient, adaptive strategies that can cope with the inherent uncertainty of fast-changing markets.

PROACTIVE;

In engaging with innovators and innovation early in the cycle to provide predictability and enable timely, proportionate responses to issues that may scale rapidly.

ITERATIVE;

In taking a test-and-evolve rather than solve-and-leave approach to novel problems, for which there may be no established playbook.

OUTCOMES-BASED;

In focusing on validating companies' efforts to achieve well-defined goals, rather than setting rules, and particularly on incentivising platforms to support regulatory objectives.

EXPERIMENTAL;

In facilitating diverse responses to regulation of early-stage opportunities and risks, and where national or global policies and standards are still to be established.

'Renewing regulation: 'Anticipatory regulation' in an age of disruption', Nesta

1.3 Why is Regulatory Science in Focus Now?

Regulation is currently a major topic in the news for several reasons. Firstly, COVID-19 has highlighted the complexities of bringing new diagnostics and vaccines to market and the flexibility and the rapidity of response by regulatory agencies to this emerging threat (9). The Government's new Vaccine Taskforce has review of regulations as one of its five key strands of activity (10).

Secondly, the UK intends to diverge from EU regulations at the end of the Brexit transition period. In the House of Commons, the Medicines and Medical Devices Bill will give the UK Government the power to amend or supplement the law relating to human medicines and medical devices. The Government recognised that this period would bring both opportunities and challenges. It therefore published its "Regulation for the Fourth Industrial Revolution" White Paper in 2019 and has recently initiated the formation of a national Regulatory Horizon Council.

Thirdly, a range of medical technologies are developing more rapidly than our regulatory frameworks. Artificial Intelligence (AI) is one prominent example (8) that has gained media attention. Forbes magazine described AI as "the hot topic of the moment in technology, and the driving force behind most of the big technological breakthroughs of recent years" (11). However, regulation of this technology has come to the fore because "its use may introduce several new types of risk to patients and healthcare providers, such as algorithmic bias, do not resuscitate implications, and other machine morality issues" (12). Understanding and allocating proportionate risk – and appropriate regulation – will critically rely on emerging real-world experience.

All of these points give a sense of urgency around establishing a coherent, coordinated approach to regulatory science within the UK, and are explored in more detail in this report.

1.4 Life After Brexit

The UK left the European Union at the end of January 2020 and is currently in a transition period lasting until 31 December 2020. During the transition, all EU laws and rules continue to apply to the UK. Before the end of the transition period (which we refer to as “post-Transition”, rather than “post-Brexit”), the UK Government plans to make new agreements for the time after 31 December 2020. These arrangements include the Government's Medicines and Medical Devices Bill, which had its first reading in February 2020 and is proceeding through Parliament. The Bill will enable the UK to change regulations for medicines, diagnostics and medical devices.

"This Bill empowers us to be able to move faster. Essentially, it empowers the UK to build a life sciences regulatory framework that is the best in the world—of course, working with EU partners, but also with partners from right around the world—and all with the intention of getting the most innovative products, as quickly as possible and as cost-effectively as possible, into the NHS. That is the goal of the entire Bill. It is a benefit of Brexit, but it is also worth doing in its own right" (13).

— Matt Hancock, Secretary of State for Health

The Bill consolidates and streamlines the existing enforcement powers of the Medicines and Healthcare products Regulatory Agency (MHRA). It aims to give the MHRA and industry greater transparency on the enforcement framework, and clarifies existing rights to appeal against enforcement actions and introduces a new regime for civil sanctions. Additionally, "the Bill will enable the regulatory framework for clinical trials and approval of medicines to be updated in line with the latest advances in science and technology" (14).

It is important to note that concerns have been expressed around some of the Bill's approaches. For example, there is no definition in the Bill as to what constitutes “the attractiveness of the relevant part of the United Kingdom”, with fears that patient safety is not being adequately prioritised, and that the delegated powers set out to enable short-term flexibility and responsiveness “risks inadequate scrutiny and oversight of major regulatory objectives and changes” unless these are time-limited (15).




1.5 Life After COVID-19

Globally, COVID-19 has severely impacted life sciences research and development, while also demonstrating the impact of a more collaborative effort and regulatory flexibility. The sector is looking at resilient recovery whilst recognising the continued risk of disruption. During this recovery phase, pharmaceutical and medical technology companies have asked for continued regulatory flexibility across international borders. They have used flexibility as they accelerate product development in medicines, devices and vaccines, and move to re-initiate trials, mitigate missing data and implement new models of working (including telehealth and remote monitoring). The unprecedented events of the pandemic have offered a paradigm shift in healthcare regulation, ripe for further exploration and learning (16).

Together, industry trade associations in the UK have set out their 'Life Sciences Recovery Roadmap', with support from the Association of British Pharmaceutical Industries (ABPI), the Association of British HealthTech Industries (ABHI), BioIndustry Association (BIA), British Generic Manufacturers Association (BGMA) and the British In Vitro Diagnostic Association (BIVDA). One of their six critical areas for action is "Taking an innovative approach to regulation". They suggest that the Medicines and Medical Devices Bill "should be reviewed to reflect innovative regulatory approaches" and that recent learning in accelerated access "could have a more permanent place in speeding up the approval of licences and variations for existing medicines, and should link into work underway to create more agile and sustained regulatory and Health Technology Assessment (HTA) systems and support patients getting fast access to new treatments". They also comment on the potential of Mutual Recognition Agreements "to extend the UK's global reputation and influence through international networks and partnerships" as well as the UK's potential "to lead new work needed on regulatory frameworks and pathways for emerging innovation, such as cell and gene therapies as well as generic and biosimilar medicines". The Medicines and Medical Devices Bill could allow some of the vital flexibilities that have been deployed to become permanent – equally, where this is not appropriate, there is a clear argument for some of these temporary regulatory flexibilities to be evaluated and prepared on file as a critical part of any future 'pandemic response plan'.

Clearly there is a huge amount of new practice, new ideas and new willingness to collaborate and innovate in regulation stimulated by COVID-19. However, given the rapid pace at which the national and global situation is continuing to evolve, this report will not dwell on this topic to any major extent, but should be seen as a complement and context to emerging findings and proposals. Regulatory science must play a key role globally both for the COVID-19 response and future threats, to support development of new tools, standards and approaches to evaluate the efficacy, safety, quality and performance of medical products and other healthcare innovations, in order to assess benefit-risk and facilitate sound and transparent regulatory decision-making.





Section 2:

Regulatory science stakeholders

2.1 The Role of Government

"This White Paper sets out our plan to maintain our world-leading regulatory system in this period of rapid technological change. We will support and stimulate new products, services and business models, with greater space for experimentation. We will uphold safeguards for people and the environment and engage the public in how innovation is regulated. And we will maintain the stable, proportionate regulatory approach the UK is rightly known for."

- Foreword to 'Regulation for the Fourth Industrial Revolution' White Paper, 2019 (17)

The UK has previously relied on two advisory bodies to Government concerning improvements in regulations:

- The Better Regulation Executive
A unit within BEIS which "works with government departments to monitor the measurement of regulatory burdens and coordinate their reduction, and to ensure that the regulation which remains is smarter, better targeted and less costly to business" (18)
- The Regulatory Policy Committee
A group of independent experts who "assess the quality of evidence and analysis used to inform regulatory proposals affecting the economy, businesses, civil society, charities and other non-government organisations" (19)

However, as part of its White Paper on 'Regulation for the Fourth Industrial Revolution' in 2019 (17), which itself built on the ambitions set out in the UK's Industrial Strategy, the government committed to establishing a new 'Regulatory Horizons Council'. The Council's stated objectives are to:

- Scan the horizon for technological innovation and trends, building on existing work and data across government;
- Work with innovators, civil society, regulators and others to identify high-potential products, services and business models and the broad implications for people, business and the environment; and
- Advise government on broad priorities for regulatory reform to facilitate the rapid and safe introduction of emerging products, services and business models.

Interestingly, the paper notes that "The Council's recommendations will be considered by the Ministerial Working Group on Future Regulation, chaired by the Business Secretary, and published by the government. The Ministerial Working Group will oversee a joined-up government response, ensuring that innovations are not hindered by the complex division of responsibilities across government departments and regulators." It also highlights that government has a range of options in how it responds, including "the introduction, adaptation or repeal of regulation, or the adoption of alternatives to regulation (such as voluntary standards), depending on the nature of the innovation".

The Ministerial Working Group itself has a wide-ranging set of responsibilities, including:

- Strengthening the Government's horizon scanning for emerging regulatory challenges arising from innovative products, services and business models
- Commissioning departments to develop regulatory reform proposals to enable innovative products, services and business models
- Promoting action by regulators to develop innovation-enabling regulatory approaches
- Seeking to resolve complex regulatory issues that cross sectoral, departmental or regulator boundaries
- Driving the exchange of best practice in innovation-enabling approaches across Whitehall

Notably, the Government's major investment in regulatory innovation - the £10million Regulators' Pioneer Fund (20) - ran its open competition in 2018, nearly a year before the White Paper was published. The successful projects from this competition informed and provided content for the document, rather than the vision laid out by the White Paper informing how significant investment in novel regulatory approaches should be targeted. The White Paper pledged to "examine the case for extending the Regulators' Pioneer Fund in future to help regulators to keep pace with technological innovation and enable the emergence of new products, services and business models.", and indeed £10million further funding was announced in the March 2020 Budget.

With the Chair of the new Council appointed (Cathryn Ross – BT's Director for Regulatory Affairs) and recruitment for members currently underway, it will be fascinating to see what the make-up of this group is and whether it provides a robust mechanism to connect the diverse stakeholders outlined in this report - which represent only a key subset of just the health arena - through to the government's regulatory machinery. The new Council support team sits within the Better Regulation Executive, so it will be a critical enabler to ensure continued cross-talk between this new activity and the two existing groups (also including the Regulatory Policy Committee), and how their activities complement the Council. Most importantly in the context of this report, it would be hugely beneficial to drive further dialogue to understand what role regulatory science can and should play in informing recommendations from each of these bodies, and how this can be strengthened moving forward.

The six key challenges identified by the Council for Science and Technology on how to enhance the regulatory oversight of technological innovation in the UK included:

- We need to be on the front foot in reforming regulation in response to technological innovation
- We need to ensure that our regulatory system is sufficiently flexible and outcomes-focused to enable innovation to thrive
- We need to enable greater experimentation, testing and trialling of innovations under regulatory supervision
- We need to support innovators to navigate the regulatory landscape and comply with regulation
- We need to build dialogue with society and industry on how technological innovation should be regulated
- We need to work with partners across the globe to reduce regulatory barriers to trade in innovative products and services

In 2019, Wellcome published its “blueprint” for the UK’s oversight of emerging science and technologies, focused extensively on actions for government (21), commenting:

“By taking an ambitious approach, and by forging stronger links with other countries, the UK can become a global leader in the oversight of emerging technologies. This will create substantial rewards here – more investment into the UK, a stronger environment for science, and faster access to innovations that transform people’s lives – but also around the world.

The UK’s approach to oversight needs to shift from being inconsistent and sometimes sluggish, to become dynamic. Now is a unique moment for reform as the UK reflects on its regulatory choices as it leaves the EU. The UK Government should seize this opportunity by setting out its vision and a package of reforms to make the UK the world-leader in the oversight of emerging science and technologies.”

The online portal for the report (21) contains a range of useful additional resources, including the cross-sector consultation findings in detail; an evidence review; and a worldwide comparative study of past and recent cases. However, despite a highly positive reception from both industry bodies and regulators, not much has been done to translate the report’s findings and associated recommendations into action.

Dynamic oversight can be delivered by reforms underpinned by the following principles:

Inclusive. Public groups need to be involved from an early stage to improve the quality of oversight while making it more relevant and trustworthy. The Government should support regulators to involve public groups from an early stage and to maintain engagement as innovation and its oversight is developed.

Anticipatory. Identifying risks and opportunities early makes it easier to develop a suitable approach to oversight. Emerging technology often develops quickly and oversight must develop with it. UK regulators must be equipped by government to anticipate and monitor emerging science and technologies to develop and iterate an appropriate, proportionate approach.

Innovative. Testing experimental oversight approaches provides government and regulators with evidence of real-world impacts to make oversight better. Achieving this needs good collaboration between regulators, industry, academia and public groups. The UK is beginning to support innovative approaches, but the Government needs to create new incentives for the testing of new oversight approaches.

Proportionate. Oversight should foster the potential benefits of emerging science and technologies at the same time as protecting against harms, by being proportionate to predicted risk. The UK should keep up its strong track-record in delivering proportionate oversight.

These changes will only be delivered effectively if there is clear leadership and accountability for oversight. This requires the Government to be flexible and decisive in responding to regulatory gaps.

- Key findings of Wellcome’s blueprint for oversight of emerging science and technologies

2.2 The Role of Regulatory Authorities

"Regulators need to have optimal tools to keep pace with scientific and technological advances and ensure the sound assessment of ground-breaking, more complex therapies."

- 'Regulatory Science to 2025', European Medicines Agency (22)

Many countries have their own regulatory authority – currently around 84 worldwide, as well as more global agencies that provide broader guidelines, such as the World Health Organisation (WHO), International Conference on Harmonisation (ICH) and International Organisation for Standardisation (ISO). Interestingly, it has been noted that. "The existence of independent regulatory agencies is justified by the complexity of certain regulatory and supervisory tasks, and the drawbacks of political interference"(23). Little mention is made of the importance of political engagement and support to empower these bodies, or of the complex ecosystem of stakeholders with whom they constantly interact both to inform and implement the regulations and standards which they enforce.

