Medicines & Healthcare products Regulatory Agency

AGENDA FOR BOARD MEETING HELD IN PUBLIC

10:00 am – 12:30 pm on Tuesday 21 May 2024

Chair: Professor Graham Cooke

	AGENDA ITEM	**PURPOSE**	**PRESENTER**
10:00	INTRODUCTION		
	1. What is the purpose of this meeting, who are the Board Directors and are there any absences?	Information	Chair
	2. Are there any new Declarations of Interest?	Information	All
	3. What were the minutes and actions from the last meeting?	Approval	Chair
	AGENCY PERFORMANCE		
10:15	4. What are the most important current activities and priorities from the CEO's point of view?	Context	June Raine
10:30	5. What was the financial and people performance of the MHRA for this year up to 31 March 2024?	Assurance	Rose Braithwaite
10:45	6. How effectively is the MHRA addressing performance on established medicines, and how will a sustainable established medicines function be established?	Assurance	Julian Beach
	PATIENT SAFETY		
11:00	7. What is the Criminal Enforcement Unit's approach to identification, prioritisation and reduction of the threat posed by the illegal trade in human medicines?	Strategic Direction	Alison Cave
	SCIENCE, RESEARCH & INNOVATION		
11:20	8. How will the new legislation strengthen the safety of medical devices?	Strategic Direction	Laura Squire
11:40	9. How will the regulation of in vitro diagnostics change to support safe access to these innovative products and how will wider engagement take place?	Strategic Direction	Laura Squire
	ASSURANCE		

12:00	10. What assurance can be provided by the Patient Safety and Engagement Committee?	Assurance	Mercy Jeyasingham
12:10	11. What assurance can be provided by the Audit & Risk Assurance Committee?	Assurance	Michael Whitehouse
	EXTERNAL PERSPECTIVE		
12:20	12. What questions do members of the public have about the items on this Board Meeting Agenda?		Chair
12:30	CLOSE OF MEETING		

MHRA Board Declarations of Interest – May 2024

The MHRA Board is responsible for advising and agreeing the strategic direction of the Agency, endorsing the Agency's recommendations to Ministers on key financial and performance targets, and advising on and monitoring plans to ensure those targets are met.

The Board supports the Chief Executive Officer in the effective delivery of services and overall performance by providing leadership, developing strategy, advising on the delivery of policies, maintaining high standards of corporate governance, scrutinising performance and ensuring that controls are in place to manage risk.

The Board and its Non-Executive Directors have no involvement in any regulatory decisions affecting medicines, medical devices or any other products or services delivered by the Agency. These decisions are the responsibility of the Chief Executive Officer, supported by the Executive Committee.

Name and MHRA Role	Name of Other Company or Organisation	Nature of interest	Paid	Current
Professor Graham Cooke Non-Executive Director & Interim Co-Chair	Imperial College NHS Trust and Chelsea & Westminster NHS Foundation Trust	Honorary NHS Consultant	Yes	Yes
	NERVTAG	DHSC NERVTAG committee member	No	Yes
	NIHR	NIHR Research Professor	Yes	No
	NIHR	Influenza platform trial in the UK	Yes	Yes
	NIHR	Chair DSMB (PROTECT-V trial)	No	Yes
	Pfizer	Pneumonia study with Imperial College Healthcare Partners	Yes	No
	30 Technology Ltd	Consultant/Advisor	Yes	Yes
	DNAnudge Ltd	Consultant/Advisor	No	Yes
	Seventh Sense Biosystems	Consultant/Advisor	Yes	No
	Sanofi CoV	Chair of End Point Review Committee for vaccine trial	Yes	Yes
	WHO	Member of Committee for Selection and Use of Essential Medicines	No	Yes
Dame June Raine Chief Executive	World Health Organisation (WHO) Committee on Safety of Medicinal Products	Member	No	Yes
Dr Marc Bailey Chief Scientific Officer	Nokia Corporation	Ex-employee shareholder	No	Yes
Dr Junaid Bajwa Non-Executive Director	Microsoft	Employed (Chief Medical Scientist at Microsoft Research), Shareholder	Yes	Yes

Name and MHRA Role	Name of Other Company or Organisation	Nature of interest	Paid	Current
	Merck Sharp and Dohme	Ex-employee shareholder	No	Yes
	Ondine biomedical	Non-Executive Director	Yes	Yes
	Novartis Industry Council	Advisory to UK Pharma Exec	Yes	Yes
	UCLH	Non-Executive Director	Yes	Yes
	Whittington NHS Trust	Associate Non-Executive Director	Yes	Yes
	NHS	GP, Physician (Sessional)	Yes	Yes
	Nuffield Health	Governor (NED)	Yes	Yes
	Nahdi Medical Corporation	Non-Executive Director	Yes	Yes
	DIA Global	Board Member	No	Yes
Julian Beach Interim Lead, Healthcare Quality & Access	None	N/A	N/A	N/A
Liz Booth Chief People Officer	None	N/A	N/A	N/A
Rose Braithwaite Chief Finance Officer	Mental Health Foundation	Treasurer	No	No
Amanda Calvert Non-Executive Director & Interim Co-Chair	Astrazeneca	Ex-employee shareholder Immediate family member	No	Yes
	Quince Consultancy Ltd	Provides consultancy services including companies in the healthcare sector.	Yes	Yes
	Athenex Pharma	Quince Consultancy providing strategic consultancy on oral oncology chemotherapy platform. ILAP applicant and Marketing Authorisation applicant.	No	No
	Cambridge Judge Business School	Member of Advisory Board	No	Yes
	Duke Street Bio	Advisory / Consultant	Yes	Yes
	Fennix Pharmaceuticals	Founder of start-up company planning to develop oral chemotherapy product into Phase 2 trial. Not yet trading.	No	No
	High Value Manufacturing Catapult	Non-Executive Director	Yes	Yes
Dr Alison Cave Chief Safety Officer	None	N/A	N/A	N/A
Dr Paul Goldsmith Non-Executive Director	Closed Loop Medicine Ltd	Shareholder, director & employee; MA submission	Yes	Yes
	Lanthor Ltd	Book publishing and medico-legal reports	Yes	Yes
	Ieso Digital Health	Shareholder	No	Yes
	Institute of Global Health Innovation (IGHI), Imperial College, London	Visiting Professor	No	Yes

Name and MHRA Role	Name of Other Company or Organisation	Nature of interest	Paid	Current
	MDU Ltd	Director	Yes	No
	MDU Investments Ltd	Director	Yes	No
	NHS	Consultant Neurologist	Yes	Yes
	NHS	Clinical Senate Member	No	Yes
	Radix Big Tent Foundation	Trustee	No	Yes
	Sleepstation	Co-founder of original programme, 2012-2014	No	No
Claire Harrison Chief Digital & Technology Officer	None	N/A	N/A	N/A
Haider Husain Non-Executive Director	Healthinnova Limited	Chief Operating Officer	**Paid**	**Current**
	Milton Keynes University Hospital NHS Foundation Trust	Non-Executive Director	Yes	Yes
	British Standards Institute	Chair – TC304 Healthcare Organisation Management Committee	Yes	Yes
	Madad UK	Trustee	No	Yes
	World Wars Muslim Memorial Trust	Trustee	No	Yes
	Microsoft Corp	Ex-employee shareholder	No	Yes
	BBC	Family Member	No	Yes
	NHS Buckinghamshire, Oxfordshire and Berkshire West Integrated Care Board	Digital and Data Advisor / Member of the System Productivity Committee	No	Yes
Mercy Jeyasingham MBE Non-Executive Director	NHS South West London Integrated Care Board	Non-Executive Member	Yes	Yes
Raj Long Non-Executive Director	Gates Foundation	Employee – Deputy Director	Yes	Yes
	Bristol-Myers Squibb	Ex-Employee Shareholder	Yes	Yes
	RESOLVE (Sustainable solutions to critical social, health, and environmental challenges)	Scientific Advisory	No	Yes
	Novartis	Ex-Employee Shareholder	Yes	Yes
	BioNTech Global Health (non-profit)	Strategic Advisory for only Sub-Saharan Africa Public Health for Equitable Access	Yes	Yes
	Gates Venture – EC Innovative Medicines Initiative (IMI) Non-Product – IMI European platform for Neurodegenerative Disorders	Advisory	Yes	Yes
	WHO – Sustainable COVAX Manufacturing Strategy for Regional Health Security	Advisory Expert	No	Yes
	UK Health Security Agency	Associate Non-Executive Board Member	Yes	Yes

Name and MHRA Role	Name of Other Company or Organisation	Nature of interest	Paid	Current
	EU Innovative Health Initiatives (IHI)	Advisory Expert for this EU public-private partnership funding health research and innovation funded by European Commission	Yes	Yes
Nicola Rose Interim Executive Director, Science and Research	Tbc	Tbc	Tbc	Tbc
Laura Squire OBE Chief Healthcare Quality & Access Officer	None	N/A	N/A	N/A
Michael Whitehouse OBE Non-Executive Director & Interim Co-Chair	South East Coast Ambulance Services NHS Foundation Trust	Deputy Chair & Senior Independent Non-Executive Director Chair of Audit Committee Chair of Charities Committee	Yes	Yes
	Cruse Bereavement Charity	Trustee Chair of Finance and Audit Committee	No	No
	Republic of Ireland Audit Office	Member of Audit Committee	No	No
	National Audit Office	Board Member and Chief Operating Officer until 17 April 2017	No	No
Glenn Wells Chief Partnerships Officer	None	N/A	N/A	N/A

Medicines and Healthcare products Regulatory Agency

Minutes of the Board Meeting Held in Public on 19 March 2024

(10:00 – 12:00)

MHRA, 10 South Colonnade, Canary Wharf E14 4PU

Present:

The Board

Professor Graham Cooke	Non-Executive Director & Interim Co-Chair
Dr June Raine DBE	Chief Executive
Dr Marc Bailey	Chief Science, Research & Innovation Officer
Julian Beach	Interim Executive Director, Healthcare Quality & Access
Liz Booth	Chief People Officer
Rose Braithwaite	Chief Finance Officer
Amanda Calvert	Non-Executive Director & Interim Co-Chair
Dr Alison Cave	Chief Safety Officer
Dr Paul Goldsmith	Non-Executive Director
Claire Harrison	Chief Digital & Technology Officer
Mercy Jeyasingham	Non-Executive Director
Dr Glenn Wells	Chief Partnerships Officer
Michael Whitehouse OBE	Non-Executive Director & Interim Co-Chair
Dr Junaid Bajwa	Non-Executive Director
Raj Long	Non-Executive Director

Others in attendance

Rachel Bosworth	Director of Communications and Engagement, MHRA
Carly McGurry	Director of Governance, MHRA
James Pound	Deputy Director, Standards & Compliance, MHRA (for item 6)
Alicia Ptaszynska-Neophytou	Head of Executive Support, MHRA

INTRODUCTION

1. Item 1: What is the purpose of this meeting and who are the Board Directors?

1.1. Professor Graham Cooke opened the meeting. The Chair set out his expectations and priorities for this Board meeting held in public which was being live streamed to the registered audience and recorded. The Chair welcomed everyone to the meeting, including a broad range of observers including patients and members of the public, representatives of patient

groups, healthcare professionals, government officials, industry, media and MHRA staff.

2. Item 2: Are there any Apologies or Declarations of Interest?

2.1. Apologies were received from Haider Husain, Non-Executive Director; Kathryn Glover, Deputy Director Medicines Regulation & Prescribing, DHS; Alison Strath, Chief Pharmaceutical Officer for Scotland; Greig Chalmers, Head of Chief Medical Officer's Policy Division in the Scottish Government; and Cathy Harrison, Chief Pharmaceutical Officer for Northern Ireland.

2.2. The Board reviewed the Declarations of Interest (DOIs) for all MHRA Board members. Dr Paul Goldsmith declared that he was no longer a shareholder in Summit, and had acquired/established a book company. There were no other new declarations this month. The Chair reviewed the DOIs and was satisfied that there were no conflicts of interest preventing any Board Member from participating in the full agenda of this meeting.

3. Item 3: What were the minutes and actions from the last meeting?

3.1. The Board reviewed the minutes and actions from the last meeting. No comments were received. The minutes were accepted as an accurate record of the last meeting.

AGENCY PERFORMANCE

4. Item 4: What are the most important current activities and priorities from the CEO's point of view?

4.1. Dr June Raine presented the Chief Executive's monthly report, which covered the following:

(i) **Partnerships** – including the cross-Agency Return to Green (RtG) programme established to eliminate backlogs in frontline service activities and lead to sustainable services;

(ii) **Digital & Technology** – including updates on the RegulatoryConnect Programme Business Case; and international recognition enhancements;

(iii) **Science, Research, and Innovation** – including updates on cross-Agency work on neurodegeneration; anti-microbial resistance grant funding;

(iv) **Patient Safety** – including the production and cascade of a letter from all four Chief Medical Officers regarding the harms of valproate.

4.2. The Board thanked Dr Raine for her report and provided comments relating to sodium valproate communication, the Innovative Devices Access Pathway (IDAP) pilot, and the visit by the US Food and Drug Administration (FDA).

5. Item 5: What was the financial and people performance of the MHRA for this year up to 31 January 2024?

5.1. The Board considered a report describing the financial and HR performance of the MHRA for this year up to 31 January 2024. The Board noted the underspend of £11.6m compared to budget and a Capital underspend of £3.3m compared to budget, and the re-profiling of £1m of the Innovation funding from this financial year into 2024/25.

5.2. The Board provided comments relating to the vacancy rate and key skills required within the Agency, predictability of spend for RegulatoryConnect, and Agency performance monitoring.

6. Item 6: How effectively is the MHRA addressing performance on established medicines, and how will a sustainable established medicines function be established?

6.1. The Board considered a paper describing how the Agency was addressing performance on established medicines. Progress had been made to clear backlogs, review resource requirements and amend processes.

6.2. The Board provided comments on key performance indicators and productivity, staff wellbeing and turnover, and prioritisation of work. It was agreed that there was a need for an operating model which would deliver sustained performance.

6.3. The Board thanked Mr Beach and the established medicines team for their work.

Action 114: Deliver an operating model for established medicines which will deliver sustained performance. Julian Beach

7. Item 7: How effectively is the MHRA maintaining its performance on clinical trials and how are plans for the new regulatory system progressing?

7.1. James Pound joined the meeting in person.

7.2. Dr Bailey gave thanks to MHRA staff who had eliminated the clinical trials applications backlog. As of March 2024, redeployed staff from across the Agency had returned to their operational areas.

7.3. The Board considered the paper summarising current performance for clinical trials and provided comments relating to stakeholder feedback received, the Lord O'Shaughnessy report, and work with national and international partners.

The Board discussed the proposed structure of the new operating model and demand forecasting.

Addition to action 101: Explore developing a model for a clinical trial hub and lead coordinator. James Pound

Action 115: Clinical trials notification scheme to be added to Board forward plan. Carly McGurry

PATIENT SAFETY

8. Item 8: How is the Yellow Card Biobank pilot progressing, to help the Agency move towards our goal of personalised medicines?

8.1. The Board considered a paper informing of progress on the Yellow Card Biobank pilot activities.

8.2. The Board provided comments relating to patient diversity and recruitment, engagement in primary and secondary care settings, and stakeholders including Genomics England.

Action 116: Add Yellow Card Biobank pilot to Board forward plan and link with clinical trial discussions on innovators. Alison Cave

SCIENCE, RESEARCH & INNOVATION

9. Item 9: How well are the Agency's innovation pathways facilitating access to new innovative products and how are these pathways being optimised?

9.1. The Board considered a paper on the two Innovative Pathways, the Innovative Licensing and Access Pathway (ILAP) and Innovative Devices Access Pathway (IDAP).

9.2. The Board provided comments relating to the sustainability of the innovation pathways, supporting stakeholders through the Agency's innovation pathways, and alignment with MedTech and diagnostics. It was agreed that a deep dive would be scheduled to agree areas of focus across the two innovation pathways.

Action 117: Provide an update on innovation pathways to future Board meeting. James Pound

ASSURANCE

10. Item 10: What assurance can be provided by the Patient Safety and Engagement Committee?

10.1. The Board considered an assurance report from the Patient Safety and Engagement Committee (PSEC). The PSEC met on 15 February 2024 and discussed patient engagement in the review of isotretinoin and the involvement of patients within the development of the New Medical Device regulations. The discussion between the Chair of PSEC and the Patient Safety Commssioner had taken place. The forward plan for the Committee had been scoped.

10.2. The Board considered the report and provided comments relating to risk communications. The Board noted the report for assurance.

11. Item 11: What were the results of the 2023 People Survey and what actions are being taken to address these?

11.1. The Board considered a report on the People Survey results from 2023.

11.2. The Board provided comments relating to productivity, staff workload and productivity, and raising concerns campaigns. Mercy Jeyasingham confirmed that she was a Raising Concerns Champion and was visible to staff in her role.

11.3. The Board noted the report for assurance.

Action 118: Additional work on Raising Concerns Champions to be carried out with Mercy Jeyasingham. Liz Booth

EXTERNAL PERSPECTIVE

12. Item 12: What questions do members of the public have for the MHRA Board?

12.1. The Board answered a range of questions which had been submitted by members of the public before and during the meeting. These questions concerned innovative pathways, finance and HR performance and long term sickness rates, the definition of established medicines, reward and recognition vouchers, clinical trials criteria, and a feedback survey on Board effectiveness.