Here we focus on three key regulatory agencies which will continue to have a major bearing on the UK landscape for life sciences and regulatory science relevant to healthcare, particularly as they represent major commercial markets for UK life sciences companies.

UK Medicines and Healthcare products Regulatory Agency (MHRA)

In the UK, the MHRA is an executive agency of the Department of Health and Social Care, "with a mission to protect and improve health through the effective regulation of medicines, medical devices, and blood products underpinned by science and research."

Recognised globally as an authority in its field, the agency plays a leading role in protecting and improving public health and supports innovation through scientific research and development. The agency has three arms:

- the Medicines and Healthcare products Regulatory Agency (MHRA), the UK's regulator of medicines, medical devices and blood components for transfusion, responsible for ensuring their safety, quality and effectiveness (24)
- the Clinical Practice Research Datalink (CPRD) (25), a data research service that aims to improve public health by using anonymised NHS clinical data
- the National Institute for Biological Standards and Control (NIBSC) (26), a global leader in the standardisation and control of biological medicines

Together, these three centres bring together expertise and evidence so that clinical practice is informed by and contributes to regulatory evidence; global standards are underpinned by and enhance regulation; and real world data underpins regulation.

The MHRA has shown leadership in helping innovators navigate the regulatory landscape through its Innovation Office. This office gives free and confidential expert regulatory information, advice and guidance to organisations of all types (27). The Innovation Office team has been working to promote its assistance to small and medium-sized enterprise (SMEs) (28) and handles around 10-20 enquiries per month. This report's authors received feedback from companies that the MHRA Innovation Office was responsive and helpful, but some SMEs were needlessly apprehensive about approaching the Innovation Office.

The MHRA set out its own actions in response to the UK's Life Sciences Industrial Strategy, including supporting advanced therapies manufacturing by developing a framework for point-of-care manufacture; leading the way on precision medicine by developing a clear UK regulatory pathway for genomic medicines and tests; and promoting patient access and safety.

The MHRA's award under the national Regulators' Pioneer Fund to create synthetic datasets which will eventually "act as a regulatory sandbox to help with product validation" was also highlighted (29). The recent summary of progress against the LSIS highlighted collaborative work between MHRA and the Health Research Authority "to deliver approvals in parallel rather than in sequence, giving researchers significantly reduced overall start-up timelines. The average approval is now less than 53 days" (19).

Importantly, the MHRA has long invested in platforms which can leverage UK assets to accelerate industry and academic innovation as well as supporting the evidence base for regulatory activities. For example, CPRD is invaluable for informing a range of Research and Development (R&D) activities (20), operating as a not-for-profit research service providing anonymised primary care records for public health research for over thirty years. These data enable observational studies, clinical trial feasibility and protocol optimisation, and post-market surveillance.

By the end of 2023, MHRA's Corporate Plan sets out a vision to:

- Continue to play a major role in protecting public health and promoting patient safety by ensuring the safety, efficacy and quality of medical goods on the market;
- Have managed the outcomes of negotiations on the UK's exit from the EU to enable the Agency to continue to deliver its statutory functions;
- Continue to support and enhance innovation, horizon scanning for scientific and technological advance, and proactively offer accelerated routes to market to benefit public health and be a magnet for life sciences;
- Continue to be a full-service regulator, providing high quality robust regulation of medicines and medical devices;
- Have built an enhanced impact across the health and care system through collaborative working, linking up actively and influencing clinical practice through provision of data/evidence and expertise and embedding vigilance in health care systems;
- Have maintained its position as a global leader in standardisation and its role in the control of biological medicines, and will have executed a comprehensive underpinning research programme; and
- Strengthened our global positioning and reach, influencing the safe production and supply of medicines and medical devices, enhancing international partnerships, influencing emerging regulations and strengthening our commercial offering

In delivering this Corporate Plan, the MHRA recognises it will need to harness wider stakeholder engagement in developing the UK's regulatory science landscape to provide input and support for these important objectives. MHRA have reaffirmed their commitment to regulatory science in their Business Plan 2020-21 (30), which flags 'Innovation and Regulatory Science' as one of five strategic goals, within which they have three strategic priorities: i) To create innovative regulatory process; ii) To develop an integrated science offer to support innovation; and iii) To improve regulatory science. They also commit to "Establish a network and financially sustainable model to deliver regulatory science across the healthcare system to evolve regulatory decision-making" within the 2020-21 period. While they have not yet laid out a specific strategy for regulatory science in the UK, the agency is developing a plan both internally and with wider collaborating bodies.

European Medicines Agency (EMA)

The EMA is responsible for the scientific evaluation, supervision and safety monitoring of medicines in the EU (31). It operates as a decentralised scientific agency (as opposed to a regulatory authority) of the European Union. It coordinates the evaluation and monitoring of centrally authorised products and national referrals, develops technical guidance and provides scientific advice to sponsors (31).

A strong partnership between the UK and the EMA is thought to be crucial to ensure the NHS can continue to secure the best possible outcomes for patients post-Transition. Leading researchers, funders such as Cancer Research UK, and respected membership bodies such as the Academy of Medical Royal Colleges have called for continued UK participation – or at the very least close alignment – in the regulatory system created by the EU Clinical Trials Regulation (CTR), including seeking full and direct access to the EU portal and database for UK trial sponsors and to recognise EMA marketing authorisations as valid in the UK. Retaining strong partnership working is proposed to facilitate recruitment across multiple countries and allow patients to access newly-approved medicines more quickly than via centralised licensing (26), and to ensure a continued stake in international public health networks in areas such as pharmacoepidemiology (32).

On 31 March 2020, the EMA launched its future vision and strategy for regulatory science in Europe (22).

EMA regulatory science strategy to 2025 - core recommendations:

- Foster innovation in clinical trials
- Reinforce patient relevance in evidence generation
- Promote use of high-quality real-world data in decision making and develop network competence and specialist collaborations to engage with big data
- Develop the regulatory framework for emerging clinical data generation
- Contribute to health technology assessment's preparedness and downstream decision-making for innovative medicines and bridge from evaluation to access through collaboration with payers

US Food and Drug Administration (FDA)

The FDA is responsible for “protecting the public health by assuring the safety, efficacy, and security of human and veterinary drugs, biological products, medical devices, our nation's food supply, cosmetics, and products that emit radiation. The FDA also provides accurate, science-based health information to the public”(33).

Importantly, the FDA puts a crucial emphasis on the role of science - and in particular regulatory science - within its remit and priorities:

“The core responsibility of FDA is to protect consumers by applying the best possible science to its regulatory activities—from pre-market review of efficacy and safety to post-market product surveillance to review of product quality. In the last few years, rapid advances in innovative science have provided new technologies to discover, manufacture and assess novel medical products, and to improve food safety and quality; FDA must both keep pace with and utilise these new scientific advances in order to accomplish its mission to protect and promote the health of our nation.”

- Advancing Regulatory Science at FDA: A Strategic Plan (34)

FDA's priorities for regulatory science, established in their 2011 Strategic Plan

- Modernise Toxicology to Enhance Product Safety
- Stimulate Innovation in Clinical Evaluations and Personalised
- Medicine to Improve Product Development and Patient Outcomes
- Support New Approaches to Improve Product Manufacturing and Quality
- Ensure FDA Readiness to Evaluate Innovative Emerging Technologies
- Harness Diverse Data through Information Sciences to Improve Health Outcomes
- Implement a New Prevention-Focused Food Safety System to Protect Public Health
- Facilitate Development of Medical Countermeasures to Protect Against Threats to U.S. and Global Health and Security
- Strengthen Social and Behavioural Science to Help Consumers and Professionals Make Informed Decisions about Regulated Products
- Strengthening the Global Product Safety Net (added in 2013)



2.2 The Role of Regulatory Authorities cont.

Other relevant UK bodies

There are a huge range of UK bodies who have formal or informal regulatory roles in healthcare, which include specific bodies, including more than 13 health and social care regulators, as well as those bodies with broader responsibilities relevant to life sciences industry activities such as HM Revenue & Customs. Each of these will be important to consider in their relevant spheres of activity where regulatory innovation may have an impact. However, two bodies in particular are extremely relevant to healthcare regulation around novel technologies, which are:

National Institute for Health and Care Excellence (NICE):

Established in 1999, "NICE's role is to improve outcomes for people using the NHS and other public health and social care services by:

1. Producing evidence-based guidance and advice for health, public health and social care practitioners;
2. Developing quality standards and performance metrics for those providing and commissioning health, public health and social care services;
3. Providing a range of information services for commissioners, practitioners and managers across health and social care" (35)

The organisation supports the NHS in England and has a service level agreement with the Welsh Government. In Northern Ireland, the Department of Health has a formal link with NICE and reviews its guidance for applicability to Northern Ireland. Except for NICE's interventional procedures programme, NICE appraisals have no status in NHS Scotland. The Scottish Medicines Consortium produces advice for Scotland (36).

Although not a regulator, NICE plays a prominent role and complements the work of the MHRA. For example, NICE guidance on interventional procedures represents a 'licence' to use them in practice. NICE regularly reviews its processes and methodology, typically drawing on a methodology working group, as well as sponsoring research into new ways to evaluate new technology.

Health Research Authority (HRA):

The HRA is an executive non-departmental public body of the Department of Health and Social Care. The HRA exists to provide a unified national system for the governance of health research, including ethics approvals for clinical research (37). The HRA ensures that research is ethically reviewed and approved, promotes research transparency, and gives independent recommendations on the processing of identifiable patient information where it is not always practical to obtain consent, for research and non-research projects (37). The HRA will play a pivotal role in future UK regulatory science innovation and already works in partnership with the MHRA and other stakeholders. The Government White paper highlights the need "to develop a more sophisticated model of engagement where ethical and moral issues arise and ensure that issues such as risk and uncertainty are discussed appropriately"(17).



2.3 The Role of Industry

Notably, the Life Sciences Industrial Strategy and subsequent Sector Deals do not explicitly mention regulatory science, although a need for apprenticeships in regulatory affairs is highlighted as an industry-led skills initiative. Interestingly, the action plan associated with one of the six key priorities within the White Paper on 'Regulation for the Fourth Industrial evolution' - "We will build dialogue with society and industry on how technological innovation should be regulated." - only mentions specific plans for new approaches to public engagement, not industry engagement and dialogue. Industry's buy-in is assumed rather than strategised.

The vast majority of initiatives around regulatory science are underpinned by strong engagements with the pharmaceutical sector - this is where most of the visible engagement for both the FDA and EMA strategies occurs, notably with pharma the only industry sector which EMA consulted with to set its 2025 strategy (38). In the UK, the Association of the British Pharmaceutical Industry (ABPI) continues to be a major advocate for the regulatory science agenda (39), with an active working group chaired by David Jefferys, who was joint chief executive of the MHRA when it was originally founded.

There is much more to do to ensure the strong engagement of other important sub-sectors of the life sciences industry. One critical industry – whose importance COVID-19 has brought to the fore – is diagnostics. The industry's trade body, the British In-vitro Diagnostics Association (BIVDA), has an active Working Party on Regulatory Affairs. From ventilators to the artificial pancreas, the Med Tech industry plays an essential role in UK healthcare, and the sector's trade association, Association of British HealthTech Industries (ABHI) has a regulatory group that acts as a forum "for developing and communicating policy on regulatory, environment and standards issues. It aims to ensure regulations provide safe and timely access to HealthTech whilst maintaining the balance between risk and benefits for patients"(40). Its outputs include a 2019 Green Paper on "Future UK Regulatory Frameworks Post Brexit"(40), which argues for the use of general principles from the International Medical Device Regulatory Forum (IMDRF) for the UK's future approach to medical technology regulation.

Sometimes regarded as a separate sector – perhaps incorrectly – UK manufacturing is integral to life sciences, particularly its supply chains. A report in 2018 noted that "Life sciences manufacturing is among the most heavily regulated industries, especially from a product lifecycle standpoint. The industry is governed by a plethora of legal requirements and consensus standards including ISO 14971, ISO 13485:2016, and FDA Q9, among many others" (41). The economy relies on manufacturing for the life sciences industries. A report for the House of Commons Committee on Exiting the European Union found that manufacturing companies employ over 90,000 people in life sciences, with many more jobs unable to be captured in the core statistics due to the classification systems used (6). Giving these companies and their trade associations a clear voice in future regulatory change in the UK means ensuring that they are firmly integrated into the emerging regulatory science agenda as key stakeholders and expert advisors. Crucially, it would help retain diagnostics, Med Tech and manufacturing jobs in the UK. COVID-19 has revealed how this capacity matters.



2.4 The Role of Academia

"The key UK attribute driving success in life sciences is the great strength in university-based research. Strong research-based universities underpin most of the public sector research success in the UK, as they do in the USA and in Scandinavia. National research systems based around institutes rather than universities, as seen in Germany, France and China, do not achieve the same productivity in life sciences as seen in university-focussed systems."

- Life Science Industrial Strategy, 2017 (19)

The UK's academic capabilities supporting industry in life sciences and the advancement of healthcare innovation more broadly are well-documented. However, individual and collective university-led opportunities around regulatory sciences remain relatively untapped. Very few universities have visible programmes in this space – the Birmingham Health Partners Centre for Regulatory Science and Innovation (CRSI), aligned with their Centre for Patient Reported Outcomes Research, and the Newcastle University Centre for Regulatory Science are focused on the topic, while other initiatives such as the Centre for Drug Safety Science at Liverpool University and the Oxford University Centre for Medical Devices Sciences have very relevant interests and expertise.


Birmingham Health Partners approach to the development of international protocol and reporting guidelines.

Birmingham's collaborative University-NHS alliance targets areas of regulatory need which have clear local academic and clinical strength as well as strong external networks. Two recent examples include leading international protocol (SPIRIT) and reporting (CONSORT) guidelines for clinical trials including: i) patient reported outcomes (25, 42), and ii) AI (43); both of which have been supported by MHRA, EMA and FDA, amongst other national and international bodies. The Birmingham team, working with patient partners, have provided:

- **Leadership:** securing funding to support activities; identification of key international stakeholders; establishing collaborative input from regulators, patients, industry, ethicists, researchers, clinicians and methodological experts
- **Evaluation of current practice and existing guidance:** Systematic review of current practice (review of trial protocols) and existing guidance
- **Development of international consensus-based guidance:** Based on EQUATOR network methodology, 2-round Delphi survey/consensus meeting for each guidance.
- **Dissemination:** Including work with regulators and other stakeholders to promote uptake and use.
- **Training:** Supporting the development of appropriate tools and training with stakeholders

Similar approaches have been used for setting consensus statements in other fields, such as the recent publication on "Effective delivery of Complex Innovative Design (CID) cancer trials"(33), led by Birmingham on behalf of the UK's Experimental Cancer Medicine Centres.





UK universities rank among the top institutions in the world for their research in healthcare, law, ethics, social policy, health economics, engineering, business, biological sciences, chemistry and a vast range of multidisciplinary programmes. Combined, these capabilities could significantly accelerate the UK's ability to regulate new drugs, medical devices and diagnostics. They also provide outstanding teaching across all these areas, as well as a range of courses directly relevant to regulatory science (see below). As well as individual universities, the UK has several national groups with relevant expertise for regulatory science. For example, the NIHR Statistics Group (44) develops more robust methodologies from early phase clinical trials to diagnostic and prognostic tests. Also, the MRC-NIHR Methodology Research Programme funds a national partnership to advance trial methodologies (45).

The rapid emergence of new technologies will demand multi-disciplinary as well as multi-sector- collaboration to understand both threats and opportunities. Furthermore, this collaboration is needed to understand how current and future regulation must adjust to enable the latter whilst minimising the former. Notably, the most visible specific UK funding call in this space was via Wellcome, which ran a single themed 'Seed Awards in Humanities & Social Sciences' call on the topic of 'Relationships between regulation and health' (46). This awarded eight grants distributed across the UK, including Nottingham, Edinburgh, London, Cardiff, Bristol and Birmingham (47). Researchers from undertook studies on a range of topics, which presciently included ethical models for global health emergencies. Other projects examined the role of big data in healthcare regulation; novel regulation for drug-resistant infections; the safety of AI in healthcare; and the opportunities in block chain to play a role in regulation. These projects demonstrate a well-distributed UK-wide interest and expertise across relevant fields and specific topics of critical importance to national capabilities and capacity in regulatory science. The availability of future funding will be vital to accelerate and connect research excellence into the national endeavour.

Over the page we examine examples from around the world demonstrating how other regions have harnessed such expertise.



2.4.1 International Exemplars of Good Practice

A. INDIVIDUAL EXCELLENCE

Copenhagen Centre for Regulatory Science (CORS)

Established in 2015, the mission of CORS is defined as “Through research and education in regulatory science, CORS will improve the drug regulatory system and thereby contribute to an improvement of the health of the society and sustainable drug innovation.” It delivers this through:

- Methodological research: Strengthening Regulatory Science as an established scientific discipline
- Applied regulatory science: Stimulating a sustainable regulatory system, by systematically studying its structure and behaviour, as well as designing new tools to facilitate regulatory decision-making
- Valorisation: Increasing societal relevance of research by utilizing the inter-disciplinary and cross-sectorial setup of CORS
- Education: Cultivating the regulatory environment for pharmaceutical innovations and emerging technologies (e.g. big data, artificial intelligence in decision-making)

The Centre has three key themes of research (<https://cors.ku.dk/research/projects/>):

- Impact of drug regulation on health
- Emerging technologies & societal trends
- Post-marketing drug regulation

CORS is also highly multi-disciplinary and cross-sector. Internal departments engaged include Clinical Medicine, Pharmacy, Drug Design & Pharmacology, Public Health, Law, Media, Health Economics. Industry partners include Novo Nordisk, Ferring Pharmaceuticals, H. Lundbeck A/S and Leo Pharma A/S, and the Danish Medicines Agency are also formal partners. All of these are represented on their Scientific Advisory Board, together with patient organisations (Rare Diseases Denmark).

Duke Margolis Center for Health Policy

The Duke-Margolis Center is at the leading edge of real-world evidence (RWE) and regulatory science. (48-50) The US “21st Century Cures Act and the sixth Prescription Drug User Fee Act (PDUFA VI) set milestones for FDA to explore the use of RWE in regulatory decision-making. To inform the FDA as it works to meet these milestones, the Duke-Margolis Center for Health Policy RWE Collaborative engages stakeholders to guide high-priority efforts aimed at improving the development and use of RWE. The Collaborative also strives to drive progress in the use of real-world data and evidence to improve patient treatment options and outcomes more broadly. Guided by an advisory group consisting of leaders representing medical product developers, payers, research groups, providers, patient networks, and regulators, the RWE Collaborative is interested in the following priorities:

- Real-World Data - Fit for Use Reporting
- Assessing Individual Study Credibility for Observational Trials
- Understanding the Role of Observational Studies in a Totality of Evidence (ToE) Approach
- Establishing Guideposts for Developing Real-World Endpoints”(3)





B. ESTABLISHING MULTI-SECTOR COLLABORATIVE NATIONAL NETWORKS

Regulatory Science Network Netherlands

(<https://www.rsnn.nl/our-network>)

The Regulatory Science Network Netherlands (RSNN) is a network of experts from industry, academia, government bodies, and the broader regulatory science field, enabling stakeholders from different backgrounds to meet and discuss regulatory science “as equal partners”. Their mission is “to advance an efficient and effective regulatory system that supports medicines development, marketing authorisation, access, and appropriate use of medicines”.

The RSNN was founded in 2015, during the FIGON (a network organisation supporting drug development in the Netherlands) Dutch Medicines Days. The initiative was started by the Medicines Evaluation Board (MEB), the TI Pharma Escher project, and the Dutch Society of Pharmaceutical Medicine. The goal was to consolidate and strengthen national research networks in the field of regulatory science. Until 2017, the RSNN was funded by the MEB with independent grants from Pfizer and Janssen. In 2018, MEB; the Association of Innovative Medicines, Utrecht University, University Medical Center Groningen, and Lygature formed a partnership in order to further strengthen and expand the network. The RSNN is co-financed by the MEB, the Association of Innovative Medicines and HollandBIO.

The RSNN Advisory Group contains relevant stakeholder representatives from industry, academia and government, as well as patient groups (PSC Patients Europe). Academic leadership has been championed by the Utrecht Centre for Pharmaceutical Policy & Regulation (51), joined recently by the Groningen University Institute for Drug Exploration (52).

C. REGULATOR-ENDORSED NATIONAL CENTRES OF EXCELLENCE

FDA Centres of Excellence in Regulatory Science and Innovation (CERSIs)

CERSIs “are collaborations between FDA and academic institutions to advance regulatory science through innovative research, training, and scientific exchanges.” The rationale for the joint FDA-academic approach is described as “A strong in-house contingent of scientific and technical experts proficient in cutting-edge science together with a network of collaborations is key to FDA's capacity to evaluate increasingly complex products and promote innovation that addresses unmet public health needs.”

The FDA sets a clear outline of research priority areas for the CERSI initiative (53), covering a range of specific topics under the following current broad headings:

- High-priority topics, with needs across product lifecycle and relevant subpopulations (sex, gender, age, race/ethnicity)
- Develop and evaluate methods to improve quality and safety of FDA-regulated products for use by patients and consumers, including methods to improve predictive value of nonclinical evaluation
- Develop methods and tools to improve and streamline clinical and post market evaluation of FDA-regulated products

Proposals to address these topics must meet a CERSI-specific set of research impact metrics (54), which build from a core of “Advancing Regulatory Science” through to “Disseminating Scientific Knowledge”, “Catalysing Action” and “Informing Regulatory Decision Making”, all with the ultimate aim of advancing public health.

Current members of the CERSI network include the University of Maryland; the University of California at San Francisco in collaboration with Stanford University (UCSF-Stanford); Johns Hopkins University; and Yale University in a joint effort with Mayo Clinic.

While the CERSI programme is undoubtedly the most advanced regulatory science support network globally, the programme did face a number of issues in its early years of delivery. Challenges included diffuse goals and divergent views on approach, insufficient engagement with the FDA's own centres, questions over sustainability, misalignment of workforce needs/gaps, and a lack of incentives for FDA staff to participate (51). Any plan to replicate current good practice should understand how these challenges were overcome by the CERSI programme.



2.4.2 Existing Educational Programmes

Only a small number of UK universities formally teach aspects of regulatory science, with visible courses including:

- The University of Hertfordshire MRegSci in Regulatory Science (Pharmaceuticals and Medical Devices) (55), as well as an MSc and PhD scheme in Regulatory Affairs delivered by The Organisation for Professionals in Regulatory Affairs (TOPRA), which are validated by the University of Hertfordshire (56).
- Kingston University BSc in Pharmaceutical Science with Regulatory Affairs (57), accredited by TOPRA
- UCL four-day course in Regulatory Science for Advanced (Gene and Cell) Therapy: Advanced Therapies – Bench to Medicine (58)
- University of Oxford module in Economics and Regulation in Translational Science (an optional course within the MSc in Translational Health Sciences) (59)

Other relevant training initiatives are captured by the ABPI's 'Industry and Academia Links Survey', which has been carried out since 2003, which also notes undergraduate placements and apprenticeships aligned to regulation within the wider context of skills, education and research (60).

It is also worth considering US universities by way of comparison, because the USA is commonly regarded as the current leader in developing and implementing regulatory science (1). A scoping study by the Centre for the Advancement of Sustainable Medical Innovation (CASMI) found several American and international centres and initiatives in regulatory science (1).

The table over the page summarises CASMI's findings, plus additional centres uncovered in the course of researching this report.

FDA ORISE

The FDA supports over 120 fellowships in regulatory sciences and related disciplines through its ORISE (Oak Ridge Institute for Science & Education) Research Participation Programme (55). This educational and training initiative "is designed to provide college students, recent graduates, and university faculty opportunities to connect with the unique resources of the FDA." Access to FDA facilities and staff - including an assigned mentor - deliver real-world experience of working in a regulatory environment' this experience is designed to make participants aware of potential future employment opportunities. It is notable that many of these Fellows go on to be employed by the FDA and become mentors for the ORISE programme in turn.

EU Coordination and Support Action on Strengthening Training of Academia in Regulatory Science (CSA STARS)

The Horizon 2020 STARS programme - which includes the MHRA as a core partner - was created in response to the fact that "Lack of specific relevant know-how in regulatory science delays the development of new treatment strategies or limits the chances that promising innovations will reach patients (57). The objective of the STARS initiative is to "complement, coordinate and harmonise regulatory efforts among Member States and at European level to support academic health research for the benefit of patients"(57).

The work plan includes:

- Development of a Comprehensive Inventory of existing support activities based on a detailed analysis of the currently established programmes.
- Development of a Common Strategy to strengthen regulatory sciences
- Two curricula, the "Core" Curriculum specifying essential knowledge for the professional training of clinical scientists, and the "Comprehensive" Curriculum defining relevant knowledge for specific post-graduate programmes.