Action 119: Undertake a review of long-term sickness rates. Liz Booth

Action 120: Feedback survey for Board effectiveness to be created, including external stakeholders. Liz Booth

ANY OTHER BUSINESS

13.1 No items of other business were raised and the Chair closed the meeting.

ACTIONS FROM MHRA BOARD MEETING IN PUBLIC – 19 March 2024

The actions highlighted in red are due this month

Action Number	Action	Owner	Date	Status
Carried Forward from previous meetings				
29	16/03/21: Present an Agency Science Strategy to the Board. 15/11/22: Revise the Science Strategy to include clear prioritisation; and greater inclusion of in-house expertise on behavioural science with a complementary expert group. Include vaccines work as a specific area of expertise, alongside biologics and the UK Stem Cell Bank, to create a distinctive offering to make the UK an internationally recognised centre of excellence in this field. A review of scientific committees should also be undertaken. Present a further update to the Board in March 2023. 21/03/2023: Science Strategy to be presented to the Board in July. 11/07/23: Present an update to the Board on progress against each of the themes in the Science Strategy at the end of 2023.	Marc Bailey	~~21/09/21~~ ~~16/11/21~~ ~~17/05/22~~ ~~15/11/22~~ ~~21/03/23~~ ~~11/07/23~~ ~~12/12/23~~ 09/07/24	
70	18/01/22: Develop and present a Data Strategy to the Board.	Alison Cave & Claire Harrison	~~17/05/22~~ ~~18/10/22~~ ~~15/11/22~~ ~~18/04/23~~ ~~12/12/23~~ ~~19/03/24~~ 18/06/24	
73	15/02/22: Develop a Sustainability Strategy.	Glenn Wells	~~17/01/23~~ ~~16/01/24~~ ~~19/03/24~~ 09/07/24	
101	11/07/23: Action: Present an update to the Board on the performance and proactive communications and engagement activities related to clinical trials which will maintain	Marc Bailey	~~21/11/23~~ ~~16/01/24~~ 09/07/24	

	trust in the Agency from industry and research customers. 19/09/23: Provide an update to the Board in November 2023 on the progress of the new clinical trial process pilot. Prepare a plan for training and upskilling of staff to increase resilience across the Agency. 21/11/23: Provide the Board with an update on the new proposed Clinical Trials process. Undertake a review of any other backlogs in the Agency. 16/01/24: Present a paper to the Board containing operational detail including a clearly defined budget; how this is resourced (skill and headcount); and demand estimation over the next year and beyond. 19/03/24: Explore developing a model for a clinical trial hub and lead coordinator.			
104	19/09/23: Develop a reputation strategy for the Agency with reputation index measures.	Rachel Bosworth	~~21/11/23~~ ~~19/03/24~~ 09/07/24	
106	21/11/23: Provide the Board with an update on the work of the Criminal Enforcement Unit. 16/01/24: The enforcement strategy should be reviewed in light of the Windsor Framework and the Falsified Medicines Directive.	Alison Cave	21/05/24	On agenda
107	21/11/23: PSEC to review the electronic Patient Information Leaflet	Mercy Jeyasingham / Alison Cave	19/03/24	Completed
108	21/11/23: Provide the Board with an update on the Trusted Research Environment	Alison Cave	~~19/03/24~~ 09/07/24	
109	21/11/23: Provide an update on the People Survey results to the Board	Liz Booth	19/03/24	Completed
110	21/11/23: Provide a further update on the progress of the Health, Safety & Wellbeing Strategy to the Board.	~~Marc Bailey~~ Nicola Rose	21/05/24	
111	16/01/24: The budget and financial reporting should be	Rose Braithwaite	21/05/24	On agenda

	linked to the Agency's statutory functions in the Performance Report. Provide the Board with further details on the decrease in CPRD income.			
New Actions				
114	19/03/24: Deliver an operating model for established medicines which will deliver sustained performance.	Julian Beach	21/05/24	On agenda
115	19/03/24: Clinical trials notification scheme to be added to Board forward plan.	Carly McGurry	21/05/24	Completed
116	19/03/24: Add Yellow Card Biobank pilot to Board forward plan and link with clinical trial discussions on innovators.	Alison Cave	21/05/24	Completed
117	19/03/24: Provide an update on innovation pathways to future Board meeting.	James Pound	09/07/24	
118	19/03/24: Additional work on Raising Concerns Champions to be carried out with Mercy Jeyasingham.	Liz Booth	21/05/24	
119	19/03/24: Undertake a review of long-term sickness rates.	Liz Booth	21/05/24	
120	19/03/24: Create a feedback survey for Board effectiveness, including external stakeholders.	Liz Booth	09/07/24	

Medicines & Healthcare products Regulatory Agency

BOARD MEETING HELD IN PUBLIC

21 May 2024

Title	**What are the most important current activities and priorities from the CEO's point of view?**
Board Sponsor	June Raine
Purpose of Paper	Context

What are the most important current activities and priorities from the CEO's point of view?

'TOP 10' HEADLINES

- Our high standard of performance on clinical trial applications continues to meet targets with an increase in first-in-human applications and intensive work on the new legislation
- Good progress reducing the backlog of established medicines applications continues, with the Commission on Human Medicines meeting on a high number of generic applications
- A major grant has been awarded for antimicrobial resistance research on novel bacterial vaccines, improved diagnostics and novel biologicals such as microbiome and phage
- WHO expert committee has endorsed a new international standard for golimumab (for arthritis) following our collaboration with European Directorate for Quality of Medicines
- We approved cabotegravir (Apretude), a new long-lasting injection for pre-exposure prophylaxis for HIV which can be given every 2 months instead of taking 'PrEP' via daily tablets
- We published patient safety alerts for finasteride (Propecia, Proscar) and montelukast (Singular), in both cases to improve knowledge of side effects, particularly psychiatric
- We are preparing the evidence requirements for a safety review into the antipsychotic medicine clozapine after concerns about its toxicity and questions about blood monitoring
- The Clinical Practice Research Datalink, our real-world data service supporting public health studies, has achieved Trusted Research Environment status
- We published our strategic approach to AI, following the Pro-Innovation Regulation for AI Whitepaper & launched our AI Airlock, a regulatory sandbox
- The RegulatoryConnect portal, live since the end of March, has received very positive feedback with access from 2,500 users of self-service tools such as 'Track my Case.'

SCIENCE, RESEARCH, AND INNOVATION

Control testing for blood safety

1.1 Blood products are made from human blood donations. Over 50 different products are widely used in the UK to treat acute blood loss, blood disorders and conditions such as anaemia or cancer. In 2023, we performed laboratory tests on almost 750 batches of blood products to ensure that they met the product specifications in the marketing authorisations. This covered 85% of the batches that were used in the UK, the equivalent of approximately 5 million doses. Additionally, we tested the >3000 plasma pools that were used to manufacture these batches, collected from approximately 12 million blood donations abroad, screening for HIV, Hepatitis and Parvovirus to prevent a recurrence of contaminated blood products.

Antimicrobial resistance

1.2 A Memorandum of Understanding has been signed that provides additional financial support for 2 programmes of work from DHSC. Through UK Vaccine Network approximately £1 million will support the CEDR activities over the next 4 years and through the Global AMR Innovation Fund approximately £1.7 million over 3 years will support our regulatory research activities focused on novel bacterial vaccines, improved diagnostics and novel biologicals such as microbiome and phage. Funding also supports additional resource in HQA. Scientists from the Diagnostics Team attended the European Society of Clinical Microbiology and Infectious Disease annual meeting in Barcelona in April to hear about developments in AMR including anti-microbial development and diagnostics. Whilst attending, they were invited to accompany a WHO team visiting Georgia to attend a workshop on Phages, which represent a novel biological medicine approach to address increasing frequency of AMR.

Pandemic preparedness

1.3 Several MHRA scientists have been invited to participate in a 10 partner European Horizon Consortium developing interventions for Non-Zaire Ebola and Marburg Viruses (EBOMAR) which is currently under review; the team will be contributing their expertise in biological standardisation of high consequence viruses for pandemic preparedness.

Golimumab international standard

1.4 An international standard for Golimumab, a fully human anti - tumour necrosis factor (TNF) monoclonal antibody approved for several indications including rheumatoid arthritis and ulcerative colitis was successfully established by the WHO expert committee at its March 2024 meeting. This material will support calibration of secondary standards, method development and qualification/validation of bioassays and assays in use for clinical monitoring to enable better disease outcomes in patients treated with the antibody. This was a successful collaboration with the European Directorate for Quality of Medicines (EDQM) under a revenue share contract and will also support the provision of a reference standard for EDQM.

Reference materials

1.5 We have completed “A Collaborative Study to Evaluate the Proposed First WHO International Reference Panel for Adventitious Virus Detection in Biological Products” using high-throughput Sequencing Technologies. Based on the data and report submitted, the WHO panel approved the virus panel to be used as reference material. This study will also be published as a scientific article. New WHO International Standards for HIV-1 p24 antigen and Thrombin activatable fibrinolysis inhibitor (TAFI) plasma became available through our biological reference materials catalogue for the first time along with the 3rd WHO International Standard for Protein S, plasma as a replacement for the 2nd International Standard.

Quality assurance of biological medicines

1.6 Control Testing representatives participated in meetings organised by the European Directorate for the Quality of Medicines and HealthCare (EDQM, a Directorate of the Council of Europe): (i) Drafting and revision of the written quality standards of the European Pharmacopoeia for human vaccines; (ii) Co-ordinate and oversee the work of a network of Official Medicines Control Laboratories (OMCLs) from >40 members states, ensuring effective and independent quality control of medicines in Europe, the UK and beyond.

NHS Chief Scientist Office Knowledge Transfer Partnership

1.7 Members of staff attended a meeting at the LGC-National Measurement Laboratory laboratories at Teddington at the launch of the NHS Chief Scientist Office Knowledge Transfer Partnership. This represented the start of an 18-month period where 5 clinical scientists from NHS laboratories will work with measurement scientists at NPL, LGC and MHRA laboratories at South Mimms on projects to improve measurement of specific problematics analytes in patient diagnostics. For the measurement scientists at South Mimms, it provides us with better understanding of diagnostics in a routine testing lab.

Metrology in Chemistry and Biology

1.8 The Head of the Diagnostics team attended the Bureau Internationale de Poids et Mesures (BIPM) in Paris to participate the Nucleic Acids Working Group of the Consultative Committee for Amount of Substance: Metrology in Chemistry and Biology (CCQM) 21-22 April. This group brings together representative from National Metrology Institutes from around the world to discuss approaches to establish reference methods for measurement of escalating disease pathogens and cancer genomic diagnoses. The group recognises the value of WHO International Standards.

Microbiological Society

1.9 Scientists from the Diagnostics and Vaccines teams attended the Microbiological Society annual conference in Edinburgh in April. Scientific progress made by the teams at the Science Campus in South Mimms, particularly in areas of Escalating Disease and Influenza were presented in a series of poster and short oral presentations. Furthermore, the conference provided the opportunity to renew and establish scientific links with academic experts from across the UK working in the areas of infectious disease and AMR.

Next Generation Organ-on-a-Chip Technologies grant funding

1.10 The Biotherapeutics and Advanced therapies team maintains its partnership with Queen Mary University of London and will collaborate on a successful “Centre for Doctoral Training in Next Generation Organ-on-a-Chip Technologies” application and a large grant on Micro-manufacturing of tissue patterned organ-chips for accelerated deployment of new medicines. Organ-on-a-chip technologies have the potential to transform the pre-clinical testing pipeline and accelerate the delivery of new medicines, enabling more accurate and reliable evaluation of drug candidates before they progress to human trials. Our regulatory expertise will provide the team with valuable insights into the navigation of the complex landscape of pre-clinical testing regulations.

Publication on cell therapies

1.11 Scientists in the Biotherapeutics and Advanced Therapies Team were senior authors on a review article published in the *Journal of Translational Medicine* on the *Mechanism of action, potency and efficacy: considerations for cell therapies.* The article focused on some of the most challenging aspects in the development of cell therapies, determining the mechanism of action, potency and efficacy of the products. The authors reviewed the information from approved cell therapy products and presented key scientific perspectives which will be useful for developers of this key class of therapy.

Biological reference material publication

1.12 An article was published in *AAPS Journa*l by our Formulation Science experts in collaboration with Purdue University, US: "*Predicting the stability of lyophilized human serum albumin formulations containing sucrose and trehalose using solid-state NMR spectroscopy: effect of storage temperature on 1HT1 relaxation times*". This study is important for our provision of stable biological reference materials and adds useful information into what is a regularly debated question as to the most appropriate stabiliser to use in freeze drying and how to assess the impacts.

UK Stem Cell Bank

1.13 The UK Stem Cell Bank (UKSCB) is the UK's only public repository for storage, banking and distribution of human embryonic stem cell lines and was established to facilitate access to high quality cells and to ensure their ethical use. These cells can be used to prepare innovative cell-based therapies. The bank was recently successfully audited by the Human Tissue Authority to ensure compliance with the HTA 2007 regulations for the use of cells for human application. As a result of considerable effort by the UKSCB team, the HTA auditors were impressed with all aspects of the UKSCB quality management system and work quality, such that we have been successful in retaining our HTA2007 licence.

Quality management systems

1.14 There is an ongoing programme of work to implement ISO 9001 Quality Management System across the wider Agency. A new Cross-Agency Quality Management Group has been established containing members of the Governance Group, the Science and Research Quality Assurance team and CPRD within Safety and Surveillance, with the role of the group being to develop and implement the requirements for the wider consistent Agency system. An early stage of this has been the Science & Research QA team members using existing S&R training modules for the ISO 9001 quality system to provide training sessions for Agency staff. Recordings have been made available as resources to help roll out the system across the Agency. Discussions are continuing to develop the requirements to be compliant for ISO 9001 and to address recommendations from BSI who audit the Agency against this standard.

HEALTHCARE ACCESS

Cabotegravir for PrEP

2.1 We approved two new formulations of cabotegravir (Apretude 30 mg film-coated tablets and Apretude 600 mg prolonged-release suspension for injection) to help prevent sexually transmitted HIV-1 infection in adults and adolescents who are at an increased risk of infection. Tablet-based pre-exposure prophylaxis or 'PrEP' is already available for those at risk. Cabotegravir long-acting injection is the first injectable treatment approved to help prevent HIV-1 infection in the UK.

Fosdenopterin for MoCD

2.2 We authorised fosdenopterin (Nulibry) for GB through the EC Decision Reliance Procedure for Molybdenum cofactor deficiency (MoCD) Type A. This is a rare genetic disorder in which the body is not able to produce cPMP (cyclic pyranopterin monophosphate). This causes a build-up of a sulphite which is toxic and damages the brain. MoCD is usually diagnosed in babies once they are born and causes symptoms such as seizures, involuntary movements and difficulties in feeding.

Established medicines performance

2.3 The Established Medicines backlog continues to be on track with projected clearance by the end of September. We are preparing to conduct a three-month review of the changes in processes we have introduced, with targeted questions for collation in June. We have a continued focus on industry engagement with both the BGMA and the other trade associations, ABPI, BIA, EMIG and PAGB, with the ongoing Established Medicines Working Group and webinars where we have broad engagement with over 350 attendees. We currently have contingent workers and we are continuing Professional Services contracts and exploring feasibility of additional contracts. Longer term recruitment is underway to right-size the organisation and we have had a large number of applications for the Pharmaceutical Assessor campaign.

International Recognition Procedure

2.4 The International Recognition Procedure (IRP) continues to successfully meet the target timeframes, with 100% of applications for Route A being approved within the stipulated 60-day timeframe. Decisions for the first wave of Route Bs are expected in June. The team delivered the first IRP webinar post-launch of the procedure, with 573 attendees and 182 questions submitted. Industry engagement with the IRP is evident with the increased number of requests for pre-submission meetings. A review of the process and tools to support industry has resulted in a new version of the eligibility checker. This has been developed and will be available for user testing in May. A checklist for IRP submissions will also be made available in the coming months, which is aimed at reducing validation issues associated with IRP submissions.

Borderline team

2.5 The Borderlines team host a twice-yearly meeting with stakeholders, historically under the auspices of Common Advertising Practice (CAP). This is a stakeholder engagement half-day event, and our attendees include representatives from OGDs / regulators including Health & Safety Executive, Food Standards Agency, Advertising Standards Agency, and representation from industry – in form of Trade Bodies – including the British Herbal Manufacturers Association and Health Food Manufacturers Association. The Medical Devices Sector was represented by BSI and TUV Sud. Our team provided updates of cases we have opened and progression of those, and those closed. In particular we discussed products which we have removed from sale from Amazon and eBay.

Artificial Intelligence strategy

2.6 On 30 April we published the MHRA strategic approach to AI, responding to the DSIT Pro-Innovation Regulation for AI Whitepaper. We have also now launched our regulatory sandbox, AI Airlock, to address the challenges in regulating medical devices that use AI. A regulatory sandbox is a tool which allows businesses to explore and experiment with new and innovative products, services or businesses under the supervision of a regulator. The MHRA initiative aims to respond to the unique challenges that AI as a medical device (AIaMD) products present.

Digital Mental Health Technologies

2.7 The Digital Mental Health Technologies Project has completed all year 1 milestone conditions for the Wellcome Trust (the sponsoring agency). This secures funding for the remaining 2 years of this vital project which has seen the formation of diverse working groups involving experts in the field alongside lived advisors and communications on the project, such as this latest one: Update on pioneering initiative on regulation and evaluation of digital mental health technologies - GOV.UK (www.gov.uk)

In Vitro Diagnostics

2.8 The MHRA is the Competent Authority for medical devices and in vitro diagnostic (IVD) devices in Northern Ireland. The Medical Devices In Vitro Diagnostic Devices etc. Amendment Regulations 2024 came into force on 21 March 2024 and in April we published updated guidance for those regulations and for IVD performance evaluation studies in Northern Ireland.

PATIENT SAFETY

Montelukast and neuropsychiatric adverse reactions

3.1 Montelukast (Singulair) is an oral add-on therapy for the treatment of asthma in patients aged 6 months and older. It is associated with reports of neuropsychiatric reactions among all age groups including sleep disorders, hallucinations, anxiety and depression, and changes in behaviour and mood. We conducted a thorough review of the evidence which confirmed that while the risk of neuropsychiatric reactions with montelukast remains unchanged, Yellow Card reports have indicated this risk is potentially not well known by healthcare professionals, patients and their caregivers. More prominent warnings are being added to the Patient Information Leaflet included in every pack of montelukast in the UK, reminding patients and healthcare professionals that they should be alert to serious behaviour and mood-related changes (neuropsychiatric reactions) associated with the treatment.

Finasteride and psychiatric and sexual side effects

3.2 Patients have raised concerns regarding a lack of awareness among patients and healthcare professionals regarding psychiatric and sexual side effects associated with finasteride, a medicine for hair loss and prostatic hypertrophy. We reviewed the available evidence, including Yellow Card reports, published scientific literature and actions by other regulators, and our independent experts agreed that these side effects are not well known by prescribers and patients. A Drug Safety Update bulletin article was published in April and a patient card will be included inside the pack, to highlight the psychiatric and sexual side effects. This will help raise awareness of the risk of psychiatric side effects and sexual dysfunction, including the potential for sexual dysfunction to persist after treatment has stopped. A press release and a Public Assessment Report were also published.

Hormone Replacement Therapy

3.3 There is an ongoing regulatory review of the importation and supply of unlicensed subcutaneous hormone replacement therapy implants manufactured by Advanced Pharmaceutical Technology in the US, in collaboration with the USFDA and other UK stakeholders. The UK importer is to provide adequate assessment and quality management systems for the products. Alternative sources of similar products are being explored with DHSC, NHS and USFDA. We are continuing to liaise with clinical groups, maintain oversight, and drive to a conclusion in collaboration with FDA.

Patient Safety Monitoring

3.4 Following receipt of adverse incident reports, drugs and events included in those reports are paired to inform statistical signal detection and analysis. In March, the number of drug event pairs generated across both established medicines and additional monitoring medicines increased significantly, with approximately 95% of all pairs having been assessed during routine signal detection activities. Following these assessments, in Q4 34 signals were identified, 29 pertaining to medicines and 5 for medical devices. Most of the signals identified originate from adverse incident reports received though the Yellow Card scheme.

Benefit Risk Evaluation

3.5 In Q4 the Benefit Risk Evaluation (BRE) team investigated 150 potential safety issues. Investigation and assessment is prompted by information received from a range of sources including signals originating from reports of adverse drug reactions for medicines and adverse incidents for medical devices, safety concerns from Field Safety Notices for medical devices and issues raised directly by stakeholders. Assessment determines whether further action is required including actions to mitigate risks for patients. Safety issues predominantly came from Field Safety Notices by medical devices manufacturers with 52 notices being received in Q4. Assessment of the safety issues raised resulted in 24 actions taken to mitigate risk of medicines/medical devices during Q4. Actions included introduction of new risk minimisation materials and updates to patient information.

Safety enquiries

3.6 The total number of enquiries about safety issues has at least doubled when compared to volumes received pre-pandemic, with a vast amount relating to COVID-19 vaccines. There has been a 200% increase in enquiries following the pandemic and the Agency transformation and substantial increases in FOI requests which require significant resource to address. Specifically, in Q4 the number of FOIs and general enquiries has increased compared to previous quarters with the vast majority being responded to within Patient Safety Monitoring.

Clinical Practice Research Datalink

3.7 Clinical Practice Research Datalink has now achieved Trusted Research Environment status in line with the Goldacre Report recommendations and the government's 'Data Saves Lives'. The CPRD continues to show strong performance and cumulative income continues to show growth year-on-year. In FY 2023/24 we consistently achieved our target of approving 75 protocols per quarter. The average time to approve a Research Data Governance (RDG) application in March was 11.3 days, 17 days lower than our target service level agreement.

PARTNERSHIPS

Clinical Trials Regulations

4.1 The work on the new Clinical Trials Regulations is making good progress ahead of the parliamentary process and anticipated implementation in 2025. The new Clinical Trial Regulations aim to support patient safety and make the submission process more agile, ensuring patients can access new and potentially life-saving medicines.