COUNTRY	ACADEMIC INSTITUTION	EDUCATIONAL PROGRAMME
	Yale University / Mayo Clinic	CERSI Scholars Program
	University of Maryland	Graduate Certificate programme in Regulatory Science Masters programme in Regulatory Science Postdoctoral Fellowships
	Georgetown University	
USA	University of Californian at San Francisco / Stanford University"	FDA Visiting Scientist Program
	Johns Hopkins University	Masters in Regulatory Science
	Cambridge Graduate University, Massachusetts	Accelerated Public Health & Regulatory Science Masters Degree Accelerated Public Health & Regulatory Science Doctorate
	Virginia Center for Translational and Regulatory Sciences	Developing programmes in regulatory sciences, although none are visible yet
	Perleman School of Medicine, Pennsylvania	Master of Science in Regulatory Science
	Harvard-MIT Center for Regulatory Science	Regulatory Science Fellowship Program
	International Center for Regulatory Science, University of Southern California	Masters in Regulatory Science

FOCUS**WEBSITE**

FDA Center of Excellence in Regulatory Science and Innovation

FDA Center of Excellence in Regulatory Science and Innovation

Focuses on modernising / improving the ways drugs and medical devices are evaluated

Postgraduate education

www.pharmacy.umaryland.edu/academics/regulatoryscience/

FDA Center of Excellence in Regulatory Science and Innovation

FDA Center of Excellence in Regulatory Science and Innovation

Research, education, outreach, and scientific exchange

Funding collaborative research projects that focus on “unmet needs” in regulatory science

Funding complemented by an Innovation in Regulatory Sciences Award from the Burroughs Wellcome Fund

<https://pharm.ucsf.edu/cersi>

FDA Center of Excellence in Regulatory Science and Innovation

Research incl. improving clinical studies and evaluation; strengthening the social and behavioural sciences to support informed decisions; and innovating the use of real-world evidence (RWE) in the life-cycle evaluation of FDA regulation

Postgraduate education

<https://advanced.jhu.edu/academics/graduate-degree-programs/regulatory-science/>

Postgraduate education

www.healthcarestudies.com/Accelerated-Public-Health-and-Regulatory-Science-Masters-andDoctoral-Degrees/USA/CGU/

Postgraduate education

<https://med.virginia.edu/phs/2017/09/07/meyer-robert-j-m-d/>

Postgraduate education

www.itmat.upenn.edu/msrs/

Fellowships, plus a wide range of research activities

<https://hmcres.org/>

Implementation/dissemination science and visual communication of educational modules

<https://regulatory.usc.edu/>

COUNTRY	ACADEMIC INSTITUTION	EDUCATIONAL PROGRAMME
	International Center for Regulatory Science, University of Southern California	Doctorate in Regulatory Science
	University of Georgia	Masters in Regulatory Science Certificate in Regulatory Science
	University of New England	Graduate Certificate in Regulatory Science Graduate Diploma in Regulatory Science
USA	University of Rochester	Advanced Certificate in Regulatory Science America's Got Regulatory Science Talent Competition (with University of Maryland) Broadening Experiences in Scientific Training: Regulatory Science track Career Development Program: Regulatory Science Training Pathway
	Burroughs Wellcome Fund	Innovation in Regulatory Science Award (up to \$0.5m)
	Arizona State University	Masters in Regulatory Science
	Pharmaceuticals and Medical Devices Agency (PMDA) Office for Regulatory Science	The PMDA has initiated education collaborations with several Japanese universities and research institutions.
JAPAN	Ministry of Health, Labour and Welfare	Establishing the "Asian Pharmaceuticals and Medical Devices Regulatory Training Center" within the Pharmaceuticals and Medical Devices Agency (PMDA) to promote understanding of pharmaceutical regulations in Japan by regulatory authority officials in Asia.
DENMARK	Copenhagen Centre for Regulatory Science, University of Copenhagen	Regulatory Science elective course in Masters programmes
NETHERLANDS	Utrecht Centre for Regulation and Enforcement in Europe, University of Utrecht	
	Dutch Medicines Evaluation Board	

FOCUS	WEBSITE
Underrepresented populations in clinical trials Adaptive clinical trials Companion diagnostic development Regulatory dissonance between US and Europe in product labelling	
Postgraduate education	https://rx.uga.edu/departments/academic/international-biomedical-regulatory-science/
Postgraduate education	https://www.une.edu.au/study/study-options/study-areas/management-and-administration/regulatory-science
Postgraduate education	
Provides up to \$500,000 over five years to investigators developing new methodologies to inform the FDA Active pharmaceutical and finished product supply chain and quality Opioid antagonists treatments	https://www.bwffund.org/grant-programs/regulatory-science/innovation-regulatory-science
Postgraduate education	
The PMDA listed 7 priority research areas (as of April 2019)	www.pmda.go.jp/english/rs-sb-std/rs/0005.html www.pmda.go.jp/english/rs-sb-std/rs/index.html
	https://www.mhlw.go.jp/english/policy/health-medical/pharmaceuticals/150827-01.html
Postgraduate education Research into the impact of drug regulation on health, emerging technologies and societal trends, and post-marketing drug regulation	https://cors.ku.dk/
Focuses on the relationship between regulation and enforcement at the interplay of national, European and other levels of government as well as private spheres of regulatory enforcement	https://english.cbg-meb.nl/
Various collaborations with Dutch universities on regulatory science	

2.5 The Role of the NHS



The NHS can be commonly viewed as a passive adopter of innovation and regulation, rather than recognising its critical existing and potential contributions to both of these areas in its own right. The NHS is the largest employer in England, with around 1.1 million full-time equivalent staff working in hospital and community services, across clinical staff, allied health professionals, administrative support and managerial roles (61). NHS staff across this breadth can provide vital insights into the effectiveness - or opposite - of regulations influencing their practice and the wider efficiencies of service.


With limited money to spend, the NHS benefits from foresight and detailed understanding of technological advances – particularly technologies that can potentially save funds. Diagnostics that enable better-targeted use of expensive drugs, for example, have enormous potential to reduce NHS costs and improve patient outcomes. NICE already assesses the budget impact to the NHS of new technologies. However, there may be more wide-ranging, or more specific, insights which regulatory science could contribute.

An illuminating keynote speech by Matthew Gould, CEO of NHSX, in October 2019 noted “Technology that meets the user needs of the NHS and care system isn’t necessarily the technology that innovators come up with... We haven’t always been great as the NHS or social care at identifying the market for innovators, what it is that we need, what it is that our patients need and articulating that in a way that’s helpful... We haven’t necessarily made it easy to innovate within the system, to sell to the system and crucially to scale innovation across the system”(59).

Innovators from small Med Tech SMEs to large-scale pharmaceutical companies recognise the huge benefits of having influential clinicians engaged with the development, testing and implementation of innovation. R&D in an NHS setting can accelerate the pace of development and delivery, as well as the ability of local (and potentially national) systems to adopt new products supported by these passionate advocates.

There are similarly significant gains to be made through the involvement of NHS leaders in development of new regulations, given their unrivalled understanding of the systems in which both the regulations and the diverse technologies which must adhere to these guidelines operate. The NHS Long-Term Plan notes under its reflections on leadership and talent management that “NHS England and NHS Improvement are already aligning our operating models, and we will continue to work closely with other regulatory bodies to ensure our expectations are clear and consistent, and to keep our assurance and oversight proportionate”(62).

It is important to remember when we think of the NHS as the enabler and adopter of much of the technology innovation that we describe in this report, that the NHS itself is highly regulated, and not always coherently. National moves towards systems-level oversight - essential for many reasons, not just technology adoption or enabling efficient responses to crises such as COVID-19 - are often at conflict with the legal framework for individual responsibility and reporting.



NHS Providers undertakes an annual survey of NHS leadership views on regulation. Reflections on its most recent report (63) note that “it is also important to remember that trusts retain formal legal responsibility for front line service delivery and, in the absence of legislative change, it will be a complex task for the national bodies and regulators to reconcile regulation and oversight at organisational level with national policy ambitions to place greater weight on collective responsibility at system levels. For the second year in a row, trusts responding to our survey highlighted the tension between the current institutionally-focused regulatory model, and policy ambitions for local systems”(45).

The Accelerated Access Collaborative

In 2017, the Department of Health and Department for Business, Energy & Industrial Strategy published its formal response to the Accelerated Access Review (64). It stated that “Selecting the best products for the pathway will be key, and we think, as proposed by Sir Hugh Taylor, it is right that this decision is taken by the national organisations responsible for regulating, evaluating and delivering new innovations to patients -- NIHR, MHRA, NICE, NHS England, NHS Improvement and Government -- with input from independent representatives for patients, industry and clinicians. This group will be referred to as the Accelerated Access Collaborative (AAC)”.

A new dedicated unit was established within NHS England and NHS Improvement, “to provide a more joined up approach, at all stages, to ensure the best, new innovations reach patients faster. This work includes horizon scanning for upcoming, cutting edge innovations that meet the needs of patients and the NHS, to providing support for providers to enable faster adoption and spread of already proven new treatments and diagnostic tools”(63).

A ‘single front door’ for innovators: We want to make it easier and faster for innovators to develop and test their prototypes and bring high-value innovations into the NHS. To do this, we’re developing an online one-stop shop, where innovators can find information and support to nurture their idea from research and testing to adoption and spread. This portal will be launched in 2020.

Demand signalling: To find the best solutions in healthcare we use ‘demand signalling’ to help researchers, innovators and funders understand what the NHS really needs to meet its challenges.


Integrated Horizon Scanning: Joining up the search for the best new innovations so that we can identify early stage products the AAC needs to foster and make sure that as a system, we are prepared to support their introduction in the NHS.

World-leading testing infrastructure: Create more opportunities for innovators to develop and improve their products, working with the NHS to provide high-quality clinical evidence.

Adoption and spread: Helping the NHS become stronger in its support for clinicians and patients to access new innovations at pace and scale.

Funding strategy: An agreed strategy to fund innovation that aligns with the work of Government, charities, research organisations and investors

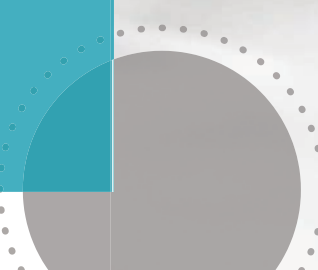
The Accelerated Access Collaborative’s “six ways of working”(65)



Chaired by Lord Ara Darzi with Dr Samantha Roberts as Chief Executive, partners in the AAC include:

- Academic Health Science Networks (AHSNs)
- Association of British HealthTech Industries (ABHI)
- Association of the British Pharmaceutical Industry (ABPI)
- Association of Medical Research Charities (AMRC)
- BioIndustry Association (BIA)
- Medicines and Healthcare Products Regulatory Agency (MHRA)
- National Institute for Health and Care Excellence (NICE)
- National Institute for Health Research (NIHR)
- National Voices
- NHS England and NHS Improvement
- NHSX
- The British In Vitro Diagnostic Association
- The Department of Health and Social Care
- The Department for Business, Energy and Industrial Strategy

While it does not have a formal role in regulation, its Board includes leaders from MHRA and NICE. The AAC commissions a range of programmes that are highly relevant to understanding how novel regulation could increase the pace of uptake of novel technologies and treatments by the NHS. The AAC is therefore a critical body to engage in the national regulatory science agenda, both as an advocate and a potential major beneficiary.



2.6 The Role of Patient and Public Partners

“In some domains, people feel that decisions about how technology is used are beyond their influence. Where technologies with far-reaching implications emerge, we need to conduct earlier engagement with the public, experts and industry to understand their views on how technological applications should be regulated.


We need to develop a more sophisticated model of engagement where ethical and moral issues arise and ensure that issues such as risk and uncertainty are discussed appropriately. We need to build trust and enable both consumers to have confidence in innovations and businesses to have confidence in our stable and proportionate regulatory system.”

‘Regulation for the Fourth Industrial Revolution’ White Paper, 2019 (17)

The importance of meaningful and sustained patient and public involvement in the co-design of medical research to ensure that research priorities and outcomes meet stakeholder needs is widely acknowledged (67-70). Patients have called for many years for patient involvement to be embedded in research and development from the earliest stages (68, 71). A call for action to partner with patients in the development and lifecycle of medicines has been made by many pharmaceutical leaders (72) and there is an industry wide movement for patient focused research and drug development (68, 70, 73-75). In 2019, the ABPI published a sourcebook to support pharmaceutical companies in working successfully and collaboratively with patients and patient organisations (76), and also inputted to the reciprocal guidance for charities working with industry, published by the Shared Learning in Involvement Group (77). Qualitative research led by the Copenhagen Centre for Regulatory Science (78) identified three main perceptions of patient involvement “a way to improve quality of life,” “a way to avoid business failure,” and “a way to foster a faster drug approval process.”. They noted that “Transparency, trust, and clarification of expectations and roles were factors perceived as prerequisites for a valuable collaboration.”


Co-production can help ensure that research protocols better reflect patient needs; and, by addressing potential barriers to patient participation, enhanced recruitment and retention (72). Patient and public involvement can drive the development of innovative medicines and devices that deliver more relevant and impactful patient outcomes and make research and development faster, more efficient, and more productive. Co-produced research may be more likely to be implemented, creating greater impact on health and well-being, particularly if patients also have an active role in implementation (79, 80). Meaningful involvement “can help avoid waste in research by ensuring it focuses on issues of importance and benefit for patients, so maximising the potential for democratic accountability to the wider public, who fund a significant proportion of UK research (80, 81).

Patient engagement and involvement can also lead to more economically viable clinical trials. Research has shown that for a pre-phase 2 project, the cumulative impact of a patient engagement activity that avoids one protocol amendment and improves enrolment, adherence, and retention is an increase in net present value (NPV) of \$62MM (\$65MM for pre-phase 3) and an increase in expected net present value (ENPV) of \$35MM (\$75MM for pre-phase 3). Compared with an investment of \$100,000 in patient engagement, the NPV and ENPV increases can exceed 500-fold the investment. This ENPV increase is the equivalent of accelerating a pre-phase 2 product launch by 2½ years (1½ years for pre-phase 3) (35).



Patient and public involvement – importantly connecting with citizens and communities beyond just those most readily-accessible in healthcare – are an essential component of regulatory science. Importantly, these must represent both meaningful and timely involvement, where possible instigated from the very start of activities, rather than a “tick-box” add-on exercise. The MHRA has long recognised their importance, including a recent consultation to review how it best engages and involves patients in its work. For example, the agency included patient and carer representatives in a patient-focused ad hoc expert meeting to consider the continued Early Access to Medicines Scheme licence for Raxone. The agency also established the Valproate Stakeholder Network, which included patient groups/research charities, as well as campaign groups and individuals representing the families affected. Since 1999, NICE has involved patients, service users, carers and the public, including voluntary, charitable and community organisations in its work. They contribute valuable input to developing NICE guidance, advice and quality standards, and support their implementation in order to ensure that guidance and other products have a greater focus and relevance for the people most directly affected by the recommendations (84).

The EMA actively interacts with patients and consumer groups acknowledging that they “bring a 'real-life' experience as well as specific knowledge and expertise to scientific discussions on medicines and on the impact of regulatory decisions. Collaborating with these groups supports transparency and improves regulatory processes.” The EMA produced a framework for interaction with patient groups and consumers in 2005 which was revised in 2014 (73, 74). The European Patients’ Academy (EUPATI) guidance documents aim to support the integration of patient involvement across the entire process of medicines research and development with regulatory agencies, health technology assessment (HTA) bodies, ethics committees and the pharmaceutical industry. This guidance is being built on by PARADIGM – a public-private partnership co-led by the European Patients’ Forum (EPF) and the European Federation of Pharmaceutical Industries and Associations (EFPIA). PARADIGM’s mission is “to provide a unique framework that enables structured, effective, meaningful, ethical, innovative, and sustainable patient engagement (PE) and demonstrates the ‘return on the engagement’ for all players (85-88).





In 2012, FDA established the Patient-Focused Drug Development (PFDD) initiative to “more systematically obtain the patient perspective on specific diseases and their currently available treatments. PFDD public meetings have a format designed to engage patients and elicit their perspectives on two topic areas:

- 1.the most significant symptoms of their condition and the impact of the condition on daily life; and,
- 2.their current approaches to treatment”(89)

In addition, the FDA is developing a series of four methodological PFDD guidance documents “to address, in a stepwise manner, how stakeholders can collect and submit patient experience data and other relevant information from patients and caregivers for medical product development and regulatory decision making”(90)

Beyond contributing to regulatory decision making patients can also play an essential role in new guideline development, innovation in regulatory science and dissemination, as exemplified by patient participation in the development of protocol guidance for patient reported outcomes and artificial intelligence trials (see section 2.4) (91, 92) and the role of National Voices in the Accelerated Access Collaborative board (91, 93). Education and support for patients and the public on the role and work of regulatory agencies and resources that help them better understand how regulatory science works will be crucial to optimise their involvement.

The background features a grayscale image of laboratory glassware, including several Erlenmeyer flasks and beakers, some containing liquids. Overlaid on this are various scientific graphics: a large green circle on the left, a green dotted pattern in the top right, a white hexagonal molecular structure in the center, and a green dotted line curving across the bottom right.

Section 3:

**UK life sciences
regulatory
challenges**

Life sciences are vital not only for the UK's health but also its economic wealth. The industry supports around 482,000 jobs in the UK. Moreover, these jobs contribute disproportionately to economic growth: the life sciences industry's Growth Value Added to the UK economy per employee is over twice the UK average. The activities of life sciences companies directly contributed £14.5bn to the UK economy in 2015, with an additional £15.9bn provided through the life sciences supply chain and employee spending (94).

As Professor Sir John Bell observed in the Accelerated Access Review in 2016: "Given the uncertainty for the financial sector and heavy manufacturing in a future potentially outside the single market, it seems clear that the life sciences industry will provide a crucial pillar for future economic growth. This will, of course, require a targeted industrial strategy and may benefit from a future regulatory regime"(95).

The UK's Life Sciences Industrial Strategy, launched November 2017, included "Regulation" as one of its three cross-cutting themes underpinning competitive growth, alongside "Skills" and "Global Britain". Both of the subsequent Sector Deals with Government flagged progress in this area, with Sector Deal 2 noting "Last year's deal included a suite of actions to support the UK environment for life sciences businesses. An effective regulatory environment that works for innovative, emerging new technologies is key to this"(29).

The Government's own White Paper on 'Regulation for the Fourth Industrial Revolution' noted that "We need to reshape our regulatory approach so that it supports and stimulates innovation that benefits citizens and the economy. At present, only 29% of businesses believe that the government's approach to regulation facilitates innovative products and services being efficiently brought to market. The need for reform is urgent: 92% of businesses from a range of sectors think they will feel a negative impact if regulators don't evolve to keep pace with disruptive change in the next two to three years".

However, significant challenges remain to UK life sciences businesses in terms of the regulatory environment - already complicated by the introduction of new regulations across the EU, now facing major uncertainty around what new, UK-specific regulations may come into play post-Transition. Here we examine some of the key current and future concerns over regulation facing the four major sectors within the life sciences industry.

3.1. Biopharmaceuticals

Market overview:

Biopharmaceutical companies supply the NHS with a wide range of medicines and vaccines. The biopharmaceuticals industry comprised 2,066 businesses that generated a turnover of £48.2bn and employed 119,000 people across the UK in 2017 (96). The UK is home to the world's seventh-and ninth-largest pharmaceutical companies, AstraZeneca and GSK, as measured market share in 2019 (97). One in five of the world's biggest-selling prescription drugs were developed in the UK (98). The Department of Health and Social Care noted that: "2018 Research and Development (R&D) spend in UK pharmaceuticals was £4.5 billion (around a fifth of total UK R&D expenditure). Pharmaceuticals is the largest product group in UK R&D spend"(99).

Regulation:

The European Medicines Agency (and its predecessor) has handled medicines regulation ever since the UK joined the EU. At the end of the Brexit transition period, the EU's legislative frameworks for medicines will remain as "retained UK Law". Supporting legislation will ensure they can operate effectively after the end of the Brexit transition. The Government wants to ensure that the UK "can maintain an up to date, dynamic system for regulating these sectors as well as enacting changes to medical devices enforcement and information-sharing powers"(100). Consequently, the Government introduced the Medicines and Medical Devices Bill.

Brexit:

It is not yet known in detail how medicines will be regulated after the transition. A briefing paper by the House of Commons Library reported in 2019 that: "The Government have stated that it is seeking a close future relationship with the EMA. The November 2018 Political Declaration said that the Parties would 'explore the possibility of cooperation' with EU agencies such as the EMA. There have been calls from health organisations, healthcare professionals, pharmaceutical companies and others for the Government to ensure regulatory alignment with the EMA on medicines in order to guarantee patient safety, public health and support the industry in the UK."

Currently, the balance between regulatory divergence and alignment with the EMA has yet to be finalised in detail. In medicines regulation, the details matter.

The Association of the British Pharmaceutical Industry (ABPI) told the authors that it is worried that the UK will lose international influence after the Brexit transition.

The association also expressed concern that the UK would diminish its ability to attract investment from big pharma companies. Two factors underpin the industry's fears for the UK.

First, companies will have to submit new medicines for approval by the EMA and the MHRA. Even if the EU and UK regulations are similar, two separate submissions for regulatory approval will need to be made by a company launching a new drug. The regulatory approval process demands considerable time and resources. Because even large companies find the process demanding, they seek regulatory approval in different countries over more than one year. 'Tier 1' countries are the largest markets and typically comprise the EU and USA, which are the first places where new medicines are launched. Countries in 'tier 2' and 'tier 3' often will not get access to new drugs until 1-2 years later. The ABPI remain concerned that the UK could become a tier 2-3 country, which would be detrimental for the UK affiliates of pharmaceutical companies and patients alike.

Second, the UK has benefitted from its regulatory approval being seen as a mark of quality, but there are industry concerns - expressed via ABPI - that Brexit jeopardises this reputation. Companies would often launch their drugs in the UK when it was part of the EU because approvals by the MHRA and NICE were seen as benchmarks. After the Brexit transition, companies will launch new medicines in other countries because UK regulatory approval will not licence a drug for use across the EU. Consequently, the MHRA will not be among the first regulatory organisations to assess new medicines and, therefore, its influence will be diminished. In the same way, NICE will not be among the first health technology evaluation agencies to review new therapies and risks a loss of international influence.

Representatives from the pharmaceutical industry have proposed several actions that UK authorities could do to mitigate these risks. To start with, the MHRA and NICE have a reputation for being, respectively, the gold standard in medicines regulation and health technology appraisal. They need to continue to maintain their high standards so that UK regulation remains a badge of quality. However, more is required. In particular, the industry has argued that the UK's regulatory processes must become significantly faster than both the FDA and EMA. Speed is the one thing that could enable the UK to remain as a 'tier 1' location for new medicines, according to the ABPI. There are several components to speed, which the table opposite summarises.

Essential opportunities for the UK to retain 'tier 1' status:

► Speed of regulation:

The MHRA has already demonstrated its agility, such as the Early Access to Medicines Scheme (EAMS) and its rapid response to COVID-19. The agency can build upon these strong foundations further.

► Speed of health technology appraisal:

NICE has evolved continuously since inception, playing an integral role in EAMS. However, resource constraints currently limit NICE from conducting appraisals more rapidly.

► Speed of NHS uptake:

It is widely recognised that the NHS can be slow to employ new medical technologies and therapies. Since 1999, successive governments have sought to address the problem of improving NHS uptake of new medicines and innovation. There have been several government reviews of this problem. However, little work has been done to ascertain how well these reviews were implemented



3.2. Diagnostics

Market overview:

Approximately 70% of clinical decisions are based on in-vitro diagnostic tests, which are generally blood and tissue tests. The NHS carries out around 300,000 of these tests per day (101). Deloitte estimates an increasing demand for in-vitro diagnostic tests, due to an ageing population and rising incidence of chronic disease (102).

In-vitro diagnostics form the largest category in the global medical technology market, with annual sales of £41bn in 2017 (103). In the UK, the in-vitro diagnostics sector was worth around £820 million in 2017 (104). The UK is a net exporter of in-vitro diagnostics, with £1.1 billion exported in 2013 according to Deloitte (103). The British In-vitro Diagnostics Association has over two hundred member companies, of which the majority are small and medium-sized enterprises (SMEs) (105).

New Regulation on In-Vitro Diagnostics (IVD):

In April 2017, the European Parliament endorsed the new In-Vitro Diagnostics Regulation (IVDR). This aims to make the regulatory process more robust, transparent, predictable and sustainable. The UK played a crucial role in influencing the latest regulatory standards, and commenting on the result at the time, the British In-vitro Diagnostics Association (BIVDA)'s Chief Executive Doris-Ann Williams said:

"We are pleased that the European Parliament has endorsed the IVDR, which has been developed to further strengthen patient safety. There will be a considerable additional cost burden to the IVD industry to comply with this regulation. However, the long development process to produce this regulation has led to much uncertainty among IVD manufacturers, and we look forward to moving forward once it is published"(106).

The regulations took eight years to develop, and 'entered into force' on 25 May 2017, which is when a five-year transition period began, with IVDR fully applying in EU Member States from 26 May 2022. The industry has invested hundreds of millions of pounds in preparing for these regulations. The UK will have left the European Union by this time, but the UK diagnostics industry has argued for regulatory alignment after Brexit. In a joint letter to negotiators for both the UK and EU, industry representatives have urged both parties to implement the regulations for their sector fully.

Since the new standards passed into law, the IVD industry has been investing heavily to meet them. One manufacturer commented: "As an organisation, we have already been preparing for the implementation of the EU IVDR. We are three years down the track and have made a significant investment in this transition." (personal communication).

Diagnostic companies told the authors it was imperative for the UK to recognise and enforce CE-marking for in-vitro diagnostics, and to implement the latest EU IVD Regulations. The MHRA initially indicated that irrespective of the outcomes of the political discussions, the UK would accept the CE-mark as a route to placing medical technologies on the UK market, although this guidance has been withdrawn as of February 2020.

Challenges for the UK in-vitro diagnostics industry

- Most British diagnostics SMEs primarily rely on selling exports to EU countries
- Companies of all sizes have already invested heavily in preparing for the new IVDR
- The UK needs more Notified Body capacity to cope with an estimated five-fold increase in product certification after 2022, and this could be a crisis issue
- Manufacturing costs will increase, thereby reducing the viability of some SMEs
- UK regulatory divergence would bring an extra 'cost of complexity' to British companies
- Regulatory divergence would weaken collaboration and post-market surveillance data sharing between EU and UK based organisations, which would hinder the development of medical technologies
- If costs of meeting new or diverse regulations are not met by sales, then companies will be forced to discontinue supplying products to the NHS. This is a real possibility in small markets, such as diagnostics for rare diseases

3.3. Medical Devices

Market overview:

Medical device companies supply the NHS with a wide range of healthcare technologies. These companies cover manufacturers of devices at all levels of complexity and sophistication, from pacemakers to the artificial pancreas. In 2017, the Med Tech sector comprised 3,583 businesses that generated a turnover of £22.2bn and employed 121,900 people across the UK. Med Tech accounts for half of industry employment (51%), one-third of turnover (32%) and 63% of businesses in the UK's life sciences sector (96). The majority of these companies are SMEs and small companies are often a vital source of innovation in healthcare.

For example, the MHRA Innovation Office reported an increase in enquiries about 3D printing (or 'additive manufacturing') in medicine manufacturing since 2017, including a growing demand for customised Med Tech (107). As well as 3D printing, the office also highlighted enquiries about the use of synthetic biomaterials in medical devices and development of scaffolds for regenerative medicine (107).

New Med Tech regulations:

The introduction of new rules brings considerable challenges for the medical devices sector. The ABHI has welcomed the new Medical Device Regulations and strongly urged the UK Government to remain aligned with them. However, the trade association is very concerned about the challenges for companies because of transition and Brexit. The MHRA initially has indicated that irrespective of the outcomes of the political discussions, the UK would accept the CE-mark as a route to placing medical technologies on the UK market, although this guidance has been withdrawn as of February 2020 (108).

New Med Tech regulations cont.:

The ABHI predicts this acceptance by the MHRA would last for two years - leaving significant future uncertainty for many small businesses (40). It is worth noting that the EMA have recently announced that the implementation of the Medical Device Regulations has been postponed by a year (109), putting it beyond the date of the transition period for leaving the EU. The implications of this will create further uncertainty for many companies attempting to prepare themselves for future trading.

The ABHI has found that UK companies are experiencing four challenges with the length of the transition period, which the table below summarises.