Point of Care Manufacture

4.2 New legislation is due to be laid in the summer on Point of Care manufacture, following innovative work led by MHRA which is now under discussion at the International Coalition of Medicines Regulatory Authorities (ICMRA).

Windsor Framework

4.3 The regulatory policy team is working across the Agency to update guidance documents ahead of the Windsor Framework implementation date of 1st January 2025, including for example on packaging and pharmacovigilance.

National and international liaison

4.4 Our national team continues to work across the UK health sector delivering information sharing and greater coordination of key activities such as medicines and medical devices horizon scanning. In addition, this team is delivering the pump priming programme for Centres of Excellence in Regulatory Science and Innovation (CERSIs), to enhance our access to relevant UK research. Our new international team is now preparing for meetings of the Access Consortium Heads of Agency (Australia, Canada, Singapore and Switzerland), ICMRA and the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH), including holding bilateral discussions with key partners ahead of these meetings.

PATIENT INVOLVEMENT

Cancer Immunotherapy vaccines

5.1 We delivered a briefing session for patient experts who sit on the Cancer Immunotherapy Vaccines Expert Working Group (EWG) the day before the EWG meeting, plus a de-briefing/feedback session straight after the EWG itself. The patient experts, who are both very experienced in committee involvement (particularly with NICE and the NHS), expressed how impressed they have been with MHRA's involvement of patients in the EWG: the quality of the briefing provided and support given, as well as the opportunity to contribute to developing the regulatory approach to cancer immunotherapy vaccines. One of them also recommended that we should publicise how we are involving patients in this kind of work.

DIGITAL AND TECHNOLOGY

Cyber security

6.1 The Agency continues to prioritise cyber risk management and has taken positive steps to improve data security against a background of ongoing and increasingly sophisticated cyber threats. The volume of cyberattacks remains high and is expected to increase in both intensity and sophistication as well-resourced attackers such nation state actors and criminal groups seek to disrupt our business, and access and compromise health and scientific data.

RegulatoryConnect

6.2 All planned releases have completed for Release 1 of RegulatoryConnect. The new portal has been live for several weeks with positive feedback from industry and over 2,500 thousand users accessing it. The new self-service tools include 'Track my Case' and Check my Data'. The use of the Inspections Universe is now planned from next quarter. Following news that the Business Case was approved by Treasury it was confirmed that the 2024/25 budget request has been fully funded. The RegulatoryConnect Programme Board is now focussed on the delivery of Release 2.

Knowledge and Information Management

6.3 The Information Security team and CPRD collaborated to prepare the Agency's Data Security and Protection Toolkit (DSPT) submission to NHS England which allows us to measure our performance against the National Data Guardian's 10 data security standards and provide assurance that we are practising good data security and that personal information is handled correctly. Review of catalogue records provided by Iron Mountain for selection of records for transfer to the National Archives (TNA) is ongoing.

DYNAMIC ORGANISATION

Business Plan 2024/25

7.1 Work is now well advanced on finalising the MHRA Business Plan 2024/25, the second year of the Corporate Plan 2023/26. This Business Plan will focus on the optimisation of MHRA services while retaining the four pillars of public trust, facilitating healthcare access, regulatory and scientific excellence, and our service culture. Inevitably a small number of Corporate Plan objectives will be postponed to next year. A 'Plan on a Page' will be available for staff to support communications.

Return to Green

7.2 The Return to Green programme has created a robust programme structure with additional resources deployed to support the business areas. The programme is focused on a) clearing the backlogs, with clear plans for each area on timelines, and b) ensuring sustainability to remain at 'green'. Root cause analysis is underway to identify the causes of the backlogs with a view to service redesign. The focus is now on the new programme dashboard detailing progress with each backlog clearance and the new interventions.

Core performance script

7.3 The first version of the MHRA performance core script was launched to key stakeholders, to positive response. This monthly update provides a rolling update of information on our performance, so key stakeholders always the most recent update on our performance in areas on which they might be questioned. The DHSC and Trade Associations have all welcomed this. A monthly schedule has been agreed, following the monthly performance reporting updates. A discussion on the usefulness of the document is also on the agenda for the next Medicines Industry Meeting to discuss further with Trade Associations.

Freedom of Information requests

7.4 Over 96% FOI requests were responded to within statutory timeframe of 20 working days. Our FOI performance metrics are now published and there will be an ongoing update each quarter. A list of MHRA response outcomes has also been made publicly available as has our action plan in response to the Information Commissioner's Practice Recommendation. The FOI eCase system went live on 18th March and MHRA groups will move over in a phased manner to eCase by the end of June. This approach will help manage and support the business change across the organisation.

FINANCIAL SUSTAINABILITY

Public Contract Regulations training

8.1 Training has started in the Commercial team for the new Public Contract Regulations that come into effect this year. We are considering now to leverage this training to increase the understanding of commercial requirements across the Agency.

AGENCY PRIORITIES

In summary, the current priorities for the Agency are to:

I. Maintain the Agency's overarching focus on delivering its core business activities, meeting assessment targets for all key services and eliminating any backlogs

II. Continuing to invest in our technology systems to improve services for our customers and patients

III. Review our regulatory science and data strategies in parallel with the CERSIs initiative to best inform regulatory benefit risk decisions and protect public health.

IV. Develop our sustainable business model through revision of our fees based on the results of activity recording

V. Continuing to collaborate with our partners in healthcare nationally and with international regulators, in particular on our approaches to new regulatory frameworks.

Dr June Raine, CEO
May 2024

Medicines & Healthcare products Regulatory Agency

BOARD MEETING HELD IN PUBLIC

21 May 2024

Title	How did the Agency perform in the fourth quarter of 2023/24?
Board Sponsor	Rose Braithwaite
Purpose of Paper	Assurance

How did the Agency perform in the fourth quarter of 2023/24?

1. Executive Summary

1.1 This paper summarises performance in quarter four of 2023/24, set out in detail in the attached Agency Performance Report. Four out of our eight key performance indicators (KPI) were 'on target' and remained at 100% performance at financial year end. Our remaining four 'off track' KPIs are being managed via the 'Return to Green' programme, which is overseeing efforts to clear backlogs which are negatively impacting these KPIs. Current programme reporting shows new items being cleared inside statutory or internal timelines and mitigation plans to clear backlogs being implemented. Of the 44 objectives set out in our Business Plan, 27 were completed at financial year end, with 10 reported as due to be completed in quarter one 2024/25.

2. Introduction

2.1 In January, we presented a new Agency Performance Report to the Executive Committee reporting on performance in quarter three. The committee were pleased with improved approach and next steps were to progress to a monthly cadence of reporting, develop a suite of top-level KPI and develop volume reporting.

2.2 All next steps were successfully implemented into the Agency Performance Report, discussed by the Executive Committee on 30 April. The attached report is a condensed version, aimed to deliver headline strategic messages to the Board summarising performance in the final quarter of 2023/24.

3. How did the MHRA perform in the fourth quarter of 2023/24?

3.1 Progress on Business Plan Objectives (Part One)

3.1.1 Of the 44 objectives set out in the 2023/24 business plan, 27 were completed at the end of the planning year. Highlights include enrolling our first participants into the Yellow Card Biobank pilot, completing the selection process for the Innovative Devices Access Pathways (IDAP) pilot, and launching the International Recognition Procedure (IRP).

3.1.2 Some minor slippages have been reported for ten objectives, these are all due to be completed in quarter one of 2024/25. Minor slippages included not fully embedding our SafetyConnect vigilance system due to challenges with migrating existing data, delays in establishing the Innovative Licensing and Access Pathway (ILAP) and a date for the publication of our Science Strategy.

3.1.3 There were seven objectives marked as late at the end of March, five of these had already been reported as late, or at risk of being late in previous performance reports. Slippages have occurred in regulatory opportunities to address health

inequalities (the expanded scope of which is being included in the new Business Plan), making Yellow Card incident report data available in the new COVID-19 interactive format (flagged previously), laying the foundation for electronic Patient Information and updating our talent management approach.

3.1.4 Business leads have summarised mitigating actions and, where possible, revised delivery dates for objectives marked as late in part one of the attached report (slides four to ten).

3.2 **Operational Performance KPI (Part Two)**

3.2.1 Of the eight top-level KPIs four were consistently on target, and all four were at 100% at the financial year end. These indicators were measuring how many assessments of clinical trials and investigations, certification of vaccine batches and blood products, medicine licences determined via the International Recognition Procedure and fatal Adverse Drug Reaction reports were processed within statutory or internal timeframes.

3.2.2 Our four remaining off target KPIs were measuring how many medicine licences were determined via the National Route, assessed national variations, granted, varied, or refused manufacturing and distribution authorisations and offers for scientific advice we processed within statutory or internal timeframes.

3.2.3 However, our KPIs are a measure of the percentage of work completed on time. Therefore, whilst we make concerted efforts to clear backlogs of older applications, our KPIs will be negatively impacted for the time being. All four ‘off target’ KPIs are being managed through our ‘Return to Green’ programme, where performance is monitored weekly (detailed at Annex A of the report). Workstream leads for every area have indicated that mitigation plans are being implemented, that means we should clear our backlogs within expected timeframes.

3.2.4 We have also forecasted our expected trajectory for clearing our backlog of Established Medicines licensing applications (also detailed at Annex A), this illustrates our sustained positive reduction of the backlog. As we clear this backlog, we should see our KPIs trend upwards. The ‘Return to Green’ programme is currently establishing similar forecasting for Variations and Inspections.

3.2.5 We continue to see ‘late volumes’ (unactioned work that is older than statutory or internal timeframes) in offering scientific advice, carrying out inspections, assessing variations, and determining medicine licences. However, all these areas showed reductions in late volumes from February to March, indicating that we are making positive strides towards clearing our backlogs.

4. Recommendation

4.1 Is the Board content with the overall delivery of the business plan and the work being done to complete the business plan objectives that have not been fully achieved during the year?

4.2 Does the Board consider it has sufficient sight of the Agency's delivery of its metrics to support its understanding of the delivery of the Agency's KPIs?

Rose Braithwaite
8 May 2024

Medicines & Healthcare products Regulatory Agency

Agency Performance Report

2023/24 - Quarter 4

Planning & Performance Team

Finance Division

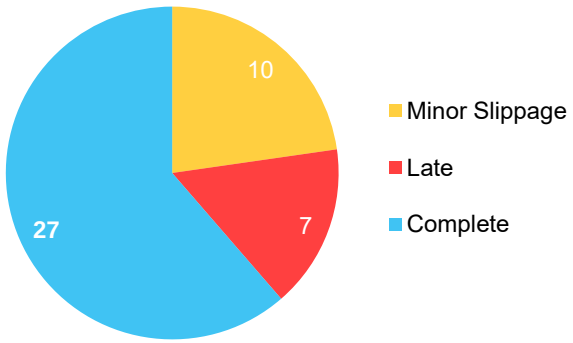
Medicines & Healthcare products Regulatory Agency

Executive Summary

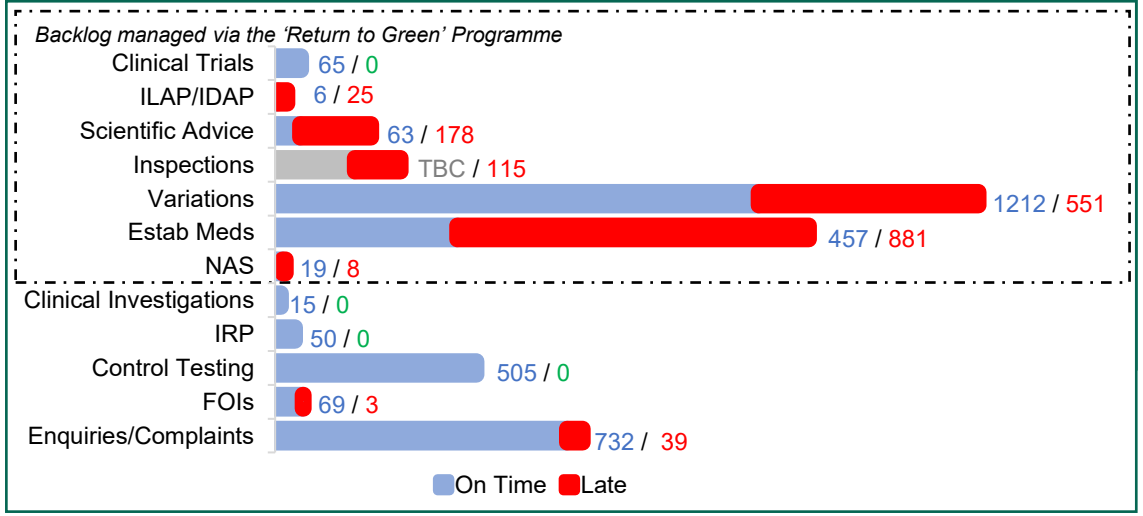
#	Key Performance Indicator	Mar-24 Performance
1	We will assess 95% of all initial Clinical Trial Authorisation (CTA) and Clinical Investigation applications within their category's statutory timeline.	100% (►0%) On Target
2	We will certify 95% of vaccine batches within 43 days and 99% of blood product batches within 15 days of submission.	100% (►0%) On Target
3	We will determine 95% of medicines license applications within 210 days via the national route.	13% (▼4%) Off Target
4	We will determine 95% of medicines license applications within 60 days via recognition Route A and within 110 days via Route B through the International Recognition Procedure.	100% (►0%) On Target
5	We will assess 95% of all national variations within their category's statutory timeline.	75% (▲8%) Off Target
6	We will grant, vary or refuse 95% of manufacturing and distribution authorisations within their category's statutory timeline.	54% (▼2%) Off Target
7	(Interim KPI) We will process 90% of Fatal Adverse Drug Reaction (ADR) reports for medicines within 24 hours,100% within 72 hours and we will process 95% of serious ADR reports for medicines within 72 hours and 100% within 5 days.	100% (►0%) On Target
8	We will offer scientific advice to 95% of requests within 70 days of the request being made.	9% (▼12%) Off Target

Progress on Business Plan Objectives

27/44 of Key Actions complete at year end.



Agency Volumes



Insight

Our Key Performance Indicators

4 out of our 8 key performance indicators (KPI) were 'on target' and remained at 100% performance at financial year end. Our remaining 4 'off track' KPIs are managed via the 'Return to Green' programme, which is overseeing efforts to clear the backlogs which are negatively impacting these KPIs. Current programme reporting shows new items being cleared inside statutory or internal timelines and mitigation plans to clear backlogs being implemented.

Progress on Business Plan Objectives

27 out of the 44 objectives set out in our Business Plan were completed at financial year end. 10 were reported to have minor slippage and are due to be completed in Q1 of next financial year. Highlights included enrolling our first participants into the Yellow Card Biobank pilot, completing the selection process for the Innovative Devices Access Pathways (IDAP) pilot and launching the brand-new International Recognition Procedure (IRP).

There were 7 objectives marked as late at the financial year end, 5 of these had already been reported as late, or at risk of being late in previous performance reports. Slippages have occurred in regulatory opportunities to address health inequalities (the expanded scope of which is being included in the new Business Plan), making Yellow Card incident report data available in the new COVID-19 interactive format (as flagged previously), laying the foundation for electronic Patient Information, preparing legislation to deliver reform of the UK clinical trials regulatory framework (in the new Business Plan) and updating our talent management approach.

For the late objectives, Leads have summarised mitigating actions and, where possible, revised delivery dates in the slides overleaf.

Agency Volumes

We continue to see 'late' volumes (unactioned work that is older than statutory or internal timeframes) in Scientific Advice, Inspections, Variations and medicine licensing (all are managed via the Return to Green workstream). However, all these areas showed reductions in volumes from February to March.

Part 1

Progress on Business Plan objectives

Medicines & Healthcare products Regulatory Agency

Progress on Business Plan objectives
Pillar 1: Maintaining public trust through transparency and proactive communication

Key Action	Objective	Q1	Q2	Q3	Q4	Insight
1.1 – Embed **patient involvement across our regulatory pathways** that is meaningful, proportionate, and impactful, to help ensure medical products reach patients without delay, accompanied by efficacy and safety info that better meets the needs of all patients. (Rachel Bosworth)	1.1.1 Ensure patient involvement activities remain ethical, meaningful and impactful by **embedding new tailored guidelines** for priority agency functions by end Q3. (Christine McGuire)	G	G	B		Objective completed in Q3 2023/24.
	1.1.2 Develop a new **risk communication strategy** to ensure more coordinated, proactive risk and safety communications to patients, the public and healthcare professionals, by end Q4. (Louise Rishton)	G	G	G	B	Risk and Safety Communications strategy has gone to board and been approved. Work has begun on the actions in the strategy including a redesign of risk and safety communication templates and additional guidance for the MHRA website.
	1.1.3 Design a new approach to **recruit and train additional lay committee members** (non-clinical, academic or scientific) to ensure our independent advisory bodies benefit from greater lay perspectives and challenge by end Q4. (Christine McGuire)	G	G	G	B	A report was commissioned to assess barriers to recruiting lay members to committees and working groups. The report was delivered in Q3. A small pool of potential new candidates has been identified but resourcing constraints have meant that further expansion of recruitment, training and support have been halted.
1.2 - **Enable diverse patient voices** to provide evidence on safety concerns on specific types of medicines and medical products. (Alison Cave and Rachel Bosworth)	1.2.1 Establish a consistent, inclusive and **systematic approach to ongoing patient involvement** in our benefit and risk evaluation assessments by end Q3. (Janine Jolly)	A	A	B		Objective completed in Q3 2023/24.
	1.2.2 Complete a **review of regulatory opportunities to address health inequalities** by end Q4. (Jenn Matthissen)	A	A	A	R	This work continues into the next business plan year. A review of women's health regulatory inequities was completed in 2023/24. The MHRA also played a significant role in an Independent Review of inequity in medical devices, largely focused on racial inequity, led by Dame Margaret Whitehead. MHRA provided its own response to the report and contributed to the overall government response. An objective has been included in the 2024/25 business plan to produce a project brief to develop strategies to implement the recommendations of the 2023/24 inequities reviews, address wider health inequalities issues including other at-risk groups, and explore the potential for intersectionality with other determinants of health outcomes (e.g. age, sex, disability, and race).
	1.2.3 Identify **two safety topics affecting underserved groups** by end Q3 and engage with patients so they can raise concerns and to inform our approach by end Q4. (Christine McGuire)	G	G	G	B	The MHRA has worked with under-served communities to input into work such as the risk-benefit review of the cystic fibrosis drug Kaftrio, and in the review of the existing guidelines for healthcare professionals on pulse oximeters and inaccuracies with darker skin pigmentation.
	1.2.4 **Broaden our communications channels** to reach under-represented and underserved populations, ensuring the contribution of more diverse voices by end Q4. (Lucy Cooke)	G	G	G	B	Communication and campaign strategies consider audience insight to inform channel selection and targeting of under-represented populations when it will directly serve the delivery of public health objectives; and work continues to establish an MHRA presence on new direct and partner-led channels.

KEY: Red – late or not possible; Amber – minor slippage; Green – on track; Blue – Complete; Delivery Date – Edged Dark Red

Medicines & Healthcare products Regulatory Agency

Progress on Business Plan objectives
Pillar 1: Maintaining public trust through transparency and proactive communication

Key Action	Objective	Q1	Q2	Q3	Q4	Insight
1.3 – **Increase transparency of safety signals and the basis of our benefit-risk decisions** by regularly publishing the safety signals on medical products and a public statement following approval of all new chemical entities within one week, plus a summary of the evidence for the regulatory approval within one month. (Alison Cave and Julian Beach)	1.3.1 Make **Yellow Card incident report data available** in the new COVID-19 interactive format for medicines by end Q2 and devices by end Q3. (Phil Tregunno)	G	A	A/R	R	Medicines functionality is on track to be delivered 4-6 weeks after Phase II SafetyConnect go-live, which is now estimated for Q1 2024/25 (May 2024). Devices functionality will follow on from medicines functionality, but will be dependent on Phase III SafetyConnect go-live during 2024/5 financial year.
	1.3.2 **Pilot publication of safety signals** assessed by our Pharmacovigilance Expert Advisory Group on our Yellow Card website and publication of accessible lay summaries of our benefit and risk evaluation assessments by end Q4. (Phil Tregunno)	A	A/G	G	A	A range of different levels and examples of text for publication have been developed, and user testing approach agreed. These will be tested and evolved during Q1 24/25 and a recommendation on approach taken to PSEC.
	1.3.3 By end Q4, establish the governance of the **Yellow Card Biobank** and successfully demonstrate procedures in action for participant recruitment, sample collection and sample storage. (Phil Tregunno)	G	G	G	B	Governance procedures for Yellow Card established and operating effectively. Participant recruitment commenced in January 2024 and our first participants enrolled into the pilot. Contract awarded to Nursing organisation for sample collection, with processes tested and first samples due to be collected in April 2024.
	1.3.4 By end Q4, regularly publish a **public statement following approval of all new chemical entities** within one week and provide a summary to provide the evidence for the regulatory approval within one month. (Andrea Johnson)	A	A/G	G	B	All new chemicals entities have their public statement and summary completed within the timeframes indicated.

KEY: Red – late or not possible; Amber – minor slippage; Green – on track; Blue – Complete; Delivery Date – Edged Dark Red

Medicines & Healthcare products Regulatory Agency

Progress on Business Plan objectives
Pillar 2: Enable healthcare access to new, safe and effective medical products

Key Action	Objective	Q1	Q2	Q3	Q4	Insight
2.1 - **Deliver predictable and reliable operational performance** having defined our priority improvements for our core services to ensure swift and robust decisions on medical products, safety signals and compliance. (All)	2.1.1 Identify **service improvements across all priority** areas with robust plans for implementation and effective change management to be in place by end Q4. (Mick Foy)	G	G	G	B	Service Improvements for short term backlog clearence have been identified for all the priority areas and change management is in place. Return to Green is being managed within SPD and work is inplace to identify long term service improvement and effectively manage the change. A Change Management Framework for the agency is in place.
	2.1.2 **Eliminate current service backlogs** by end of 2023/24. (Penny Carter)	A	R	R	R	Return to Green now set up to monitor and eliminate current service backlogs and this work will continue throughout 2024.
	2.1.3 Deliver phase one of our innovation-enabling and risk-proportionate **medicines compliance strategy** including the development of a pilot project for an outcome-based model by end Q4. (James Pound)	A	A/G	G	B	Pilot population identified and engaged, kick off scheduled for May. GXP model to follow based upon outcomes of pilot. A period of review and refinement will allow building of requirements with other pilot partner(s). Objective complete.
	2.1.4 Fully embed our new **SafetyConnect** vigilance system and realise patient and operational benefits by end Q4. (Phil Tregunno)	G	G	A/G	A	Challenges were identified with the Agency's Business Intelligence solution, alongside difficulties in data migration, which have delayed go-live. These issues have now been addressed and phase 2 go-live is on track for Q1 2024/25. The Phase 2 go-live will also deliver a number of enhancements to Device Incident processing to deliver operational efficiencies identified since the initial go-live.
2.2 - **Develop and embed system cooperation with UK partner organisations**, including the NHS, to ensure the gap continues to be narrowed between regulatory and health ILAP technology approval with a clear path to patient deployment. (James Pound and Julian Beach) Continued overleaf	2.2.1 By end Q3, work with stakeholders to lay the foundation for **electronic Patient Information** (ePI) by 2026 to ensure more accessible information for patients. (Andrea Johnson)	G	A/G	R	R	Significant progress has been made during the last quarter. A number meetings have been held and progress is being made to define a pilot. There is a lot of Industry interest in this area, and we will work with the ePI Task Force to move this forward. We are now regularly attending the monthly legislative work stream meetings.
	2.2.2 Establish the **UK healthcare systems priorities** for medicines and medical devices in terms of patient need and proactive supply chain management and to inform our priorities by end Q3. (Bernadette Sinclair-Jenkins)	A	R	A	A	Delivery of Medicines of Concern List (MoCL) compromised by external partners priorities (NHSE/DHSC) Internal group established, Terms of Reference, processes, scope in place. Plan activity has been Deprioritised to address multiple external compliance incidents/demands

KEY: Red – late or not possible; Amber – minor slippage; Green – on track; Blue – Complete; Delivery Date – Edged Dark Red

Medicines & Healthcare products Regulatory Agency

Progress on Business Plan objectives
Pillar 2: Enable healthcare access to new, safe and effective medical products

Key Action	Objective	Q1	Q2	Q3	Q4	Insight
2.2 - **Develop and embed system cooperation with UK partner organisations**, including the NHS, to ensure the gap continues to be narrowed between regulatory and health ILAP technology approval with a clear path to patient deployment. (James Pound and Julian Beach)	2.2.3 Establish the **Innovative Licensing and Access Pathway (ILAP) and the Innovative Devices Access pathway (IDAP**) by delivering a partnership governance that delivers ILAP activities and the IDAP pilot project by end of Q4. (Louise Knowles) Split into: **ILAP**	A	R	A	A	The partners (MHRA, HTA bodies, NHS) are working collaboratively to refine the scope of ILAP for the next phase to address the recommendations of the McLean review and to ensure that products entering the pathway receive enhanced levels of support. Plans to relaunch ILAP in Q4 have been delayed as work commenced to reestablish the partnership arrangements and bring in new NHS partners, alongside increased activity to clear backlogs that had built up over 2023. We are on track to launch a refreshed ILAP by the end of Q1 2024/25, subject to finalising and approvals for the new approach. This revised date has been agreed with partners and presented to DHSC and PAMP. This is included in the 2024/25 Business Plan.
	IDAP	A	G	G	A	Selection process completed with the 8 technologies selected for the IDAP pilot announced in mid-February 2024. Have completed the initial meetings with all 8 companies to develop their Target Development Profile Roadmaps. Pilot will continue into 2024/25. This is included in the 2024/25 Business Plan.
	2.2.4 Work with the Health Research Authority to **implement the 60-day review period** of clinical trial applications in line with the recommendation of the O'Shaughnessy review. (Andrea Manfrin)	G	G	B		Objective completed in Q3 2023/24.
2.3 - Launch the **improved regulatory management system** to make our services more streamlined, as the first phase of the replacement of legacy IT systems, enabling all new product licences, variations, inspections, and process licences to be efficiently handled, maximising the use of self-service for low-risk decisions. (Mick Foy)	2.3.1 Launch the first release of our new **regulatory management system** – **RegulatoryConnect** by end Q4 23/24. (Adam Sykes)	G	G	A	B	Delivery of the first Release 1 milestones of LA Search, LA Reporting, eCTD Docubridge, Self-Service Portal, UKSRS and Inspections Universe all complete. Note: Release 2 activities are running in parallel, however delivery for November: (Q3 '24/25) is at risk. Velocity and elaboration is below plan due to quality issues in the data model. Risk around the original estimates vs the forecast once elaborated, the risk on completing data migration in this period. Action is being taken to prioritise resource and unblock issues affecting velocity in this quarter to mitigate any delays to the R2 go-live dates.

KEY: Red – late or not possible; Amber – minor slippage; Green – on track; Blue – Complete; Delivery Date – Edged Dark Red

Medicines & Healthcare products Regulatory Agency

Progress on Business Plan objectives
Pillar 3: Deliver scientific and regulatory excellence through strategic partnerships

Key Action	Objective	Q1	Q2	Q3	Q4	Insight
3.1 - Introduce the **MHRA Science Strategy**, establish and build on partnerships in key priority areas with national and international partners with measurable benefits that support prompt and robust regulatory decision-making. (Nicola Rose, Glenn Wells, Alison Cave)	3.1.2 Launch our **MHRA Science Strategy**, including engagement with key stakeholders, and delivery of key themes by Q4. (Nicola Rose)	G	G	A	A	A publication date for the Science Strategy is to be determined.
	3.1.1 Publish a **Data Quality Strategy**, including proposals for revised and extended data quality checks, for our Clinical Practice Research Datalink services and refresh our data quality webpage by end Q3. (Puja Myles)	G	G	G	B	The CPRD data quality strategy has been completed and a summary has been published on the CPRD website.
	3.1.3 Establish processes to **identify future areas of innovation, working with national and international partners** to align priorities with patient need by end Q4. (Louise Knowles and Harriet Teare)	A	A/G	A	B	New regulatory science staff have joined the innovation office team and are initiating workstreams addressing different areas of innovation. Work is underway to align with existing horizon scanning processes (including with MMD Access) and with partners including NHSE, to determine how best to action innovation signals.
3.2 - **Re-prioritise standards, control testing and underpinning research** to ensure support for priority areas of our MHRA Science Strategy and Corporate Plan. (Nicola Rose)	3.2.1 Run a trial from Q2 to end Q4 aimed at **improving our distribution approach**, increasing the volumes of standards we provide globally and raising awareness of our offer. (Paul Bowyer)	A	R	A	R	Intensive correspondence to recruit strategic distributors for global marketing campaign trial. 4 distributors in China and Korea have commenced implementation of campaign using our Marketing eToolkit complete with all branded assets. An ongoing cross-functional team assigned to deliver improvements in customer experience/fulfilment and to conduct regular business review meetings for the duration of trial. Delay in the launch due to the backlog. The backlog is now cleared thereby ensuring our customers can have a positive end-to-end customer experience when ordering our NIBSC standards. Further expansion of distributors planned for FY 24/25 to potentially cover regions such as the US and Latin America.
	3.2.2 Develop a new **strategy for the British Pharmacopoeia and associated laboratory services** for consultation by end Q4 including income investment plans to improve services. (James Pound)	G	A/G	G	B	Strategy document with recommendations complete. Consultation and refinement to be completed with SMT hierarchy through April.
	3.2.3 Link the **Innovation Accelerator activities** with academia and other stakeholders by Q4 to provide support for the CERSI recommendation in the McLean Report. (Louise Knowles)	G	G	G	B	Formation of CERSIs is on track. MHRA in partnership with OLS and other cross-government partners have provided funding to support this initiative. The competition call, supported by Innovate UK, closed at the end of January, identifying for its first stage – the Discovery Phase – 17 applications on human health and 1 cross-cutting with the net zero initiative. The applicants have received the seeding fund of £50 K and are currently in the second month of the Discovery Phase. MHRA, OLS and Innovate UK will hold an information webinar in early May to: (i) communicate details of the second stage of the competition, the Implementation Phase; (ii) introduce candidate networks to their area-expert MHRA regulatory specialists (or MHRA sponsors) for their future collaborative regulatory-science activity; (iii) lay expectations for the established CERSIs; and (iv) answer applicants' questions. Meanwhile, MHRA and OLS work with Innovate UK in shaping the Implementation Phase application form, which will be open to applicants from July 2024. At this point, all 18 networks will be invited to develop full applications for determining which networks will progress to become CERSIs. About 6 awards will be made and announced in September 2024.
	3.2.4 Implement a new **risk-proportionate approach for the independent control testing** of biological medicines to expand our ability to perform laboratory assessments by end Q4. (Silke Schepelmann)	G	G	G	B	The risk-proportionate approach for control testing has transitioned from project implementation to business as usual.

KEY: Red – late or not possible; Amber – minor slippage; Green – on track; Blue – Complete; Delivery Date – Edged Dark Red

Medicines & Healthcare products Regulatory Agency

Progress on Business Plan objectives
Pillar 3: Deliver scientific and regulatory excellence through strategic partnerships

Key Action	Objective	Q1	Q2	Q3	Q4	Insight
3.3 - **Legislate on Point of Care Manufacture** and drive international regulatory progress in key scientific areas commensurate with scientific and technological advances such as mRNA technology, AI and in silico data generation. (Glenn Wells)	3.3.1 Deliver a new framework for **UK Point of Care Manufacture**, lay legislation before Parliament and publish guidance by end Q4. (Cathy Lenihan)	A	A/R	A/R	A	This work continues into the next business plan year. The legal text has been drafted, and we are aiming to lay the legislation in Q2 2024. Next Business Plan objective "lay legislation in Q2 and implement from October 2024"
	3.3.2 **Establish active bilaterals and wider collaborations** nationally and internationally with work programmes in place on healthcare product innovation areas of interest by end Q4. (Harriet Teare)	G	G	G	B	A new post has just started looking at closer alignment of MA / HTA processes, which will support bilateral interactions with HTA organisations. The partnerships team, with support cross-agency, continue to support and develop bilaterals and wider collaborations to enable harmonisation and alignment in medicines and medical devices, with a focus on innovation.
3.4 - The second year of our Corporate Plan 2023-26 will have a focus on the introduction of **new guidance and legislation** to build our status as an independent regulator in a global environment and to ensure the UK remains a great environment to develop novel and innovative medical products. There are also some milestones for this year: (Glenn Wells and Laura Squire)	3.4.1 Implement the **Windsor Framework** for a commencement date of 1 Jan 2025: issue essential guidance by end Q3, place legislation before Parliament in 2024 and issue further guidance and comms as needed up to the commencement date. (Rachel Arrundale)	G	G	G	B	Work will continue into the next business plan year. Essential pieces of guidance on labelling and licencing requirements have been completed and published on gov.uk alongside Q&A documents. Work continues to review existing guidance and updates are being published at intervals through 2024 ahead of the commencement date. MHRA are supporting DHSC to prepare the implementing legislation.
	3.4.2 Prepare legislation by Q4 to deliver reform of the **UK clinical trials regulatory** framework. (James Pound/Glenn Wells)	A	A/R	A/R	A	This work continues into the next business plan year. Drafting the legislation is progressing, with the aim to lay legislation in Q2.
	3.4.3 Drive forward reform of **medical devices regulation** to ensure that medical devices are subject to future requirements for quality, safety and performance, whilst allowing increasing numbers of patients to benefit from innovative products placed onto the UK market. This includes laying regulations for transition provisions by end Q2 to maintain the supply of devices in GB and for future regulations to strengthened Post Market Surveillance (PMS) by end Q4 to strengthen requirements for devices on the market and increase patient safety, and clarifying plans, including consulting if needed, for international recognition of devices approved in other jurisdictions by end Q3. (Eve Hutchinson)	G	G	A/G	A	The programme continues to progress - Communications have been increased in Q4 with the publication of a roadmap in Jan 2024, a series of blogs, webinars and trusted advisor group meetings to discuss the detail of the new legislation planned, including exemptions for devices made in health institutions, scope, classification, essential requirements. This is to provide stakeholders with greater certainty to enable them to plan and inform MHRA guidance. Due to issues outside the Agency, we were unable to consult on International Recognition in 2023, however work continues this policy, and we are on track to meet our commitment to issue a statement of policy intent in Spring 2024. Transition legislation came into force in June 23. WTO notification for PMS took place in Autumn 23 and collective agreement is being sought to lay coming weeks.
	3.4.4 Launch a new **international recognition route** by 1st Jan 2024 for medicines utilising pre-existing approvals from Australia, Canada, the EU, Japan, Switzerland, Singapore and the United States. This new framework will support patients in the UK with expedited access to safe and effective medicines that have been approved by trusted regulatory partners. (Leo Both)	G	G	G	B	Objective complete in Q4.

KEY: Red – late or not possible; Amber – minor slippage; Green – on track; Blue – Complete; Delivery Date – Edged Dark Red

Medicines & Healthcare products Regulatory Agency

Progress on Business Plan objectives
Pillar 4: Become an agency where people flourish alongside responsive customer service

Key Action	Objective	Q1	Q2	Q3	Q4	Insight
4.1 - Deliver a range of **core and specialist learning opportunities** and implement and review the agency leadership development plan, to ensure we have the right capabilities across the organisation. (Liz Booth)	4.1.1 Introduce an **MHRA-wide workforce plan** by end Q3 to ensure our workforce needs are known and can be acted on. (Sarah Read)	G	G	A/G	R	Updated workforce planning discussions have taken place in the majority of areas. However, some remain outstanding and the recent approval of additional resources in HQ&A will necessitate revisions to the information gathered. All discussions to take place by the end of Q1 with a view to incorporating succession planning information obtained in the My Progress Review discussions held. Outline of an Agency-wide workforce plan to be collated by end of Q2.
	4.1.2 **Refresh our Culture Action Plan** by end Q2 and deliver its actions by end Q4 to support our strategic priorities and the delivery of our redesigned services. (Malgosia Malach)	G	G	G	B	The Culture Action Plan is a dynamic 3-year Plan with Y2 actions currently being refreshed. A paper will be presented at April's P&CC to report on progress against Y1 actions.
	4.1.3 Deliver a **plan for core learning and development** for 2023/24 that identifies and strengthens capabilities in priority areas by end Q4. (Malgosia Malach)	G	G	G	B	Confirmed activities on the core learning and development plan were delivered. Highlights were LEAP, Line manager capability learning programme and Strengths Development Inventory learning.
	4.1.4 Update our **Leadership Development Plan** by end Q2 and deliver new actions to strengthen leadership capability across the agency by end Q4. (Malgosia Malach)	G	G	G	B	Leadership Development Plan actions delivered – an update will be shared with P&CC in April and the plan will be updated for 24/25.
4.2 - **Attract and develop talent** by strengthening existing or creating new recruitment channels such as a graduate scheme and increasing apprenticeships (Liz Booth)	4.2.1 The **first graduate scheme** cohort to commence our new 3-year programme and complete the on-boarding of 8 new graduates by end Q2. (Malgosia Malach)	G	B			Graduates have been in post since September 2023. They have settled in well and are making a strong contribution.
	4.2.2 Increase the number of **apprenticeships** towards the target of 40 by end Q4. (Malgosia Malach)	G	G	G	B	There are now 40 signed apprentice contracts with 27 active apprentices on 31st March but this number will become 40 in April.
	4.2.3 Update our **talent management approach**, aligning it to workforce planning and ensuring a clear link with business planning by end Q4. (Malgosia Malach)	G	G	A/G	R	Talent management approach to be timetabled for ExCo discussion. Challenge is finding the bandwidth across agency to meaningfully engage with talent assessments/succession planning processes in view of the current set of pressures agency leaders are currently working through.
4.3 - Develop a **new financial plan** to ensure we continue to deliver value for money, invest in people, maintain our financial sustainability and recover the costs of all our services, with updates to our fees to be in force by 1 April 2025. (Rose Braithwaite)	4.3.1 **Staff activity recording** to commence in fee earning areas by end Q3 to ensure we have a greater understanding of our costs to serve. (n.b. Q3 will be changed to Q4 following ExCo agreement to roll out from Jan) (Maham Masood)	G	G	G	B	Activity is now complete as of 31st March.
	4.3.2 Produce new improved **financial management reporting** using DataRails by end Q2 to ensure better data and more informed decision-making. (Peter Ralls)	G	B			Objective completed in Q2 2023/24.
	4.3.3 **Develop new pricing for services and products** by Q4 to improve cost recovery across the Agency and consult on and deliver the next uplift in our fees by 1 April 2025. (Maham Masood)	G	G	G	A	First draft of new pricing is being developed following the completion of Activity Recording - a fee order proposal will go to Exco on 4th June for their approval to launch public consultation during July 24

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Medicines &
Healthcare products
Regulatory Agency

Part 2
Operational Performance KPIs

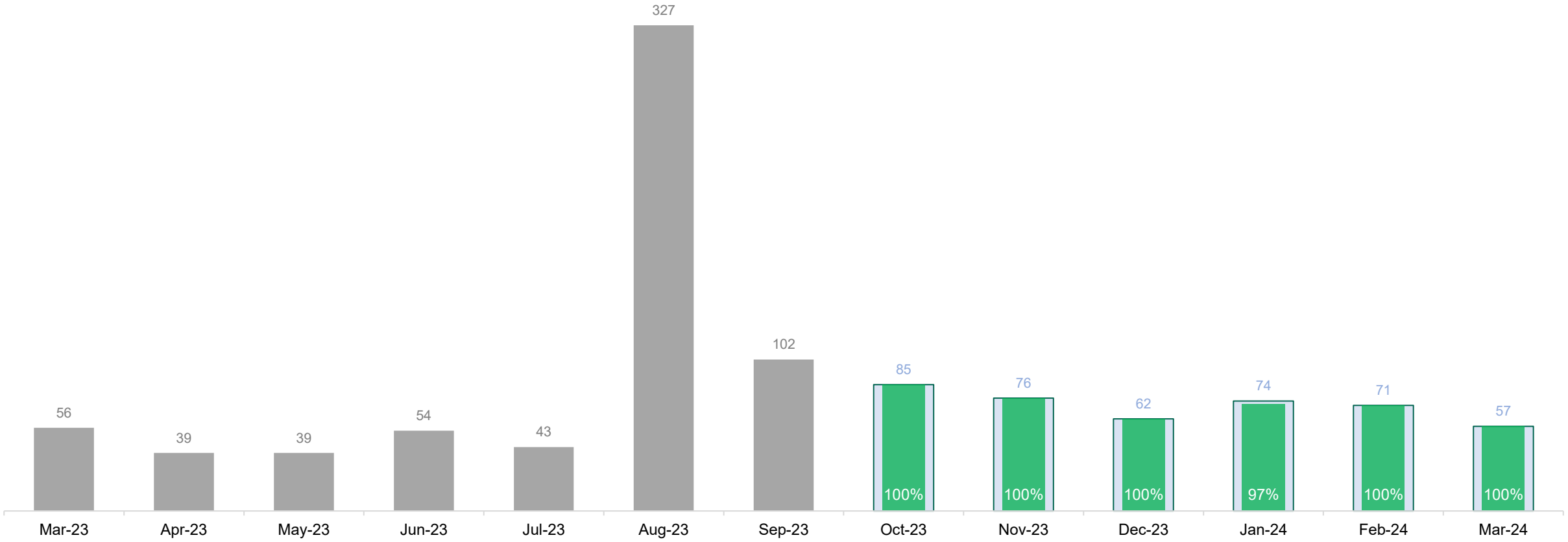
Medicines & Healthcare products Regulatory Agency

Operational Performance KPIs
Clinical Trials and Investigations

KPI 1: We will assess 95% of all initial Clinical Trial Authorisation (CTA) and Clinical Investigation applications within their category's statutory timeline.