Challenges for medical technology (Med Tech) companies with the length of transition period:

- Capacity to deal with new regulations for Med Tech
- Complexity of new Med Tech regulations
- Competence to deal with new regulations
- Cost of dealing with new regulation (noting that Med Tech profit margins are considerably lower than Pharma, in a sector dominated by small SMEs)

To address these challenges, companies have clearly articulated the need for more time than the 11-month transition. The ABHI is already reporting that SMEs do not yet understand the new regulations, which is resulting in a reduction in innovation because of companies' focus on compliance. Crucially, there has not been time to harmonise standards for medical devices across European countries - this ranges across safety and performance requirements to the criteria for undertaking the clinical trial of a device. This situation is highly problematic for many UK-based Med Tech companies.

Furthermore, COVID-19 has worsened the regulatory difficulties faced by SMEs because the pandemic has hampered work by existing Notified Bodies, and the designation of new Notified Bodies is not taking place.

After transition:

UK industry had contributed significantly to the new Medical Devices Regulations and welcomed them. Just like the diagnostics sector, British Med Tech companies also rely on exports to EU countries. Companies will continue to make CE-marked products long after Brexit because they depend on these sales.



3.4 Digital Health

“There should be an ambition to develop the regulatory environment and digital capability to enable the evidence generated in healthcare systems to improve the speed and efficiency of regulatory studies. Few things could have such a major impact on the cost effectiveness of trials ultimately feeding through to better data and potentially much less expensive drugs.”

- Life Sciences Industrial Strategy, 2017 (110)

Market overview:

This sector includes businesses involved in making products for both hospitals and consumers including products such as hospital information systems and mobile medical devices and apps. Classified as a subsegment of the UK's Med Tech sector, digital health is nevertheless a vibrant part of the economy - in 2017 (the most recent Government report), it comprised 491 businesses, employed ~10,000 people and had a turnover of £1.2billion, the most significant part of Med Tech (96). Reports predict a rapid increase in the net worth of the sector, with forecasts of \$639.4 billion by 2026 (111) - likely to be further enhanced as an impact of the COVID-19 pandemic and increasing reliance on population monitoring and consumer interest/involvement in health data.

Digital Health Regulations:

The main source of formal regulation will come from the Medical Device Regulation (MDR), which changes both the law and process of certification for medical software, including key changes for digital health technologies which are medical devices. This is complemented - albeit not seamlessly - by a range of other guidance:

- The NICE evidence standards framework for digital health technologies, which focus on effectiveness and economic impact, and explicitly note that they are “not intended to assess the safety of digital health technologies, which is the responsibility of other frameworks such as the Medical Device Regulations or the NHS digital clinical safety regulations (DCB0129 and DCB0160) (112).
- The Care Quality Commission (CQC) regulation of online provision of healthcare (113), as well as their recent report on the future of digital triage in health services (114), following investment from the Regulator's Pioneer Fund.
- The Government's official code of conduct for data-driven health and care technology, which outlines 10 principles “to enable the development and adoption of safe, ethical and effective data-driven health and care technologies”(115).

NHSX also recently published its draft open Digital Health Technologies Standard, “intended to speed up and streamline how health technologies are reviewed and commissioned by the NHS and social care, and enable innovation to flourish”(116).

Digital Health Regulations cont.:

Unsurprisingly, given major public relations challenges around previous programmes such as the government's controversial and ultimately abandoned care.data NHS information sharing scheme (117), much of the formal regulatory work has been complemented by major initiatives focused on public trust. This includes the Data Ethics Framework (launched when Matt Hancock was Secretary of State for Department for Digital, Culture, Media & Sport), and the new Centre for Data Ethics and Innovation, established "to identify the measures needed to strengthen and improve the way data and artificial intelligence (AI) are used and regulated. This will include articulating best practice and advising on how we address potential gaps in regulation"(17). Important work was also undertaken recently by the Office for Life Sciences with the Shelford Group around creating the right framework to realise the benefits for patients and the NHS where data underpins innovation. The draft framework is awaiting ministerial approval this year, but sets out a vision to complement existing regulatory bodies with a new national centre of expertise and ongoing patient and public involvement and engagement.

After transition:

As a subsector of Med Tech, the Digital Health sector faces the same challenges around the new MDR directive, including capacity, competence and cost. However, they may face even more significant challenges around complexity, given the range of guidelines and regulations outlined above specifically focused on this sector - for example, one recent review commented on the NICE standards "Whilst these are stated to be complementary to the new MDR, the framework has different assessments and evidence requirements (118).





The background features a grayscale molecular model with spheres and connecting lines, creating a sense of depth. Overlaid on this are several pink geometric elements: a large semi-circle on the left, a dotted pink pattern in the top right, and a solid pink circle in the bottom right. A dotted line also curves from the bottom right towards the center.

Section 4:

**Strategic
areas for
development**

4.1. Identification of Emerging Science and Technologies

“There has been much discussion about the opportunity of the UK to develop an innovative regulatory approach to emerging technologies outside of the EU. This would follow on from the MHRA role in supporting the innovation of various elements of the EMA system such as the adaptive licensing system. It will be important for any future regulatory system to regulate emergent and convergent technologies such as cell and gene therapies and algorithms, as well as digital medicines. While this innovative strand in the MHRA approach might be theoretically desirable from a UK life sciences ecosystem point of view, it would only be additive if it did not jeopardise the UK’s participation in the EU systems and processes. Relatively speaking, the UK market is too small even with the fastest and most innovative regulatory system in the world, to stand alone from a larger decision-making bloc.”

- Life Sciences Industrial Strategy, 2017 (110)

Innovation is inherently risky for all stakeholders - the inventors, the “beneficiaries” and the buyers (who may not be the same, particularly in the case of healthcare thanks to the UK’s NHS system). There are challenges in how to simultaneously reduce risk for all of these groups - for example, human ‘organ-on-a-chip’ technology can provide quicker and more human-relevant data than rodent assays (119), and the technology is developing apace, such as lungs on chips that can mimic breathing movements (120). The technology is poised for take-off, but it is unclear what organ-on-chip data would be considered valid by regulators. Without this clarity, the technology is caught in a Catch-22. Many investors and innovators want to know what data will be acceptable to regulators, yet regulators are looking for more data on which to base such decisions.

Similarly, the concept of extending healthspan in older adults - the last years of life are typically spent in poor health with a range of multimorbidities and consequent polypharmacy - is a major challenge for the NHS, industry and regulators. The potential benefits to all of these is huge - for the NHS alone, acute care fills 90% of hospital beds at a cost of £17 billion per year (121), and in the models of future health trends and spending predicts that the effect of delayed ageing resulting in 2.2 years additional healthy life expectancy would yield \$7T in savings over 50 years (122). However, industry has struggled to grapple with a concept which crosses multiple therapeutic indications. Many large pharmaceutical companies have this area in their 5-10 year plans rather than their near-term investment streams (excepting companies such as Calico in the US). One of the most difficult challenges has been establishing appropriate methodologies for patient stratification and appropriate biomarkers for outcomes in clinical trials, particularly where these approaches are preventative rather than treatment-based. Only by working across current industry and academic silos with strong NHS buy-in and regulators willing to innovate will this thorny challenge be overcome.

Regulatory science offers a way to provide clarity and collaboration between stakeholders, providing that it is appropriately targeted. There are several emerging technologies and trends in regulation which need collective visions on how best to move forward, as highlighted by recent IMI-EMA-FDA Regulatory Science Summits (123, 124). These include advanced therapy medicinal products (ATMPs), artificial intelligence, digital tools for data collection and analysis, digital therapeutics, immunology and the microbiome, big data and digital health, as well as real-world evidence and clinical trials.

For example, the 2019 summit sets out the comparative lack of trials in Europe for ATMPs, noting that complex and diverse regulation may be a key factor. Through collaborative discussions, it then sets out key potential actions in non-clinical, clinical and manufacturing sectors, including defining regulatory convergence on product quality and comparability and managing long-term effects and safety. Through its strong Cell & Gene Therapy Catapult and national network of Advanced Therapies Treatment Centres, supported via the Industrial Strategy Challenge Fund, the UK is well-placed to actively contribute to these challenges and demonstrate international leadership - but could crucially benefit from the proactive support of regulatory scientists to support new thinking.

A coherent UK-wide approach to coordinate, accelerate and deploy regulatory sciences has to balance risk and reward for all stakeholders. Here we discuss in detail four emerging areas where the pace of innovation in the UK's regulatory sciences could enable near-term national benefits to health and wealth through global market opportunities. These are intended as illustrative examples to stimulate further discussion amongst national stakeholders, rather than formal recommendations.





4.1.1 Artificial intelligence

"I believe wholeheartedly that we are in the early stages of a revolution that is going to change all of our lives."

— The Rt Hon Matt Hancock MP (125)

"Artificial Intelligence (AI) has the potential to make a significant difference to health and care." AI has already established itself in early R&D for new medicines. For example, Pfizer has worked with IBM Watson in immuno-oncology research, Sanofi has signed a deal to use Exscientia's AI platform to find metabolic disease therapies, and Genentech is using an AI system from GNS Healthcare in cancer research. However, AI-led research has now moved into the clinic. British company BenevolentAI recently completed patient recruitment for what could become the first drug discovered through AI. BenevolentAI uses machine learning "to design new molecules, extracting new hypothesis based on a knowledge graph composed of over a billion relationships between genes, targets, diseases, proteins and drugs". Now that AI-led research has reached the clinic, regulatory science must keep pace. The MHRA Innovation Office reported that queries about the use of AI had leapt from two in 2017 to fourteen in 2018. The office commented that: "This includes novel software solutions for use in clinical trials as well as use in healthcare applications to monitor the progression and identify treatment options for a range of medical conditions"(28).

In all likelihood, it is in diagnostics where AI will impact the NHS first. The UK has been a key player in the development of AI diagnostics, notably with the Moorfields Eye Hospital collaboration with DeepMind, which led to the world's first automated diagnostic of high-dimensional imaging data, in which a two-step algorithm provided retinal image segmentation and labelling, and diagnosis with triage capability and diagnostic accuracy equal to retinal experts. A 'State of the Nation' survey by NHSX revealed that "diagnosis and screening are the most common uses of AI, with 132 different AI products identified as being designed for diagnosis or screening purposes covering 70 different conditions". A £250 million UK investment in NHSX to establish an AI Lab aimed at improving the health and lives of patients is actively searching for applications in diagnosis and testing, alongside "health promotion and prevention" and "system efficiency", coordinated via the Accelerated Access Collaborative (130).

For example, clinicians need the results of diagnostic tests to help determine the right treatment for patients. Diagnostic capacity affects how long this takes, and there is a shortage of radiologists in the NHS. Additionally, "the interpretation of diagnostic tests is unavoidably subject to human error"(131). In radiology, for example, AI brings hope for reducing human error and freeing up radiologists' time.

AI can help at different levels of sophistication, each of which requires appropriate regulation underpinned by sound regulatory science:

- Tools that identify signs of disease from diagnostic images, underpinned by AI: These tools should be relatively straightforward to regulate, and the AI lab hosted by NHSX is well resourced. Simon Stevens, NHS England's chief executive, said, "Carefully targeted AI is now ready for practical application in health services" (132).
- AI tools that prompt clinicians to act: In theory, these should be moderately easy to regulate because there remains a final human decision. In practice, regulation may prove trickier because these AI tools are not always tested in well-controlled comparative studies with appropriate follow-up time. NICE faced this problem with its first Med Tech briefing on AI software, an AI tool for analysing CT brain scans. The software detects and notifies healthcare professionals of abnormalities after analysis of brain CT scans, with automated patient prioritisation and alert systems for critical cases. Also, preliminary findings from some of this software populate radiology reports (133). NICE would not have had enough evidence to issue formal guidance but was able to issue a briefing about the technology.
- AI tools that diagnose and determine patient treatment: The regulation of these tools will require significant advances in regulatory science.
- AI tools which are not static but continuously learn from the input data with a view to improving performance: Regulators have raised this as an area of concern, and existing frameworks for evaluating digital health technologies usually overlook or explicitly exclude these types of adaptive AI system.

Accordingly, Notified Bodies will require increasing expertise in AI, usually in the context of software as a medical device. What is more, research by NHSX found there were few issues with the regulation itself but problems centred on "the lack of coordination of regulatory bodies along the innovation pathway. In addition, the absence of a guidance and regulation navigator makes it difficult for people to figure out what they need to do and with whom they need to interact with at each stage of the process"(129), tying in with our earlier summary of the complexities of regulation for the Digital Health industry.

THE NHSX AI report has highlighted a number of challenges in the regulatory system for AI:

1. No one body is responsible for the overall process, making it hard to ensure coordination between regulators
2. Regulation can often be wrongly interpreted on the ground, particularly data regulation
3. In particular instances, the regulation is not fit for purpose
4. The remit of regulators is unclear or overlapping, and no regulator has direct oversight of the quality of data used to train algorithms
5. There are uncertainties about how to regulate certain aspects of AI, such as 'adaptive' algorithms

If the UK can nourish its capabilities and reputation in AI and regulatory science, this would generate a significant benefit. The House of Lords Select Committee report "AI in the UK: ready, willing and able"(134)? noted that many of the start-ups in this sector were acquired by foreign-owned companies, which "reinforce the sense that the UK environment and investor expectations encourage the sale of technologies and technology companies before they have reached their full potential". The Government's White Paper highlights that a partnership has already been agreed with the World Economic Forum Centre for the Fourth Industrial Revolution in San Francisco to work on regulatory approaches for AI and machine learning (17). However, there may be some opportunities for regulatory innovation, which may not involve significant divergence, that would enable a world-leading environment for AI clinical testing through which we may be able to better anchor private/public sector innovation in the UK.