March 24: 100% (►0%)

On Target



	Mar 23	Apr 23	May 23	Jun 23	Jul 23	Aug 23	Sep 23	Oct 23	Nov 23	Dec 23	Jan 24	Feb 24	Mar 24
Assessed (total)	56	39	39	54	43	327	102	85	76	62	74	71	57
Assessed (on time)								85	76	62	72	71	57

Medicines & Healthcare products Regulatory Agency

Operational Performance KPIs
Clinical Trials

Output

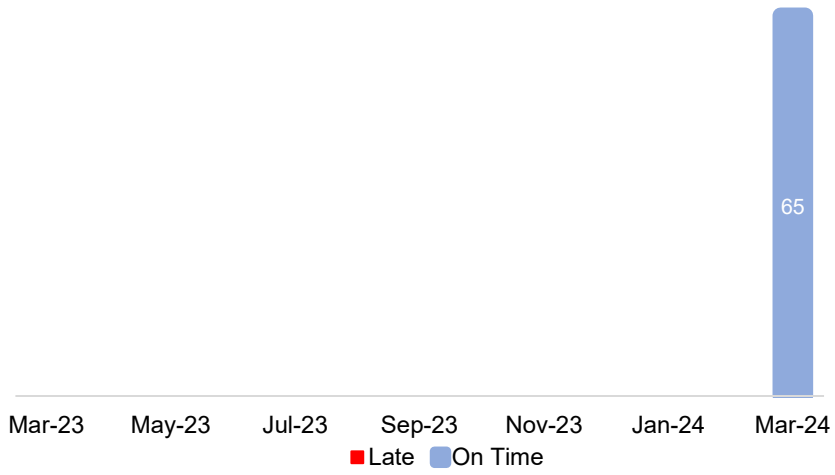
Clinical Trial Authorisation (CTA) applications assessed in and outside of statutory timeframes.

Target: "We will assess 95% of all initial Clinical Trial Authorisation (CTA) applications within their category's statutory timeline".

	Mar 23	Apr 23	May 23	Jun 23	Jul 23	Aug 23	Sep 23	Oct 23	Nov 23	Dec 23	Jan 24	Feb 24	Mar 24
CTA Applications (Assessed on time)	0	2	0	2	0	4	11	76	70	60	69	67	48
CTA Applications (Assessed late)	49	30	30	44	38	316	82	0	0	0	2	0	0
% Completed on Time	0%	6%	0%	4%	0%	1%	12%	100%	100%	100%	97%	100%	100%

Volume

Current volume of CTA applications that are unassessed, split into those that are younger and older than the statutory timeframes.



Turnaround Times

Current time taken to assess a CTA application or ammendment.

Description	Target	Mar-24 Actual
Average time of assessment of a Clinical Trial **application.**	**30** days	**28 (▼1)** On Target
Average time of assessment of a Clinical Trial **amendment**.	**35** days	**28 (▲1)** On Target

Insight

Key Performance Indicator

100% of Clinical Trial Authorisation applications were processed within statutory timeframes in March.

Volume

Volume tracking of CTA applications is a new metric that cannot be ran historically, historical volume data will build in each iteration of this monthly report.

We had 65 CTA applications unassessed as of April 1st, these were all within regulatory deadlines.

Misc.

Clinical Trial Initial Applications have a 30-calendar day statutory timeframe to issue an outcome from the Application Received Effective Date (Day 0).

The 'output' data from October 2023 onwards, represents the number of Initial clinical trial authorisation (CTA) applications received from 1st September 2023 onwards, assessed in that month.

Volume data represent the number of pending applications received in that month currently under assessment at the time when the data was extracted. The 'live apps' is a constant variable as applications are received and assessed live.

Medicines & Healthcare products Regulatory Agency

Operational Performance KPIs
Clinical Investigations

Output

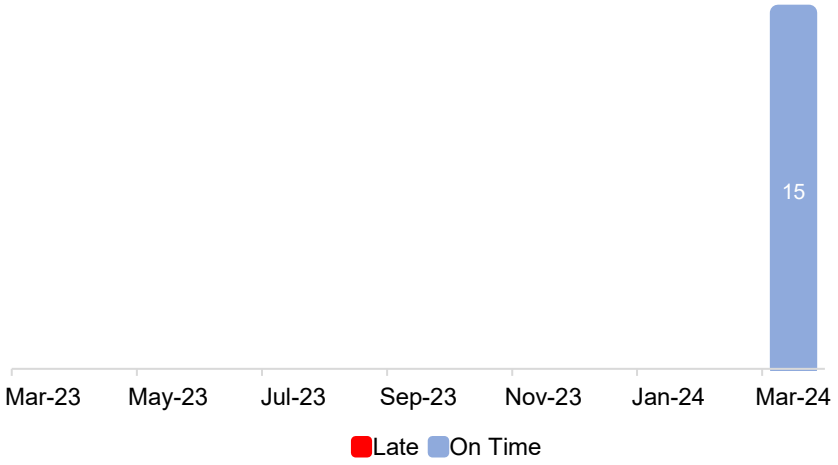
Clinical Investigation applications assessed in and outside of statutory timeframes.

Target: "We will assess 95% of all Clinical Investigation applications within their category's statutory timeline".

	Mar 23	Apr 23	May 23	Jun 23	Jul 23	Aug 23	Sep 23	Oct 23	Nov 23	Dec 23	Jan 24	Feb 24	Mar 24
Clinical Investigations (Assessed on time)	7	7	9	8	5	7	9	9	6	2	3	4	9
Clinical Investigations (Assessed late)	0	0	0	0	0	0	0	0	0	0	0	0	0
% Completed on Time	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%

Volume

Current volume of Clinical Investigation applications that are unassessed, split into those that are younger and older than the statutory timeframes.



Turnaround Times

Current time taken to assess a Clinical Investigation application.

Description	Target	Mar-24 Actual
Average time of assessment of a Clinical Investigation **application.**	**60** days	**50 (▲9)** On Target
Average time of assessment of a Clinical Investigation **amendment**.	**21** days	**11 (▲7)** On Target

Insight

Key Performance Indicator

100% of Clinical Investigation applications were processed within statutory timeframes in March.

Volume

Volume tracking of Clinical Investigations is a new metric that cannot be ran historically, historical volume data will build in each iteration of this monthly report.

We had 15 Clinical Investigation applications unassessed as of April 1st, these were all within regulatory deadlines and the team are confident this is a healthy and manageable volume.

Misc.

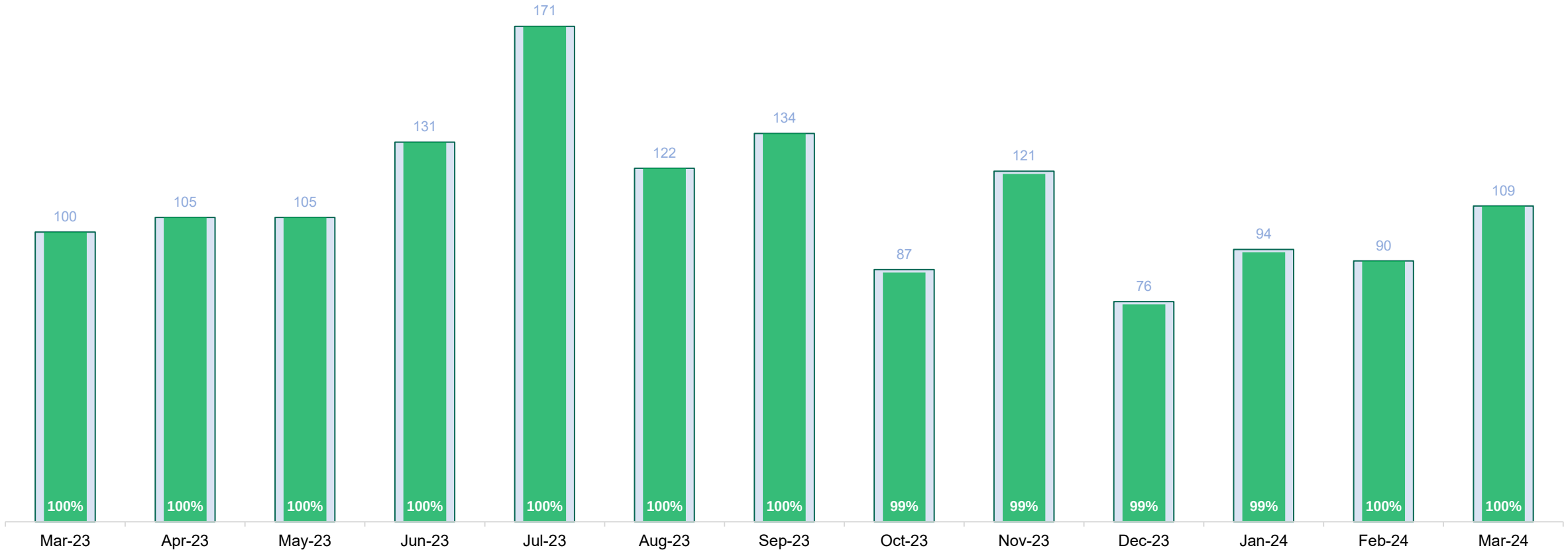
Regulatory timelines are as follows, 60 calendar days for GB studies. For NI studies we have 45 days plus 3 clock stops of 7 days each where we may seek expert advice giving a maximum review period of 66 days. Note, the 'Intake' only refers to applications received and deemed valid as some may be rejected at the point of internal validation. The review period (60 or 45 days) begins the first day after the submission of a valid application

Operational Performance KPIs
Control Testing

KPI 2: We will certify 95% of vaccine batches within 43 days and 99% of blood product batches within 15 days of submission.

March 24: 100% (►0%)

On Target



	Mar 23	Apr 23	May 23	Jun 23	Jul 23	Aug 23	Sep 23	Oct 23	Nov 23	Dec 23	Jan 24	Feb 24	Mar 24
Certified (total)	100	105	105	131	171	122	134	87	121	76	94	90	109
Certified (on time)	100	105	105	131	171	122	134	86	120	75	93	90	109

Medicines & Healthcare products Regulatory Agency

Operational Performance KPIs
Control Testing

Output

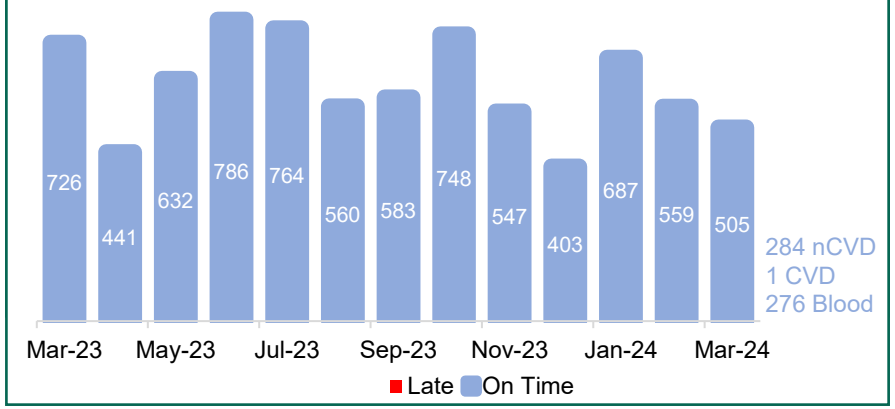
Vaccine and blood product batches certified in and outside of statutory timeframes.

Target: "We will certify 95% of vaccine batches within 43 days and 99% of blood product batches within 15 days of submission".

	Mar 23	Apr 23	May 23	Jun 23	Jul 23	Aug 23	Sep 23	Oct 23	Nov 23	Dec 23	Jan 24	Feb 24	Mar 24
n-COVID Vaccine (on time)	43	35	39	65	108	59	56	32	44	19	28	22	45
n-COVID Vaccine (late)	0	0	0	0	0	0	0	0	0	0	0	0	0
% Completed on Time	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%
COVID Vaccine (on time)	23	8	6	1	0	14	40	23	19	4	0	1	0
COVID Vaccine (late)	0	0	0	0	0	0	0	0	0	0	0	0	0
% Completed on Time	100%	100%	100%	100%	N/A	100%	100%	100%	100%	100%	N/A	100%	N/A
Blood Products (on time)	49	70	60	65	63	63	56	52	64	54	65	67	64
Blood Products (late)	0	0	0	0	0	0	0	1	1	1	1	0	0
% Completed on Time	100%	100%	100%	100%	100%	100%	100%	98%	98%	98%	98%	100%	100%

Volume

Number of batches awaiting testing



Turnaround Times

Current time taken to certify vaccine and blood product batches.

Description	Target	Mar-24 Actual
Average time to certify a **non-COVID vaccine** batch	**43** days	**5 (▼1)** On Target
Average time to certify a **COVID vaccine** batch	**43** days	**1 (▼1)** On Target
Average time to certify a **blood product** batch	**15** days	**7 (►0)** On Target

Insight

Key Performance Indicator
100% of batches were certified within timeframes in March 2024, meaning we exceeded our targets of 99% of vaccines and 05% of blood products certified on time.

Output
The turnaround of blood products remained steady in March. The number of vaccine batches continues to follow seasonal trends. There was little demand for new batches of COVID vaccines for the spring campaign this year.

Volume
We continue to hold a healthy volume of batches that are awaiting testing. With no batches awaiting testing that are older than statutory timeframes.

Turnaround Times
We continue to certify all vaccine and blood product batches well within statutory timeframes.

Medicines & Healthcare products Regulatory Agency

Operational Performance KPIs
Medicine Licensing via the National Route

KPI 3: We will determine 95% of medicines license applications within 210 days via the national route.

March 24: 13% (▼4%)

Off Target

	Mar 23	Apr 23	May 23	Jun 23	Jul 23	Aug 23	Sep 23	Oct 23	Nov 23	Dec 23	Jan 24	Feb 24	Mar 24
Determined (total)	50	52	32	46	37	47	53	23	43	27	34	86	55
Determined (on time)	8	22	2	7	0	2	7	4	4	8	13	15	7

Medicines & Healthcare products Regulatory Agency

Operational Performance KPIs
Medicine Licensing via the National Route

Output

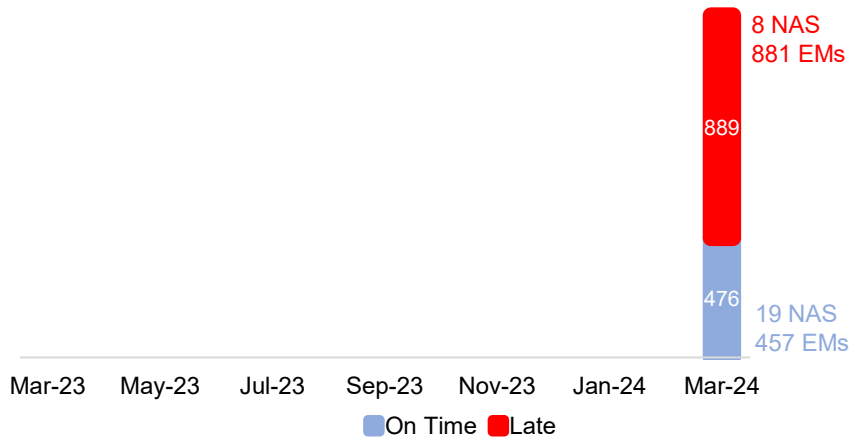
New Active Substances (NAS) and Established Medicines medicine license applications determined via the National route, in and outside of statutory timeframes.

Target: "We will determine 95% of medicines license applications within 210 days via the national route".

	Mar 23	Apr 23	May 23	Jun 23	Jul 23	Aug 23	Sep 23	Oct 23	Nov 23	Dec 23	Jan 24	Feb 24	Mar 24
New Active Substances (Determined on time)	2	0	0	0	0	0	0	1	1	1	0	0	0
New Active Substances (Determined late)	1	0	4	0	0	2	0	2	1	0	0	0	0
% Completed on Time	67	N/A	0%	N/A	N/A	0	N/A	33%	50%	100%	N/A	N/A	N/A
Established Medicines (Determined on time)	6	22	2	7	0	2	7	3	3	7	13	15	7
Established Medicines (Determined late)	41	30	23	39	37	43	46	17	38	19	21	71	48
% Completed on Time	13%	42%	7%	15%	0%	4%	13%	15%	7%	27%	38%	17%	13%

Volume

Undetermined NAS and Established Medicines medicine license applications via the National route, split into those that are younger and older than the statutory timeframes.



Turnaround Times

Current time taken to determine NAS and Established Medicines license applications via the National route.

Description	Target	Mar-24 Actual
Average time to determine a medicine license application via the National route that **contains a New Active Substance.**	**210** days	**0 (►0)** Target N/A
Average time to determine a medicine license application via the National route that contains an **Established Medicine.**	**210** days	**433 (▼19)** Off Target

Insight

Key Performance Indicator

13% of medicine licenses were determined via the National Route on time in March. Our KPI performance showed a continuous decline for each month of Q4.

Our KPIs measure the percentage of work completed on time and therefore whilst we focus on a backlog of older established medicine license applications, our KPIs will show a low performance score for the time being. Established Medicines are managed via our 'Return to Green' programme, reported on weekly. We continue to see a sustained positive reduction of backlog. The workstream lead has indicated that there is currently a mitigation plan being implemented to clear our backlog by September 2024.

Turnaround Times

No NAS applications were completed in Q4, so no turnaround times have been provided. This reflects resourcing issues (vacancies and knock-on effects of redeployment). Focus has been put on reducing time to allocation and ensuring that timetables for applications received from now on are strictly adhered to, to restore compliance with statutory timelines at the earliest point.

Established medicines remain well over our statutory timeframe of 210 days via the National Route, although we did see the average in March reduce by 19 days. Over the coming months we expect to see further reductions in average turnaround times, reflecting the positive impact of the introduction of initiatives and process changes. Based on the composition of the backlog and current prioritisation strategy (review of applications in age order), only applications for first generic and products that could alleviate supply issues will be completed within target times for the foreseeable future.

Operational Performance KPIs
Medicine Licensing via the International Recognition Procedure

KPI 4: We will determine 95% of medicines license applications within 60 days via recognition Route A and within 110 days via Route B through the International Recognition Procedure.

March 24: 100% (►0%)

On Target

	Mar 23	Apr 23	May 23	Jun 23	Jul 23	Aug 23	Sep 23	Oct 23	Nov 23	Dec 23	Jan 24	Feb 24	Mar 24
Determined (total)	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	1	3
Determined (on time)	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	1	3

Medicines & Healthcare products Regulatory Agency

Operational Performance KPIs
Medicine Licensing via the International Recognition Procedure

Output

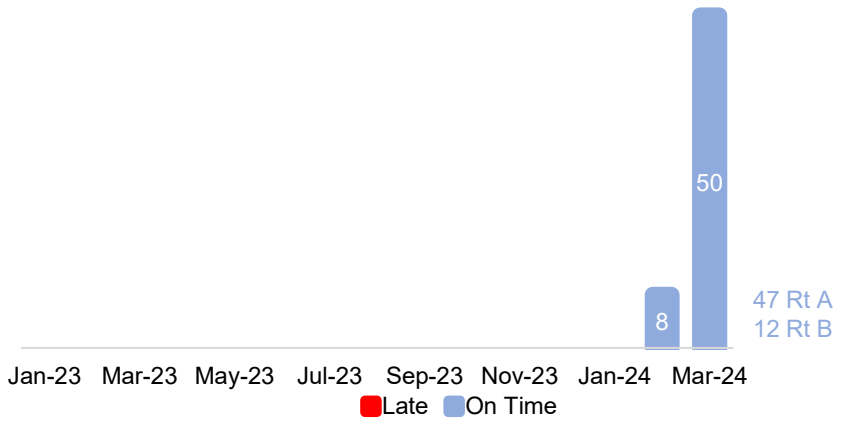
New Active Substances (NAS) and Established Medicines medicine license applications determined via the International Recognition Procedure (IRP) in and outside of statutory timeframes.

Target: "We will determine 95% of medicines license applications within 60 days via recognition Route A and within 110 days via Route B".

	Mar 23	Apr 23	May 23	Jun 23	Jul 23	Aug 23	Sep 23	Oct 23	Nov 23	Dec 23	Jan 24	Feb 24	Mar 24
Via Route A (Determined on time)	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	1	3
Via Route A (Determined late)	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	0	0
% Completed on Time	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	100%	100%
Via Route B (Determined on time)	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	0	0
Via Route B (Determined late)	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	0	0
% Completed on Time	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A

Volume

Undetermined NAS and Established Medicines medicine license applications via the IRP, split into those that are younger and older than the statutory timeframes.



Turnaround Times

Current time taken to determine NAS and Established Medicines license applications via the IRP.

Description	Target	Mar-24 Actual
Average time to determine a medicine license application via the International Recognition Procedure's **Route A.**	**60** days	**53 (▲23)** On Target
Average time to determine a medicine license application via the International Recognition Procedure's **Route B.**	**110** days	**0 (►0)** Target N/A

Insight

Key Performance Indicator

100% of medicine licenses via our new International Recognition procedure were determined on time since the new route opened in January.

Volume

There are currently 50 medicine license applications awaiting determination via the IRP, however none of these are currently outside of statutory timeframes.

Volume tracking is a new metric that cannot be ran historically, historical volume data will build in each iteration of this monthly report.

Turnaround Times

The average time to determine a medicine license via Route in the IRP is currently at 53 days, this is 7 days below our statutory target of 60 days. March's average turnaround did increase by 23 days, but this is largely due to low volumes of applications being determined impacting averages.

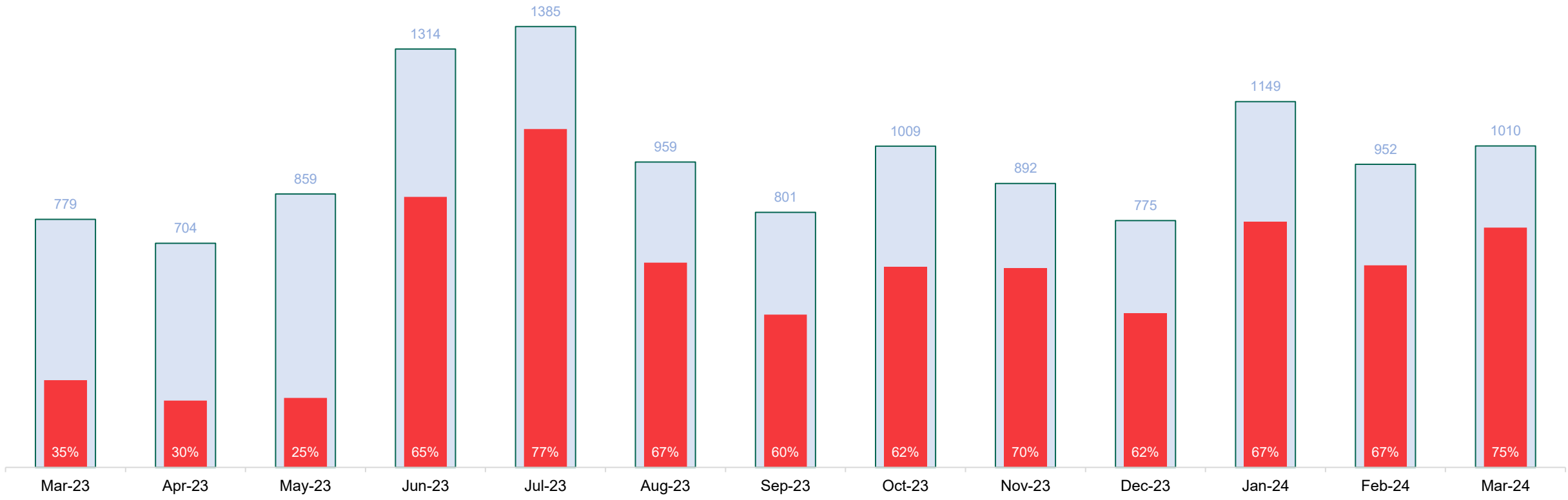
No applications were completed via IRPs Route B in Q4, so no turnaround times have been provided.

Operational Performance KPIs
National Variations

KPI 5: We will assess 95% of all national variations within their category's statutory timeline.

March 24: 75% (▲8%)

Off Target



	Mar 23	Apr 23	May 23	Jun 23	Jul 23	Aug 23	Sep 23	Oct 23	Nov 23	Dec 23	Jan 24	Feb 24	Mar 24
Assessed (total)	779	704	859	1,314	1,385	959	801	1,009	892	775	1,149	952	1010
Assessed (on time)	4	210	218	850	1,063	643	480	630	625	484	771	635	753

Medicines & Healthcare products Regulatory Agency

Operational Performance KPIs
National Variations

Output

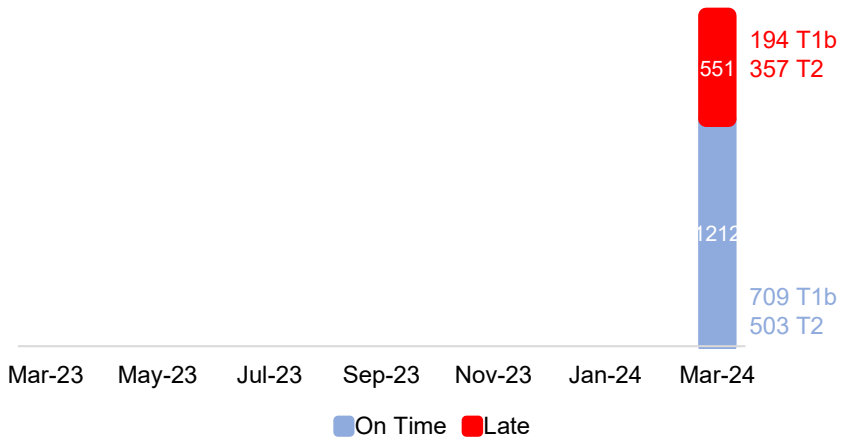
National Variations assessed in and outside of statutory timeframes.

Target: "We will assess 95% of all national variations within their category's statutory timeline".

	Mar 23	Apr 23	May 23	Jun 23	Jul 23	Aug 23	Sep 23	Oct 23	Nov 23	Dec 23	Jan 24	Feb 24	Mar 24
Type 1b Variations (Assessed on time)	209	178	165	771	987	584	406	538	552	439	689	571	604
Type 1b Variations (Assessed late)	460	461	580	381	275	289	243	276	185	229	261	183	156
% Completed on Time	31%	28%	22%	67%	78%	67%	63%	66%	75%	66%	73%	76%	79%
Type 2 Variations (Assessed on time)	65	32	53	79	76	59	74	92	73	45	82	64	149
Type 2 Variations (Assessed late)	45	33	61	83	47	27	78	103	82	62	117	134	91
% Completed on Time	59%	49%	46%	49%	62%	69%	49%	47%	47%	42%	41%	32%	60%

Volume

Unassessed National Variations that are younger and older than the statutory timeframes.



Turnaround Times

Current time taken to assess National Variations.

Description	Target	Mar-24 Actual
Average time to assess **Type 1b National Variations.**	**30** days	**22 (▼19)** On Target
Average time to assess **Type 2 National Variations.**	**90** days	**129 (▲9)** Off Target

Insight

Key Performance Indicator

75% of National Variations were assessed on time in March. Performance did however show some signs of positive improvement (+8%).

Our KPIs measure the percentage of work completed on time and therefore whilst we focus on a backlog of older variations, our KPIs will show a low performance score for the time being. Variations and safety amendments are managed via our 'Return to Green' programme, reported on weekly. We continue to see a rise in our output and the workstream lead has indicated that there is currently a mitigation plan being implemented to clear our backlog by expected clearance dates.

Output

Output of both Type 1b and Type 2 variations showed positive increases for every month in Q4, therefore the % completed on time has continued to move in a positive direction.

Volume

There remains a backlog of 194 Type 1b variations and 357 Type 2 variations that are older than our statutory timeframes.

Volume tracking is a new metric that cannot be ran historically, historical volume data will build in each iteration of this monthly report.

Turnaround Times

On average in March, we processed Type 1b National Variations in 22 days, this was 19 days quicker than February and brought us within our statutory timeframe of 30 days.

Type 2 National Variation average in March worsened by 9 days and remains outside the statutory timeframe of 90 days.

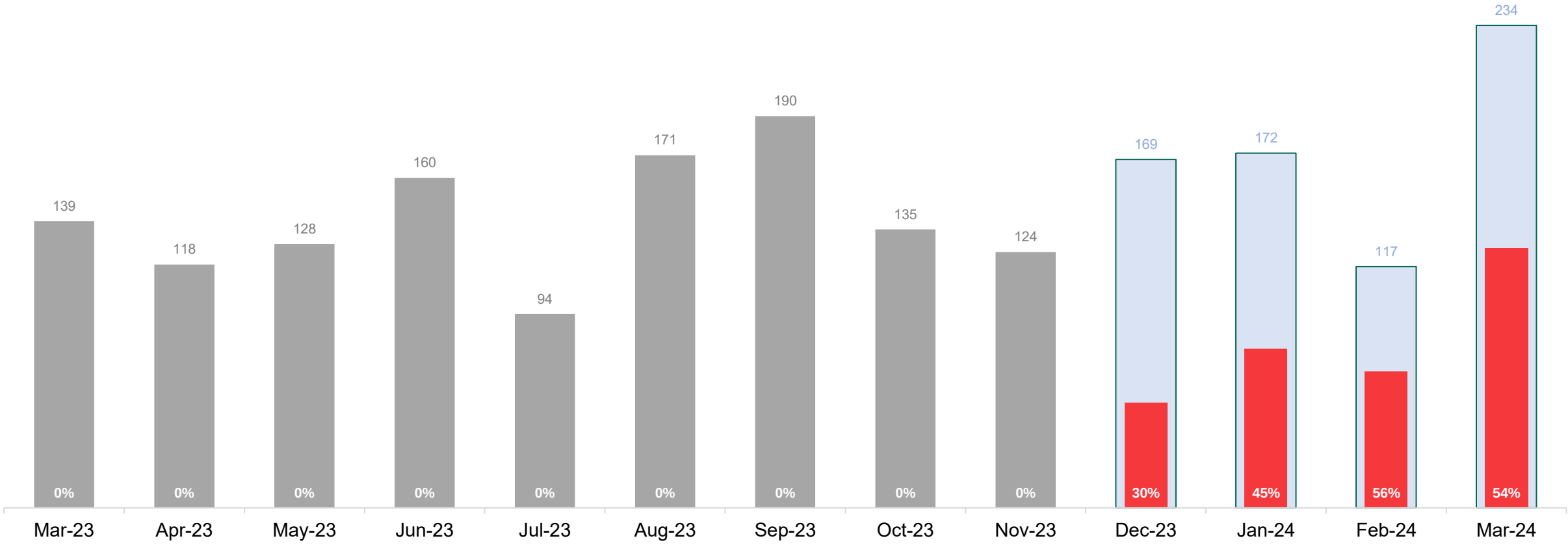
Medicines & Healthcare products Regulatory Agency

Operational Performance KPIs
Manufacturing and Distribution Authorisations

KPI 6: We will grant, vary or refuse 95% of manufacturing and distribution authorisations within their category's statutory timeline.

March 24: 54% (▼2%)

Off Target



	Mar 23	Apr 23	May 23	Jun 23	Jul 23	Aug 23	Sep 23	Oct 23	Nov 23	Dec 23	Jan 24	Feb 24	Mar 24
Authorisations (total)	139	118	128	160	94	171	190	135	124	169	172	117	234
Authorisation (on time)										51	77	66	126

Medicines & Healthcare products Regulatory Agency

Operational Performance KPIs
Manufacturing and Distribution Authorisations

Output

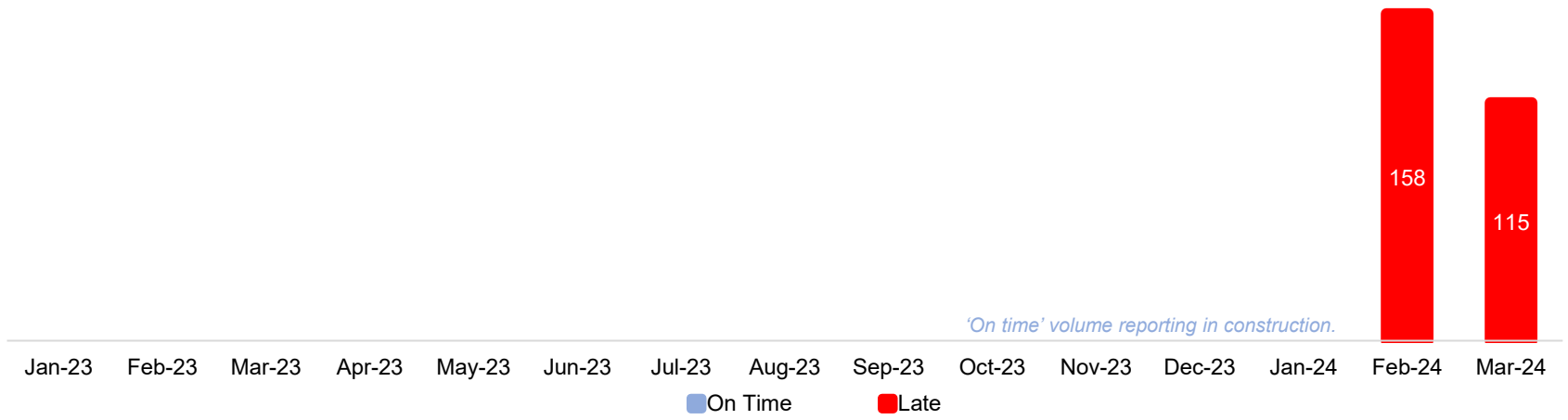
Wholesale Dealer and Manufacturing Licenses granted, varied or refused in and outside of statutory timeframes.

Target: "We will grant, vary or refuse 95% of manufacturing and distribution authorisations within their category's statutory timeline".

	Mar 23	Apr 23	May 23	Jun 23	Jul 23	Aug 23	Sep 23	Oct 23	Nov 23	Dec 23	Jan 24	Feb 24	Mar 24
Wholesale Dealer Licenses (Granted etc. on time)										29	44	42	54
Wholesale Dealer Licenses (Granted etc. late)										40	41	25	28
% Completed on Time	139	118	128	160	94	171	190	135	124	42%	52%	63%	66%
Manufacturing Licenses (Granted etc. on time)										22	33	24	72
Manufacturing Licenses (Granted etc. late)										78	54	26	80
% Completed on Time										22%	38%	48%	47%

Volume

Sites awaiting triage, assessment or inspection.



Insight

Key Performance Indicator

54% of Manufacturing and Distribution Authorisations were granted, varied or refused within our statutory timeframes in March. This figure remained relatively static through Q4.

Our KPIs measure the percentage of work completed on time and therefore whilst the inspections teams focus on a backlog of older applications, our KPIs show a low performance score for the time being. Inspections are a workstream that are managed via our 'Return to Green' programme, reported on weekly. Output in March was 234, this was 117 higher than February and the backlog of work reduced to 72 inspections, 43 lower than February. The workstream lead has indicated that there is currently a mitigation plan being implemented that means we should clear our backlog of initial triage work by May and will have implemented a compliance strategy by December 2024.

Volume

The number outside statutory is 115 at various stages with 72 awaiting inspection.