4.1.2 Patient Reported Outcomes

A patient-reported outcome is "any report of the status of a patient's health condition that comes directly from the patient, without interpretation of the patient's response by a clinician or anyone else"(90). International regulatory authorities, health policymakers and patients have all recognised the importance of patient reported outcomes (PROs) (25). PRO trial results, if captured in a scientifically rigorous way, may inform clinical decision-making, pharmaceutical labelling claims, product reimbursement and influence healthcare policy (25, 90, 135, 136). PROs may also be "the only way of assessing and demonstrating treatment benefits (e.g. pain therapy, fatigue, sleep disturbances)"(137). Consequently, interest and the use of PROs has increased over the last decade. Laurie Burke, former Associate Director at the FDA, reported that "the growth has been... almost exponential, showing the importance of the field in the biomedical literature"(138).

The FDA has been at the forefront of regulatory developments for PROs. It produced its first guidance about PROs over a decade ago (90) and is currently drafting a suite of advice on patient-focused drug development_(139). The FDA have also recently released the Project Patient Voice platform (140) - an online platform for patients and caregivers along with their healthcare providers to look at patient-reported symptom data collected from cancer clinical trials. The EMA has also guided the use of PROs in oncology studies (137), and there has been a strong push by regulators to drive greater use of PROs, as well as collaboration between regulators to align how they evaluate PRO data. For example, representatives from the US, UK and Canadian regulatory authorities jointly wrote that "sustained international collaboration is underway to advance regulatory science related to PRO measurements"(141).

As noted earlier, the Centre for Patient Reported Outcomes Research, University of Birmingham UK is working in close collaboration with regulatory agencies (MHRA, FDA and EMA) on the development of international guidelines for the use of PROs in clinical trials. The Centre has played a key leadership role in the development of PRO protocol guidance (SPIRIT-PRO) (25) and reporting guidelines (CONSORT-PRO) (142). Representatives from the Centre and other UK organisations are also contributing to:

- i) the European Organisation for Research and Treatment of Cancer led Setting International Standards in Analysing Patient-Reported Outcomes and Quality of Life Endpoints Data (SISAQOL) Consortium, which is developing recommendations for standardizing the analysis and interpretation of PRO endpoints in randomized cancer clinical trials (141); and
- ii) the PROTEUS consortium which is leading efforts to promote the uptake and use of these and other tools by international stakeholders including regulatory agencies such as the FDA, EMA, MHRA and Health Canada (143).

There are several opportunities for collaborative research to further advance innovation in regulatory science for PROs, and the UK is well-placed to contribute to, or lead on, such initiatives. Examples include the development of recommendations to improve PRO study objectives, analysis and reporting of results to facilitate uptake and use by multiple stakeholders as identified in a recent Innovative Medicines Initiative (IMI) call (144), and the use of PROs for real-world evidence generation (145). Many of these initiatives to date have focused on oncology. However, there is a growing need to advance this science across other clinical disciplines (146).

4.1.3 Medications for Use in Pregnancy

During 2015-17 in the UK, 9.2 women per 100,000 died during or up to 6 weeks after pregnancy, from causes associated with pregnancy, while there were 2,840 stillbirths and 1,267 neonatal deaths (147). Worldwide, these figures grow to 215 per 100,000 women and around 6.5 million newborn and child deaths per year.

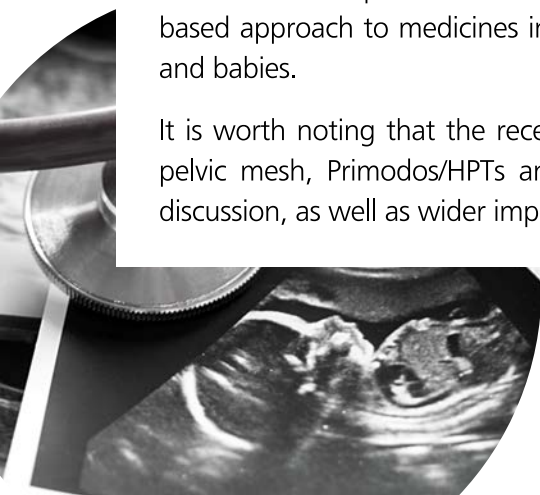
Medication use in pregnancy is fundamental for making pregnancy safer for women and improving short and long-term outcomes for mother and baby. 4 out of every 5 women are prescribed one or more medications in pregnancy, while many more self-medicate with over-the-counter medicines. Despite this, 98% of available drugs have insufficient safety and/or pharmacokinetic data in pregnancy and breastfeeding, including long-term outcomes, with most safety data sourced from pregnancy exposure registries – limited by numbers, completeness of follow-up and lack of appropriate controls.

There is also a critical lack of drugs designed specifically for pregnant women and for obstetric conditions. Pregnancy complications such as preterm labour and preeclampsia are the largest cause of baby deaths and pose health risks for women in later life. For the past 25 years there has been no development in new therapeutics because the pharmaceutical industry has been reticent to invest in new drugs due to the significant risks of being sued if a baby or mother suffers from health defects, even if these do not occur until years after birth. There is a real case for investment as new drugs could mitigate and reduce the rates of infant mortality and health problems for women in later life - but currently the risk falls entirely on the pharmaceutical industry.

In December 2018, the UK Government announced new wide ranging maternity plans to improve safety, quality and continuity of care to halve stillbirths, maternal and infant deaths and serious brain injuries in new-born babies by 2025 (148). New drug development was not included in the announcement. There is a huge unmet need in the space of maternal health globally - a large and largely-untouched market for the pharmaceutical industry - which should cover the use of patients' existing medications; new drugs not specific to pregnancy; and novel drugs targeted at pregnancy-specific conditions.

The UK is extremely well-placed to tackle this. We have a long-established tradition of well-managed clinical trials in pregnancy; a clear priority for maternal health funding; a unified end-to-end system of NHS health care delivery which provides the potential for bringing together the data required for long-term follow-up following drug exposure during pregnancy of both the mother and their child. A specific "Maternity Investigation Plan" (or "Maternity and Paediatric Investigation Plan") could be established to ensure robust, coordinated approaches. If we can demonstrate a willingness to adapt regulation to encourage targeted, well-managed innovation in a way no other country has before - in careful coordination with patient groups such as the Royal College of Obstetrics and Gynaecology's Maternity Voices Partnership and National Childbirth Trust - the UK could become a global beacon for an evidence-based approach to medicines in pregnancy that would improve, and possibly save, the lives of mothers and babies.

It is worth noting that the recent independent Medicines & Medical Devices Safety Review report into pelvic mesh, Primodos/HPTs and sodium valproate (149) is likely to have an impact on this area of discussion, as well as wider impacts on the field of regulation and regulatory science.



4.1.4 Emerging Threats

The MHRA responded to COVID-19 swiftly and pragmatically, demonstrating that regulation can move with pace. By 23rd March 2020 the agency had produced guidance on managing clinical trials during the pandemic, application guidance for COVID-19 clinical trials, new arrangements for MHRA inspections, the specification for ventilators to be used in UK hospitals during the outbreak, and regulatory approval for COVID-19 test kits (150). No mean feat. The EMA and FDA have also responded rapidly to this crisis (151, 152). This regulatory flexibility and rapid response presents the chance to learn what went right that could apply under normal circumstances. Speed matters and innovation in regulatory science will help regulatory agencies to act with appropriate swiftness.

The COVID-19 pandemic reminds us of the importance of being able to develop and deploy diagnostic tests for the virus and medical technologies such as ventilators. The first CE-marked test for COVID-19 did not come from a large company like Siemens or Roche Diagnostics, but a smaller company called Novacyt.

It is worth noting that even before COVID-19 pandemic, the MHRA Innovation Office had reported increasing enquiries about vaccines. It stated that: "Enquiries regarding vaccines seem to be on the increase. Already in 2019, we have received about 20% of total enquiries received in 2018." The office reported vaccine enquiries across a wide range of subjects:

- novel delivery devices, including needle-free delivery
- design of vaccine manufacturing facilities, e.g. the Vaccines Manufacturing Innovation Centre at Harwell
- platform technologies for vaccine manufacture
- synthetic vaccines
- formulations/ stabilisers to eliminate cold-chain requirements
- toxicology programmes for vaccine Marketing Authorisation

The Government's new 'Vaccine Taskforce' - which will be led by Chief Scientific Adviser Sir Patrick Vallance and Deputy Chief Medical Officer Professor Jonathan van Tam, and includes Life Sciences Champion Sir John Bell, AstraZeneca and Wellcome, and will be working closely with the Bioindustry Association - includes "reviewing government regulations to facilitate rapid and safe vaccine trials" as one of its five core strands of activity, emphasising how core the UK's approach to regulation will be in overcoming this pandemic. There may also be learning for the UK from Canada and the US about regulation and a systematic approach to research on vaccine effectiveness (153).

Importantly, while COVID-19 represents the most immediate threat at the time of writing this report, other emerging threats could have a far more significant impact in the near future. For example, antimicrobial resistance presents a clear and present danger that may be far worse than COVID-19 (154).

"Antimicrobial resistance... is a very important area, and we are under-investing in sorting it out. Antibiotics underpin modern medicine - you can't have gut surgery, replacement hips, all sorts of surgery without risking infection. At least 10 million could die every year if we don't get on top of this."

— Dame Sally Davies, then Chief Medical Officer for England (155)

4.2 Evaluating Regulatory Science Initiatives

Antimicrobial resistance cont.

The pharmaceutical industry is committed to tackling AMR working alongside governments and NGOs (156). The UK Government has launched their National Action Plan to tackle antimicrobial resistance (157).

Several publications have argued that regulation is a vital part of the solution to antimicrobial resistance. For example, Livermore et al concluded that "The dwindling supply of new antibiotics largely reflects regulatory and commercial challenges"(158). Also, Metlay et al argued that "Regulatory bodies have roles within collaborative responses to improve the prevention and treatment of infections caused by resistant bacteria. However, in an era of emerging drug resistance, controlled clinical data are often not available to guide regulatory policy"(159).

Brexit may present an opportunity for innovation in regulation to help. After the Brexit transition, there may be opportunities where the UK could show leadership through agile regulation. Advances in regulatory science are needed to help facilitate - and promote investment in - AMR research, develop a sustainable R&D pipeline while keeping patients safe (160, 161).

"Regulation seeks to make such improvement by changing individual or organisational behaviour in ways that generate positive impacts in terms of solving societal and economic problems.

At its most basic level, regulation is designed to work according to three main steps:

1. Regulation is implemented, which leads to changes in
2. The behaviour of individuals or entities targeted or affected by regulation, which ultimately leads to changes in
3. Outcomes, such as amelioration in an underlying problem (162) or other (hopefully positive) changes in conditions in the world"(163).

In 2012 the Organisation for Economic Co-operation and Development (OECD) published a framework for systematically evaluating the performance of regulations and regulatory policies. In order to measure regulatory progress in a meaningful and excreducible way, requires both indicators to measure relevant outcomes (163) and research designs to support inferences about the extent to which a regulation or regulatory policy under evaluation has actually caused any change in the measured outcomes. Indicators may include:

- i) Impact/effectiveness (changes in the problem or other outcomes of concern such as patient safety, mortality);
- ii) Cost-effectiveness (costs for a given level of impact);
- iii) Net Benefits (all beneficial impacts minus all costly impacts); and
- iv) Equity/distributional fairness of impacts.

In addition to equity or distributional concerns, sometimes other outcomes of concern are used as criteria, such as impacts on technological innovation, macroeconomic growth, and employment.



Building on the OECD framework the EMA have developed a conceptual framework for the review of the impact of regulatory science projects on regulatory processes and activities and implications for resources and further iterative improvements.

Key considerations include:

- i) When are results of regulatory science projects matured enough to form a basis to implement changes in regulatory or clinical practice?
- ii) Depending on the types of outcomes, to what extent should results/recommendations from regulatory science projects be validated, scrutinised and peer reviewed in the scientific community before their implementation?
- iii) Should there be a trade-off between timing of implementation and scientific replication/validation?
- iv) Which outcomes should be prioritised for implementation?

Regulatory science projects that will have the highest impact and be an efficient use of resources should be prioritised (162). The EMA established a panel to develop a methodology for the assessment of the impact of regulatory science projects, using the IMI funded PROTECT (Pharmacoepidemiological Research on Outcomes of Therapeutics by a European ConsorTium) study as an example, in order to make recommendations to EMA and its committees for an appropriate action on PROTECT results and evaluate its generalisability to other projects (see case study below). A full report on the regulatory impact of PROTECT was published in 2016 which may serve as a useful model for future evaluative work (164).

Case study:

EMA development of a conceptual framework for the review of the regulatory impact of results of regulatory science projects

Pharmacoepidemiological Research on Outcomes of Therapeutics by a European ConsorTium (PROTECT): partnership of 34 public and private partners supported by IMI Joint Undertaking with funding from European Commission and in-kind contribution from European Federation of Pharmaceutical Industries Associations (EFPIA).

Goal of PROTECT:

Strengthen the monitoring of Benefit / Risk of medicines in Europe by testing methods to collect data on drug utilisation and safety directly from patients, enhance signal detection, evaluate methods to decrease variability of results of pharmacoepidemiological studies and support the integration and presentation of data on benefits and risks (<http://www.imi-protect.eu>)

Impacts of PROTECT:

On innovation, benefit-risk evaluation of medicines and ultimately public health need to be evaluated.