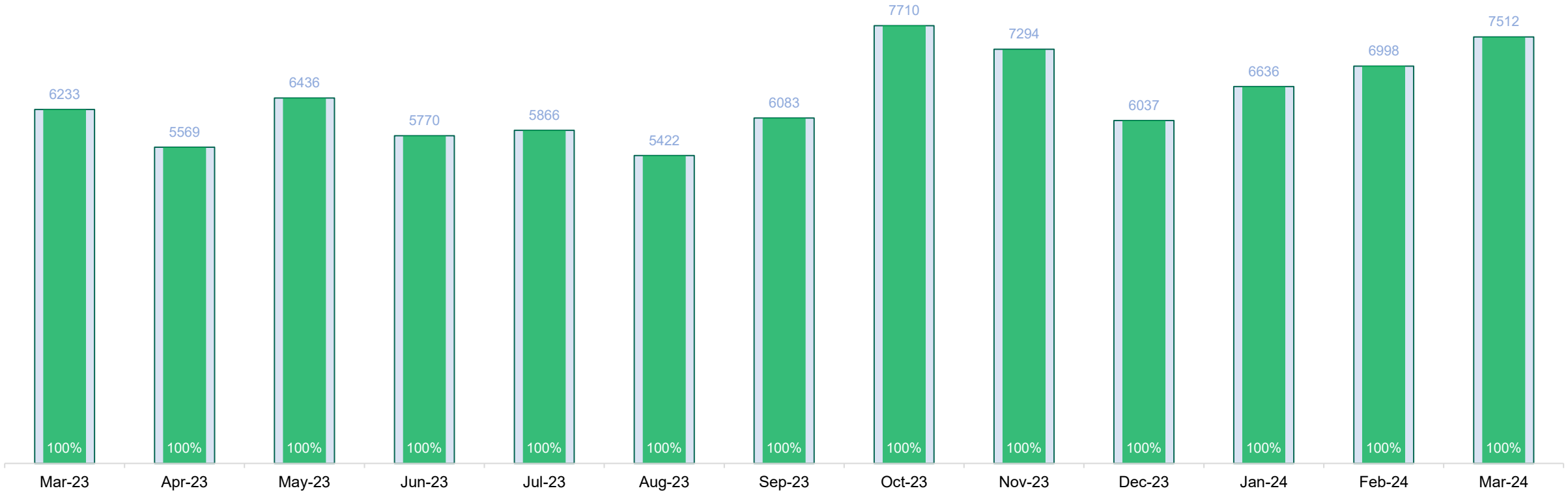
The inspections team are currently exploring ways to enhance reporting on the inspections process holistically, including how to report on the current volume of work end-to-end that is 'on time' but within statutory timeframes. Data reporting on the backlog of inspections is also aligned through the Return to Green programme, the team has identified and prioritised several interventions to accelerate triage and assessment and release resource to support inspections.

Operational Performance KPIs
Patient Safety Monitoring

KPI 7: (Interim KPI) We will process 90% of Fatal Adverse Drug Reaction (ADR) reports for medicines within 24 hours,100% within 72 hours and we will process 95% of serious ADR reports for medicines within 72 hours and 100% within 5 days.

March 24: 100% (►0%)

On Target



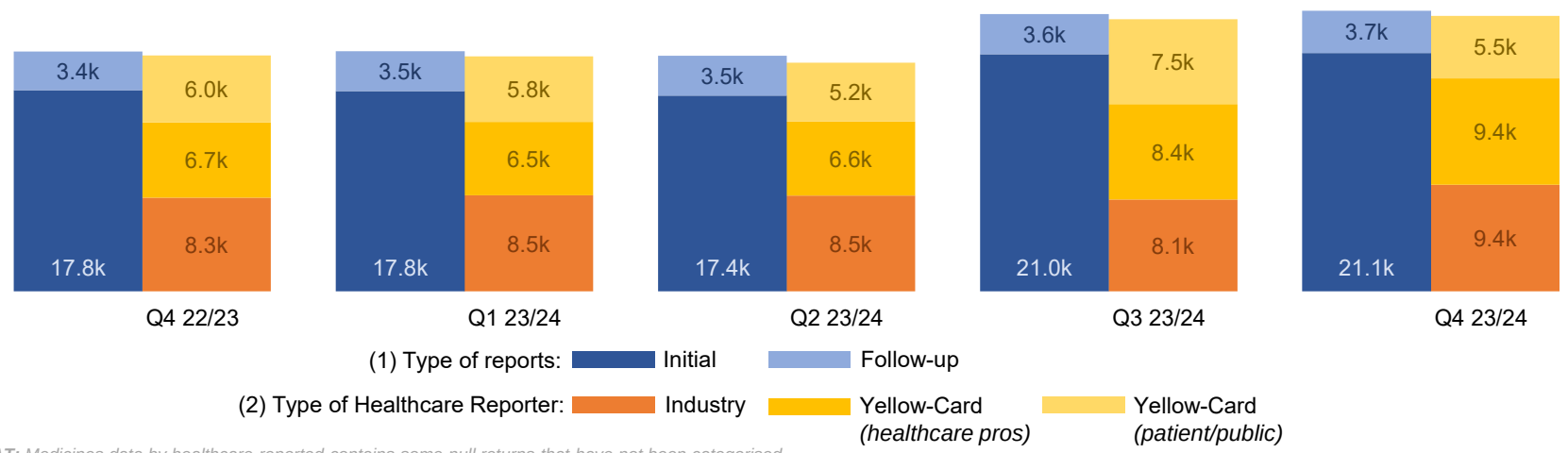
	Mar 23	Apr 23	May 23	Jun 23	Jul 23	Aug 23	Sep 23	Oct 23	Nov 23	Dec 23	Jan 24	Feb 24	Mar 24
Reports Processed (total)	6,233	5,569	6,436	5,770	5,866	5,422	6,083	7,710	7,294	6,037	6,636	6,998	7,512
Reports Processed (on time)	6,233	5,569	6,436	5,770	5,866	5,422	6,083	7,710	7,294	6,037	6,636	6,998	7,512

Medicines & Healthcare products Regulatory Agency

Operational Performance KPIs
Patient Safety Monitoring

Adverse Incident Reports Received - Medicines

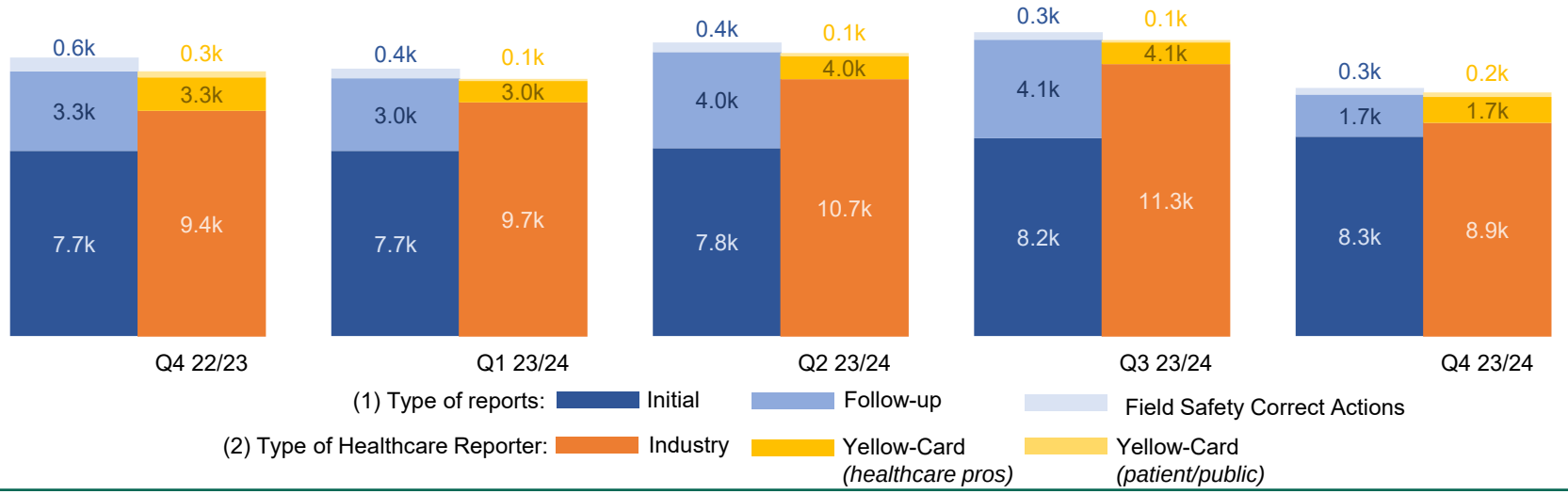
Number of adverse incident reports related to medicines received split by (1) the type of report and (2) the type of healthcare stakeholder who made the report.



CAVEAT: *Medicines data by healthcare reported contains some null returns that have not been categorised.*

Adverse Incident Reports Received - Devices

Number of adverse incident reports related to devices received split by (1) the type of report and (2) the type of healthcare stakeholder who made the report.



Insight

Key Performance Indicator

We are currently internally crafting a Key Performance Indicator that will allow us to track the time taken for us to respond to safety signals. Current workload systems do not allow for timebound reporting. The new SafetyConnect System should provide us with this capability. We intend to have the new KPI set out for next year's Business Plan publication.

Our interim KPI, which measures the % of fatal and serious Adverse Drug Reaction reports for medicines, continues to show 100% performance month-on-month.

Adverse Incident Reports Received

Adverse incident reports for medicines and medical devices remain steady with all reports processed within 15 days. Any reports for medicines which meet a certain level of data validation can by-pass manual processing which aids completion of reports within the statutory timelines. The Adverse Incident and Signal Analysis team currently have six contingent workers to help process the volume of adverse incidents for medical devices given all of these require manual review.

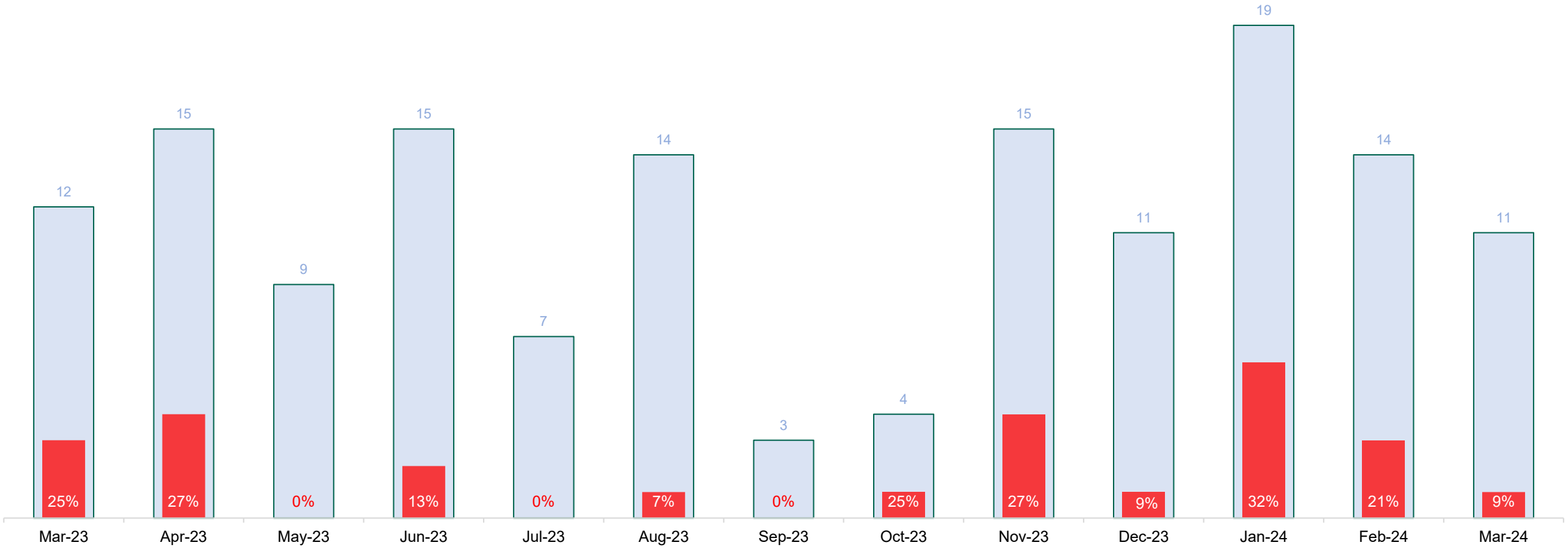
The number of adverse drug reactions reports for medicines increased in March 2024 compared to the beginning of this year. Notably over the past few months we have seen an increase in reports from healthcare professionals, the highest number of reports we have seen in over a year which is encouraging. The total number of reports includes medicines, COVID-19 vaccines and all other vaccines, with only 3% of reports relating to COVID-19 vaccines in March. s. It is encouraging to see reports from patients, parents and carers remain as the highest volume of reports received from a single reporter group via the Yellow Card scheme. The number of adverse incidents reports for medical devices received as initial reports remains consistent, with the number of follow-up reports required decreasing significantly. The number of Yellow Card reports from members of the public concerning medical devices remains low which is an area for improvement.

Operational Performance KPIs
Scientific Advice

KPI 8: We will offer scientific advice to 95% of requests within 70 days of the request being made.

March 24: 9% (▼12%)

Off Target



	Mar 23	Apr 23	May 23	Jun 23	Jul 23	Aug 23	Sep 23	Oct 23	Nov 23	Dec 23	Jan 24	Feb 24	Mar 24
Scientific Advice Offered (total)	12	15	9	15	7	14	3	4	15	11	19	14	11
Scientific Advice Offered (on time)	3	4	0	2	0	1	0	1	4	1	6	3	1

Medicines & Healthcare products Regulatory Agency

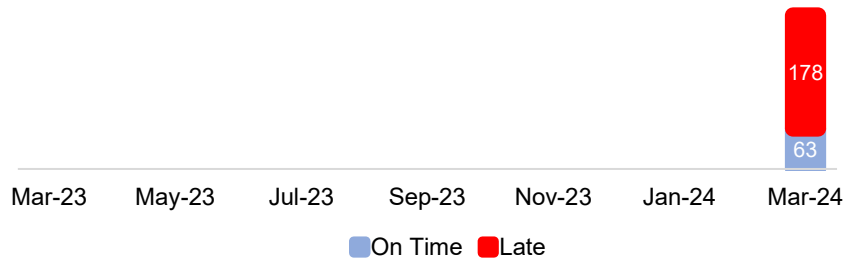
Operational Performance KPIs
Scientific Advice

Output

Target: "We will offer scientific advice to 95% of requests within 70 days of the request being made".

Scientific advice offered on…	Mar 23	Apr 23	May 23	Jun 23	Jul 23	Aug 23	Sep 23	Oct 23	Nov 23	Dec 23	Jan 24	Feb 24	Mar 24
Clinical Trials (on time)	0	0	0	0	0	0	0	0	1	0	2	0	0
Clinical Trials (late)	7	3	6	9	2	7	2	1	3	4	4	6	4
% Completed on Time	0%	0%	0%	0%	0%	0%	0%	0%	25%	0%	33%	0%	0%
NAS (on time)	4	2	1	3	2	2	0	0	1	0	0	0	1
NAS (late)	1	2	0	3	2	3	1	1	2	2	2	2	2
% Completed on Time	80%	50%	100%	50%	50%	40%	0%	0%	33%	0%	0%	0%	0%
Population Health (on time)	1	0	0	1	0	1	0	1	0	0	2	2	0
Population Health (late)	1	5	2	2	3	1	0	1	4	2	5	3	4
% Completed on Time	50%	0%	0%	33%	0%	50%	N/A	50%	0%	0%	29%	40%	0%
Biologicals (on time)	2	3	0	1	0	0	0	0	2	1	2	0	0
Biologicals (late)	1	3	1	2	2	5	1	1	4	4	2	0	0
% Completed on Time	67%	50%	0%	33%	0%	0%	0%	0%	33%	20%	50%	N/A	N/A
PIQ (on time)	0	1	0	0	0	0	0	0	0	0	0	1	0
PIQ (late)	0	0	0	0	0	0	0	0	0	0	0	0	0
% Completed on Time	N/A	100%	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	100%	N/A

Volume



Turnaround Times

Average time to offer advice on	Target	Mar-24 Actual
Clinical Trial applications	70 days	270 (▼92)
New Active Substances (NAS)		207 (▼70)
Population Health		240 (▲25)
Biologicals		N/A (▼N/A)
Patient Information Quality		N/A (▼N/A)

Insight

Key Performance Indicator
Performance in Q4 declined month-on-month and remains well below the target of 95%.

Our KPIs measure the percentage of work completed on time and therefore whilst we focus on the backlog of older requests for scientific advice, we are showing a low performance score against our KPI. Scientific Advice is a workstreams managed via our 'Return to Green' programme, reported on weekly. The workstream lead has indicated that there is currently a mitigation plan being implemented that means we should clear our backlog of requests for scientific advice by December 2024.

Turnaround Times
While the time to deliver scientific advice in all areas remains above our target of 70 days on average; delivery of Scientific Advice letters in Clinical Trials and New Active Substances have both shown positive gains in March. Innovative medicines (Biologicals and NAS) have agreed and assigned meeting dates to stakeholders for most of their allocation and continue to drive improvement in time to deliver advice.

Quality of Delivery
Direct feedback through a standard form from stakeholders averaged at 8.2/10 for the Quality of the advice received. Feedback is requested with the delivery of every 'Scientific Advice Meeting' letter.

Misc.
The Executive Committee have confirmed that this workstream has been deprioritised against the concerted efforts to clear backlogs in all workstreams via the 'Return to Green' programme whilst leads in the area consider a new model for how we offer scientific advice.

Medicines & Healthcare products Regulatory Agency

BOARD MEETING HELD IN PUBLIC

21 May 2024

Title	How effectively is the MHRA addressing performance on Established Medicines, and how will a sustainable established medicines function be established?
Board Sponsor	Julian Beach
Purpose of Paper	Assurance

How effectively is the MHRA addressing performance on Established Medicines, and how will a sustainable established medicines function be established?

1. Executive Summary

1.1 This paper provides an update on progress made in delivering the current plan to eliminate the Established Medicines backlog and achieve sustainable operations to agreed targets within statutory timelines.

1.2 Following the update to the Board in March 2024, further significant progress has been made in Established Medicines in terms of performance, people and process. Modelling figures show that the project to clear the established medicines backlog is on track.

1.3 Stretching targets to reduce the original backlog to 750 (749 as of 28th March) and the overall backlog to 900 (881 as of 28th March) by the end of March 2024 were met. The original backlog is defined as applications that were overdue (over the statutory limit of 210 days) on 9th January 2024. The overall backlog is all overdue applications, including those that have fallen over 210 days since 9th January 2024. This is a significant achievement in building confidence in our ability to eliminate the original backlog and is the direct result of a number of process changes.

1.4 Over the course of 2023, we made a number of internal process changes to improve how we assess pending national marketing authorisation applications (MAAs). We also communicated the most common application errors for the benefit of industry and made checklists available on gov.uk to support right first-time submissions. From 1 March, following consultation with Trade Associations, we issued guidance making clear we will not process incomplete applications; we will only send one request for further information (RFI); and, following approval, we require applicants to submit a prepopulated lay summary for the UK public assessment report (UKPAR).

1.5 The positive impact of these interventions on throughput is being realised with further improvements forecast in the coming months. Early evidence includes a record high number of applications being considered at CHM in April and an increase in number of applications refused for failing to provide responses to questions raised in the allotted time.

1.6 In April, our performance monitoring continued to demonstrate improvements in the numbers of applications completed at each stage of the national assessment process. The Established Medicines applications backlog was reduced to 805 applications. Assessment of company responses to questions were prioritised to achieve the target reduction in backlog numbers.

1.7 Since January, circa 50 applications have been converted from a national to reliance route. We anticipate further conversions as European procedures conclude in the coming months.

1.8 The plan to eliminate the backlog is underpinned by new ways of working and increased resources. Appropriately trained resources have been onboarded via contingent labour or professional service contracts to increase capability in the short term. A recruitment campaign has been launched to source additional assessor resource to support long-term sustainability.

2 Current status

2.1 The Established Medicines performance data for April are shown below.

Work type	Median time in days	Numbers granted	% in target
Type IB variations – national,	35	659	71%
Type II variations – national, Project Orbis	69	178	76%
Established medicines national MAA	430	82	5%

2.2 Output as measured by number of completed first assessments (RFI) and number of applications determined has significantly increased to approximately 35 applications per week since January and reflects the positive impact of initiatives implemented to date.

3 Backlog clearance plan update

3.1 Following achievement of the 31 March targets, a clearance rate that takes account of new work falling overdue and existing backlog cases has been modelled. The backlog is a dynamic situation with an average of 16 applications falling overdue every week. In order to eliminate the backlog, a target has been set to reduce the original backlog to 500 by the end of June. Achieving this stretching target will be dependent on there being a sufficient number of company responses for assessment. 22% of backlog applications are with companies to compile responses to the identified outstanding issues and it is anticipated that many of these will be submitted and assessed by the end of June.