Panel evaluated the PROTECT adverse drug reaction database on key criteria:

INDICATORS

Intended target

- Process (evaluation of adjustment of statistical signals for known ADRs, and of the effect of background restriction on the performance of statistical signal detection) ++
- Behaviour -
- Outcome (Improvement of the efficiency of signal detection by filtering or flagging electronic reaction monitoring reports (eRMRs) for signals related to unlisted reactions only) +++

Impact of change

+++

Maturity

+

Feasibility

+

- Impact on resources
- Acceptability +++
- Alignment with legislation +++

Timing

++

The HM Government White Paper 'Regulation for the Fourth Industrial Revolution' (17) highlighted: "Outcome-focused, 'tech-neutral' legislation involves a focus on the achievement of 'real-world' outcomes for citizens and the environment. It increases flexibility for business on how they can achieve those outcomes, enabling them to find the most efficient way to comply and reducing costs for consumers. It can encourage innovation since firms have greater freedom to try out new ideas, technologies, business models and practices. It can also encourage businesses to think more carefully about how best to achieve a regulatory goal, and not mechanistically follow rules laid out by the regulator. It can also give regulators greater flexibility in how they use their powers to achieve the best outcomes for citizens and the environment. It can enhance stability and predictability for business, as public policy goals are set for the long-term." Achieving this within the context of healthcare setting whilst ensuring patient safety will be crucial.

The Government "will develop tools for regulators to support them to review their guidance, codes of practice and other regulatory mechanisms to ensure that they provide flexibility for those businesses that want to innovate, while ensuring a clear route to compliance for other businesses. We will support business, policymakers and regulators to make effective use of standards where appropriate as a complement to more outcome-focused legislation"(17).

Academic institutions with extensive knowledge of research and outcomes methodology including health economic evaluation could be well placed to develop and evaluate regulatory science initiatives.



4.3. Creating Our Future Workforce

“Underpinning the advancement of the sector is also a need for people with regulatory skills, across industry, the health service and academia as well as regulators, not only to do the core work of medicines development, regulation and delivery to patients but to be resourced to develop standards for emerging technologies and methodologies.”

- Skills Action Plan, Life Sciences Industrial Strategy (110)

Our overview of available training in regulatory science (commonly as regulatory affairs) in the UK highlights just five visible offers - two full MSc programmes (both supported by a single university, although one delivered by TOPRA), a module within an MSc, part of an undergraduate degree, and a CPD offer. The Science Industry Partnership, which takes a leadership role in UK skills policy and lobbying, highlights the need for growth in skills aligned to regulation across a range of educational mechanisms in its 2030 Skills Strategy (165), including “skills updates to reflect technological and regulatory change”, noting particular gaps and shortages in this area within the wider workforce. All of these elements are critical to establish a full portfolio of lifelong, flexible learning to build up national capacity and capability in regulatory science - but they are currently critically underpowered. The Government’s White Paper makes no reference to any form of training.

The FDA offers a huge programme of internships and fellowships via its ORISE partnership, allowing it to target and accelerate key areas of regulatory science which will support its future activities, with successful Fellows often going to work for the regulator and in turn mentoring future Fellows. The EMA is currently designing two curricula through the STARS initiative to support both the professional training of clinical scientists and a broader programme to support a shared post-graduate educational agenda.

The role of TOPRA – the global association for people working in Regulatory Affairs (formerly the British Institute for Regulatory Affairs) is key in this space. They already offer significant training opportunities, not only the noted MSc and PhD programme, but also their own extensive CPD offering and a Competency Framework for regulatory professionals (166) as well as a recently-developed apprenticeship scheme across the UK (167). It will be crucial to leverage their expertise, insights and professional standing to create an appropriately competitive and ambitious, forward-looking training programme for UK professionals.

Developing a coherent UK programme of training in regulatory science will be crucial to delivering workforces for industry, the NHS, policy and academia, providing a sustainable skills pool to ensure that technological innovation in healthcare can be supported effectively, and that the corresponding health and economic benefits are realised while robustly protecting patients. However, we also need to understand what each of these diverse stakeholders relevant to regulatory science in healthcare need - and what they can offer - in terms of training so that we can assemble a clear national framework and strategy.

This training offer does not need to be developed in isolation - through the MHRA we can draw learning from the STARS programme, and we could consider whether any fellowship scheme might include international elements in collaboration with the FDA, TOPRA and other bodies. We can look to offer something distinctive to complement existing international good practice - for example, ORISE fellowships predominantly focus on drug development, so the UK might create focused programmes around healthcare technologies or diagnostics, or methodologies such as PROs in which we have world-leading centres.

Even just within the UK we should look to be as collaborative as possible - whether this is at the level of shared training elements within the increasingly cross-institutional Doctoral Training Programmes funded via UKRI, or whether this is something more ambitious, for example connecting regulators, Catapults, manufacturers and patients with our academic, industry and NHS teams to co-create accelerated frameworks for novel product development.

4.4. Leveraging Assets Across the UK: Infrastructure and Collaboration

For the UK to make best use of its opportunities in future regulation of healthcare innovation - which includes understanding challenges and limitations caused by existing, emerging and future political, technological and disease environments - it must work cohesively and collaboratively, while enabling and taking advantage of specific contexts which might allow accelerated demonstration of benefit. We therefore frame this overview through the lenses of national versus local activities, noting that both will be necessary for success, together with an ongoing commitment to international collaboration.

A. The potential of the UK's national environment for regulation and innovation

The MHRA, NICE, the Scottish Medicines Consortium, and the NIHR all play roles in evaluating technological innovations from the life sciences industry. It is easy to see how someone in an SME, for example, could be confused. On the surface, the NIHR Office for Clinical Research Infrastructure, MHRA Innovation Office and NICE Scientific Advice services all look like a "single" point of entry for the industry. The Accelerated Access Collaborative is beginning to make major inroads on cross-organisational working to support those innovations submitted via its HealthTech Connect platform, but businesses looking for regulatory input into their R&D processes still struggle to find a consistent entry point, and many of them still fear to engage in the first place.

Beyond life sciences, the Government's new Regulatory Horizon Council seeks to ensure that UK regulation keeps pace with innovation and enables it to thrive while safeguarding the public. However, the breadth of its scope means that the council cannot cover any single area - including life sciences - in significant depth. They must identify effective ways of sourcing and integrating diverse multi-stakeholder expertise into rapid and responsive change, while monitoring the effectiveness of their recommended interventions on the ground. The UK must look to leverage the profile and strong engagement practices that existing bodies such as the MHRA as well as industry groups such as ABPI, ABHI and BIVDA have established, while supplementing these

with expert regulatory science support. For example, NICE operate a Horizon Scanning programme which focuses on medicines that have progressed through to clinical trials - connecting this with a robust regulatory science network could allow them to look much further ahead at future medicines, diagnostics and medical devices which need significant regulatory preparation time. The Regulatory Horizons Council will need significant foresight to maintain a competitive UK position, something which cannot just rely on a small group of multi-sector experts, but rather requires deep-rooted and well-integrated sector-specific expertise across multiple representative bodies to channel effective and timely information.

Up to the present time, the US has been recognised as the global leader in regulatory science because the FDA has supported research programmes and centres specifically endorsed to deliver their objectives in a full partnership. This national-level approach has enabled the shared prioritisation of goals and discrete topics for study. In contrast, the UK has no coherent UK strategy for regulatory science in healthcare; no defined models for recognition or funding of excellence, whether in response to agreed priorities or open to ideas; and is arguably under significantly more pressure than the US or Europe to define these sufficiently quickly to maximise the opportunities and mitigate the risks of regulatory divergence post-Transition. Collaboration will be critical if we are to remain competitive.

B. The opportunity of the UK's local ecosystems for regulation and innovation

The UK benefits from expertise across the country and devolved administrations. Moreover, the Government is committed "to ensure all corners of the country drive the economy, and fully benefit from prosperity in years to come"(168). This commitment to the regions comes right from the Prime Minister. In July 2020, Boris Johnson made his first speech outside the steps of 10 Downing Street and promised to unleash "the productive power not just of London and the South East but of every corner of England"(169).

We are increasingly seeing a move within the UK for more integrated local working - this extends from the NHS move from individual Trusts through to Sustainability & Transformation Partnerships (STPs) and eventually

Integrated Care Systems (ICSs); to the work of regions (particularly those with devolved mayoral powers in the Combined Authorities) to develop Local Industrial Strategies. The emergence of major academic-NHS partnerships has been complemented by the growth of the Academic Health Science Networks, while major industry centres of gravity have been endorsed through initiatives such as the Life Science Opportunity Zones. Such areas have become ready-made 'clusters' for innovation - and an ideal springboard for regulatory sciences to flourish in the UK.

Through the ease of collaboration and sharing know-how, clusters foster shared knowledge and talent pools, support collaborative cross-sector innovation, and generate significantly more value than the mere sum of their parts, providing critical accelerators and test-beds to inform broader systems thinking. There are around 15 American centres delivering against the regulatory science agenda (several of which have the CERSI badge from the FDA), with a diverse range of research and education offers. In comparison, the UK has only two visible 'clusters' – geographical concentrations of related disciplines, collaborating organisations and networks – in Birmingham and Newcastle. However, there are many additional flags which could be used to highlight ready-made clusters for regulatory science - the presence of major Memorandums of Understanding with industry bodies such as ABHI and ABPI, which would also connect in Cambridge, Leeds, Manchester and Nottingham. The Office for Life Sciences has also undertaken work to support the regional clusters - including the Northern Health Science Alliance; the Great Western 4; and Midlands Innovation - with their approach to engaging life sciences industries, representing another lens for distinctive but complementary approaches across the UK with shared learning embedded.

Interestingly, the Government's White Paper notes that "We will examine the case for extending the Regulators' Pioneer Fund to local authorities in future, in order to help them support greater testing and trialling of innovations in their area"(17).

C. Retaining international excellence and collaborative approaches

"As we leave the European Union and forge a new path for ourselves, we will continue to play an important role in shaping how regulation is developed internationally. We will collaborate with like-minded international partners to reduce regulatory barriers to trade, through mechanisms such as the adoption of international standards, mutual recognition agreements and free trade agreements. We will encourage our regulators to play an active role in shaping international thinking on how innovation should be regulated."


- 'Regulation for the Fourth Industrial Revolution' White Paper, 2019 (17)

As has been articulated throughout this report, it would be highly damaging for the UK to attempt to operate in isolation of other regulatory systems and international excellence in approaches to supporting emerging technologies and regulatory science. The loss of access to major collaborative programmes such as the EU's Innovative Medicines Initiative (IMI) would put us on the back foot in terms of driving both the science and the regulatory frameworks to enable its rapid translation. In addition, there may be new models for collaboration which could be explored with European and US priorities - for example, could a model of the CERSI badge be extended outside of the US?

The Government's White Paper notes that "Standards open up new markets, connect companies to international supply chains and are a passport to trade. As a global leader in standards, guidance and good practice, we will work with international partners and multilateral fora to develop and promote standards for new and emerging technologies, capturing knowledge from publicly-funded R&D pilots, testbeds and technology adoption programmes"(17). The approach we take to sharing evidence and demonstrating an open, collaborative approach to informing regulation will decide how much of a voice we have in enabling our innovators and life sciences industry to access and compete in a global market.

The background is a complex digital composition. It features a grayscale image of a city skyline at night, with lights reflecting on water. Overlaid on this is a glowing, wireframe brain, suggesting neural activity or data processing. A large, solid purple circle on the left side contains the word 'Conclusion'. Another purple circle is partially visible at the bottom right. The right side of the image is filled with a grid of small purple dots, some of which are arranged in a curved path. Thin white lines and dots connect various points across the image, creating a network-like structure.

Conclusion



Regulatory science is more important than ever before. With its departure from the EU, the UK must strike the right balance between taking control of its regulatory frameworks without adding any delay or further risks to patients receiving new interventions, diagnostics and treatments, as well as avoiding adding unwarranted cost to R&D. Striking a balance which allows us both to be globally competitive as well as internationally collaborative – enabling ground-breaking products developed here to be efficiently deployed around the world - will not be straightforward, and finding the best outcomes will rely on forward-thinking UK innovation in regulatory science.

Advances in regulatory science are needed to develop and evaluate new approaches to regulation. This report argues that the UK should take a coordinated approach to foster and prioritise innovation in regulatory science and build a corresponding workforce to ensure its sustainability and continuing evolution. We should also actively support the emergence of both existing and new clusters in regulatory science, drawing on world-leading academic expertise connected with increasingly integrated regional ecosystems connecting industry, policy and crucially our unique NHS.

These actions will put the nation in a leadership position for regulation, which will attract the most exciting ideas and key resources from global industry; will further accelerate the co-creation and adoption of innovation by the NHS; will create vibrant, well-networked and multi-disciplinary academic insights into tools, technologies and methodologies; encourage an enabling and collaborative approach from regulators and policy-makers; and most importantly embed the support and guidance of our patients, communities and citizens through a clearer, central voice in the design, development and delivery of innovative new treatments, diagnostics and medical devices.

The UK's current situation brings incredible complexities, challenges and risks - but our uniquely collaborative and dynamic national ecosystem for regulatory science is more than capable of rising to these and ensuring this is a time of unique opportunity and benefit.

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The background features a grayscale image of several old, leather-bound books standing on a shelf. The spines of the books are visible, with some showing the word 'CYCLOPÆDIA' and others 'CAS = CHR'. Overlaid on the left is a large teal circle. In the top right corner, there is a gray rectangular area with a grid of teal dots. A diagonal line of teal dots runs from the top right towards the bottom center. In the bottom right corner, there is another teal circle.

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