A “Net Projected Clearance Rate” of c20 cases a week is required from April to May. From June to July this rises to c.68 a week, as a result of “Green” cases clearing the system. The clearance rate falls to c.26 a week from August, as a result of residual, more complex cases remaining. Increased clearance rate from April to May is a result of the new process changes – specifically the RFI round being reduced to 1, better scrutiny upfront of non-compliant applications, and reduced report writing – alongside additional resources and overtime uptake.

For the future the increased clearance rate over June / July is based on expected 3-5 month gap in c270 “Green” RFI responses being received back from first assessments completed between January and March.

3.2 The prioritisation strategy is unchanged. Applications will continue to be assessed in age order with the exception of applications for first generics or products that can alleviate shortage issues which are being prioritised.

4 Future Plan for Established Medicines backlog

4.1 The focus is now on eliminating the remaining backlog to the modelled trajectory and embedding the new process. As the review of low-risk/low-resource applications is largely complete, a number of new workstreams are being developed and implemented as detailed below to ensure progression of the medium and high risk/resource applications:

Optimisation of assessment process and utilisation of existing and new resource

4.2 To improve efficiency, pending medium and high risk/resource MAAs have been divided into sections and dedicated teams of existing and new resource have been set up to process discrete parts of the dossier. For example, a discrete team to deal with unallocated most complex ‘red’ applications (narrow therapeutic index drugs, complex pharmaceutical forms e.g. inhalers, topical products). In addition, skilled staff have been redeployed from the British Pharmacopoeia to assess pending active substance master files. Assessment of the clinical data is being covered by ongoing professional services contracts, allowing existing pharmaceutical assessors to conduct a targeted assessment of the critical aspects of the drug product.

4.3 To ensure that recent high performance for variations is maintained, assessors in training will focus solely on the assessment of variations to existing marketing authorisations for a period of 3 months. By taking a different approach to how these assessors are supported, experienced assessors will be able to dedicate more time to assessment work of new MAAs leading to a higher output.

Definition of Clearly defined targets / delivery timelines

4.4 First assessments: team targets are set a week in advance based on available resource; if full time, broad expectation is completion of 3.5 green, 1.5 amber or 0.5 red applications per person. Total target ≥ 36 applications per week. As we now have cleared most of the oldest responses, the aim is to maintain the rapid turnaround of responses received with each individual having a target to complete all response assessment within 2 weeks of receipt. In April the CHM provided advice on the safety, quality and efficacy of over 40 licence applications. All MHRA assessments had the recommended action agreed by CHM.

5 Risks

People

5.1 A number of risks exist within the people category. These are being actively managed to ensure actions have the required impact.

- **Recruitment**: to ensure we have the required numbers of assessors coming on to support with assessments, focus is continuing to find and recruit professional services contracts, contingent labour and, most importantly, permanent staff.
- **Retention**: ensuring active resolution of issues, managing high continuous workload in a pressured environment, supporting staff under considerable pressure. Ensuring communication of a revised Competency Development Framework to recognise individuals.
- **Culture**: addressing change management/culture has been a focus and the change in ways of working is continuing to be seen and accepted. Focused communication sessions and opportunity to question, challenge and make suggestions have continued to be robustly used to introducing the new processes.

Process

5.2 Detailed internal guidance on the process changes has been documented and shared with the operational team to support consistent processing of applications in the backlog. We are currently scoping out a plan which will define measures of success. The efficacy of the interventions and changes to process will be reviewed against these measures; and decisions will be taken on which of the changes should be taken through into the sustainability phase.

6 External Engagement

6.1 Significant external engagement has been conducted over the last 3 months. A list of events was presented in the March Board paper. Alongside the regular meetings listed below, an Industry webinar on the 24th April 2024 was held to provide updates on our improved performance and handling of applications for medicines in shortage and respond to questions on the new process and future plan for eliminating the backlog. Extensive Q+A was conducted which was open in nature answering any topics raised. The webinar was well attended with excellent feedback obtained with >95% giving positive feedback.

Ongoing / future meetings	When
DHSC/BGMA/MHRA meeting	Bi-weekly
Established Medicines Working Group, successor to the Trade Association Task & Finish Group (ABPI, BIA, BGMA, EMIG, PAGB)	Monthly

7 Future sustainability

7.1 With the improvement in the clearance of the backlogs in Established Medicines and Variations for products being marketed, we are starting to see a rising number of applications being submitted. As part of the future review of anticipated volumes, companies are seeing a projected rise in applications to the MHRA. We expect this increase to continue as we release constrained demand, through completing applications, as existing and new companies decide the UK is a market they wish to be operating in.

7.2 Current estimates are for approximately a 20% rise in applications in 2024 and currently a further 10% rise annually in both 2025 and 2026. The training deficit and dealing with the backlog would see a demand for additional internal Medical Assessors and Quality Assessors. There is currently an evergreen advert which is being used to recruit Pharmaceutical Assessors. This is to mitigate the risk of historically finding appropriate candidates hard to recruit.

7.3 We also need to address the need for flexible resources to cope in the future with unexpected increases in demand, and to supply already trained assessors at short notice when required. We are also looking to external sources of supply for this flexible resource.

7.4 Work to define the long-term review of what licencing pathway is needed for the appropriate assessment of Generic Medicines is continuing. A review of the process changes introduced in 2024, is being conducted in June and July. Workshops will be completed with industry in September and October 2024 to confirm the changes which can be made once focus shifts from reduction of the backlog to reliable delivery of sustainable performance.

8 Recommendation

The Board is asked to:

8.1 Advise on the progress of current and planned activities to eliminate the backlog of applications for established medicines.

8.2 Consider sufficiency of the plans to ensure that we have a sustainable operation for established medicines licencing.

Julian Beach
May 2024

Medicines & Healthcare products Regulatory Agency

BOARD MEETING HELD IN PUBLIC

May 2024

Title	**Does the Board support the Criminal Enforcement Unit's approach to the identification, prioritisation and reduction of the threat posed by the illegal trade in human medicines?**
Board Sponsor	Alison Cave
Purpose of Paper	To update the Board on the strategic direction of the CEU to protect the public from the threat posed by the illegal trade in human medicines.

Does the Board support the Criminal Enforcement Unit's approach to the identification, prioritisation and reduction of the threat posed by the illegal trade in human medicines?

1. Executive Summary

1.1 In public health terms, it is likely that the illegal trade in medicines is the cause of significant, often largely unreported, harm to the UK public. The MHRA is one of a very small number of regulators globally equipped with a dedicated criminal enforcement capability. The Criminal Enforcement Unit (CEU) works in partnership with cross-sector partners at home and abroad to defeat the illegal trade – protecting the public and maintaining regulatory integrity.

1.2 This paper outlines, in broad terms, the unit's understanding of the nature and scale of the current criminal threat from the illegal sale and supply of medicines and describes how the unit prioritises and delivers its response[1]. Measuring the success of this activity in a manner that is externally and outcome focused is a critical part of the unit's innovative approach to its business. The paper outlines the unit's bespoke performance measurement model.

2. A picture of the criminal threat

2.1 Although variants and sub-threats are observed, the threat to the UK from the illegal trade in medicines is dominated by the online sale and supply of unlicenced medicines to retail customers outside the legitimate supply chain (LSC).

2.2 At any time, there are estimated to be between 30,000 and 40,000 active websites illegally offering medicines for sale to UK customers. Most are hosted overseas, often in hard-to-reach jurisdictions. The majority are believed to be under the control of a relatively small number of well-established transnational organised criminal groups (OCG). The resources, reach and expertise frequently available to these criminal groups support sophisticated online store fronts and customer experiences comparable to standard legitimate e-commerce offerings. This can often make it challenging for the public to distinguish between the licit and illicit trades. The CEU is currently working with Digital and Technology colleagues on an IT solution to help customers make this determination and stay safe online.

[1] The strategic approach outlined in this paper is common to threats from regulatory fraud and serious offences involving medical devices. As these threats are assessed to be significantly smaller, they are not separately addressed in this paper.

2.3 Most illegally traded medicines (ITM) sold online are unlicenced generic products sourced from Asia. Although some websites purport to offer UK branded stock, the customer invariably receives the generic unlicenced version. The perception of UK licenced medicines as premium can also drive the dishonest misappropriation of such products from the LSC for subsequent sale online. Theft and diversion of LSC product, sometimes facilitated by corrupt professionals and others acting inside the industry, is not uncommon in intelligence reporting. Criminals are also known to exploit insufficiently robust stock management and destruction regimes, and targeted thefts of and from logistics vehicles also play a part in the misappropriation of UK stock.

2.4 Unlike in many low-and middle-income countries, CEU intelligence currently suggests that the threat to the UK from cross-border trafficking in counterfeit medicines is not significant. The widespread availability of inexpensive generic versions of the most in-demand medicines largely undermines the economics of the counterfeit business model. The counterfeit trade can occasionally make sense for criminals where a licenced product experiences unusually high UK demand recreationally (or otherwise for misuse), and there is no generic version available. This effect was seen most recently in 2023, when a sudden and exponential rise in demand for semaglutide among the general population for use in weight loss led to the appearance of relatively unsophisticated counterfeit versions of branded Ozempic products. This case study is described in greater detail later in this paper.

2.5 Robust compliance and enforcement work by the Agency, has helped the LSC remain extremely resistant to penetration by falsified medicines. Just two relatively minor incidents have been identified in the last three years, with a third identified before the falsified product entered the LSC.

2.6 A variety of push and pull factors combine to sustain a substantial UK demand for ITM. Recreational use, addiction and dependence all play a part, as those ITM also controlled as drugs can present an inexpensive, superficially lower risk alternative to traditional narcotics. Unlicenced generic benzodiazepines and medicines containing the nonbenzodiazepine zopiclone appear to be in particularly high demand at present.

2.7 For other medicinal products, speed of access, convenience, choice, self-diagnosis, and anonymity are also likely to influence individual buying decisions. Acute supply challenges and difficulties in accessing primary healthcare may also contribute to the demand. CEU analysis of the footfall on twenty-two illegally trading websites advertising medicines to the UK identified approximately 250,000 combined visits from global customers in a single month. Recent analysis of just nine illegally trading websites estimates a combined annual turnover of nearly £5m.

2.8 Whether sourced from Asia or diverted from the LSC by criminal groups, once ordered online, ITM are generally transported into the UK via international parcel post. The trafficking of larger consignments of medicines concealed in air freight and RoRo has also been identified.

2.9 Annual ITM seizures at the border are at their highest levels to date, and this is likely a consequence of improved information sharing and interoperability between the CEU and Border Force. As with any trafficked commodity, a change in seizure levels is a very unreliable bellwether of a similar change in either demand or supply.

2.10 It is estimated that more than 100m doses of ITM are trafficked into the UK every year. Erectile disfunction medicines and those used for pain management and in the treatment of anxiety and sleeping disorders are the most frequently observed. These products generally account for between 80% and 90% of total annual ITM seizures.

2.11 Although the overall threat from the illegal trade in medicines is assessed to be substantial, it is not believed to be especially dynamic in its business model. Both the demand and supply sides of the economic equation appear relatively entrenched and stable, with only pockets of acute informal demand for specific products, particularly those used for aesthetic and recreational purposes, driving changes in behaviour.

2.12 The activities of well-established OCGs continue to pose the broadest threat, and this is highly likely to continue in the years ahead. Many OCGs have established appreciable footprints in trafficking medicines into the UK and in distributing them across the country. Senior actors in OCGs sometimes base themselves overseas, adding a further level of complexity in securing lasting upstream disruption. OCGs often demonstrate high levels of capability and sophistication with vertical integration of the sourcing, sale, importation and distribution of ITM and the laundering of criminal proceeds, common.

2.13 There are indications that websites operated by OCGs are becoming increasingly sophisticated in terms of customer experience with many offering instant customer assistance and support through chat messaging and telephone helplines, and exclusive discounts and incentives. By enhancing customer perceptions of credibility and legitimacy, this can lead to greater repeat trade.

2.14 Criminals are likely to exploit offending opportunities presented by new and emerging technologies. Intelligence suggests an increasing use of cryptocurrency as a method of payment and to hold and launder criminal profits. Although sales transactions through encrypted messaging applications are frequently observed, there is currently no intelligence to suggest the widespread criminal use of Artificial Intelligence (AI). There is a realistic

possibility that the increasing availability of consumer-focused AI tools will change this assessment.

Case study – the illegal trade in counterfeit Ozempic

In the spring of 2023, significant mainstream and social media discourse led to an exponential and unprecedented rise in popular demand for semaglutide products to treat overweight. To meet this informal demand, a small but pernicious illegal trade emerged in counterfeit Ozempic branded self-injectable pens (active ingredient semaglutide).

While some of the websites offering these products for sale were assessed as fraudulent, others appeared to be offering the POM for sale without a prescription. Working with partners, the CEU identified and removed from circulation almost 900 inauthentic Ozempic pens during 2023. Of these, 500 were identified at two UK wholesalers in a single incident in September with the remainder seized in fast parcel interceptions at the UK border.

Examination of the seized products confirmed them to be relabelled insulin glulisine pens which shared visually similar light blue plastic containers. A very small number of suspected adverse reactions to these products were reported to the MHRA. These reports were consistent with the inadvertent administration of insulin glulisine above the therapeutic dose.

Informal demand for Ozempic, and the illicit trade in the product, are assessed to be relatively transient and fragile. To influence both behaviours, the CEU committed significant resource to public messaging through regional, national, and global media outlets. The activity was targeted at those demographic groups identified through open-source research as most vulnerable to the illegal trade, and the largely unsophisticated criminal actors responsible for it.

Intelligence indicates that the prevalence of inauthentic Ozempic pens in the UK is now very low. Robust and sustained preventative and disruptive interventions by the CEU and its partners underpinned by increased vigilance and deterrence messaging are assessed to have materially depleted stocks, reduced demand, and displaced emerging criminal activity. It is also likely that NHS and private prescribing of Wegovy (a second semaglutide product launched in September 2023) contributed to reducing the demand for illegally traded Ozempic.

3. The CEU response to the criminal threat

3.1 Recognising that the success of the CEU response is predicated on having the clearest possible picture of the threat and that this, in turn, is predicated on having the richest possible intelligence pipeline, the CEU works closely with other government departments and agencies, both nationally and globally.

3.2 At a tactical level, the CEU enjoys particularly strong bilateral relationships with the Home Office Border Force (BF). Through combined efforts to enhance joint and single agency working at the border, this remains one of its most valued and productive. Over the last two years in particular, the CEU has deployed resources on multiple occasions to border posts in support of BF counter-medicines crime activity. These 'intensification' operations have proved highly effective in terms of seizures and have also strengthened interoperability. Day-to-day two-way intelligence sharing has helped better target BF interdictions and bolstered mutual understanding of trafficking trends. The resulting BF seizures have also initiated and supported multiple CEU investigative interventions.

3.3 Close working relationships with territorial police forces across the country are also critical to the unit's success. Police presence significantly enhances the effectiveness of all operational CEU search and arrest deployments.

3.4 The CEU continues to leverage robust partnerships with international regulatory and law enforcement agencies to effectively fulfil its mission of mitigating threats. Emphasising the exchange of intelligence and best practice at a strategic level, the unit has maintained particularly strong ties with European partners by securing formal observer status for the EU's Working Group of Enforcement Officers (WGEO) and, through the National Crime Agency, with Europol in The Hague.

3.5 On a global level, the CEU takes a leading role in the annual Operation Pangea initiative, which it helped conceptualise fifteen years ago. Coordinated by Interpol, Operation Pangea has evolved into a significant multinational effort focused on disrupting the illicit online trade of counterfeit health products. Its objectives extend to reducing demand by educating the public about the hazards of purchasing medications from unregulated websites. Preparations are currently in progress for the CEU's active involvement in the next iteration of Pangea. The CEU currently sits on the Permanent Forum on International Pharmaceutical Crime (PFIPC). The PFIPC is an international enforcement forum with the aim of protecting public health through the exchange of information and ideas to foster mutual cooperation.

3.6 The CEU also has effective information-sharing relationships with key stakeholders throughout the medicines industry. Many pharmaceutical companies maintain their own brand protection functions, and these provide a valuable bilateral docking point for CEU intelligence and investigative staff. The

CEU also uses its close association with the Pharmaceutical Security Institute as its primary route into this industry capability at a strategic level.

3.7 Given the assessed nature, scale and resilience of the prevailing medicines crime threat to the UK, robust prioritisation of the CEU's response is vital. To ensure that both tactical and strategic prioritisation is consistent, risk-led and defensible, the CEU uses the MoRiLE risk assessment tool. The tool, which is very much the standard across the law enforcement profession, assesses individual and thematic manifestations of medicines crime against a range of factors to determine the level of unmitigated risk they present. Whilst prioritising public safety, MoRiLE considers a broad range of harms associated with medicines crime.

3.8 The CEU sets strategic priorities each year to help ensure the public continue to enjoy access to effective and acceptably safe medicines, untarnished by the egregious activities of criminals. These priorities inform both high-level and day-to-day decision-making in the unit - driving proactive delivery and managing reactive demand.

3.9 Using the MoRiLE tool, and based on a current understanding of the threat, the strategic priorities of the CEU for 24/25 are:

- To reduce the criminal threat from falsified medicines entering the regulated supply chain
- To reduce the criminal threat from the illegal supply of the most harmful UK licensed medicines
- To reduce the criminal threat from the illegal supply of the most harmful unlicensed medicines

3.9 Driven by its strategic priorities, the CEU's operating model focuses on using the most efficient and effective means to reduce the criminal threat. In a law enforcement context, 'threat' is the extent of individual (or more commonly, group) capability and capacity to commit specified criminal offences, or a class of offences, at some point in the future. Threat can be thought of as the likelihood side of the risk equation. Assessments of criminal threat levels are generally based on intelligence of past or known present conduct and behaviours.

3.10 In respect of the illegal trade in medicines, threat is the product of an individual's (or a group's) means[2], motivation[3] and opportunity[4] to offend. If just one of these is absent, an offence cannot generally occur. As preventing future crime is rightly the dominant purpose of all progressive law enforcement functions, the strategic focus of CEU activity is on compromising one or more of these

[2] The tools and ability required to commit a crime

[3] A reason to commit a crime. Normally based on the perception of a favourable risk/reward ratio.

[4] Adequate chance to commit the crime. Normally because of the absence of a capable guardian

enablers. In practical terms, the CEU delivers this mission through the Threat Reduction Intervention (TRI).

3.11 TRIs fall into three broad categories distinguished by their focus. 'Universal' TRIs target the general population, 'selective' TRIs target groups whose members have a higher risk of offending behaviour or becoming victims, and 'indicated' TRIs target individuals already offending. Universal and selective TRIs tend to be most effective against strategic threats, whereas indicative TRIs generally have utility in addressing specific tactical threats.

3.12 To optimise the overall threat reduction yield from its work, the CEU leads, supports and coordinates a wide cross-section of TRIs to prevent or disrupt offending, and to bring offenders to justice where necessary. The unit adopts a multi-dimensional and intelligence-led approach, with the precise tactical response determined by the particulars of the individual threat. Whilst not appropriate in every case, a full scale investigation towards criminal charges remains an important and effective tactical option on the unit's menu. In addition to threat reduction, the resulting prosecution also serves an important secondary purpose of visibly maintaining the credibility of regulation and upholding the rule of law.

3.13 All CEU TRIs target one or more of the three enablers. This might include activity to dismantle criminal capabilities, to deny the rewards of crime or to design out victim vulnerability. Over time, innovative and sustained TRIs, each addressing a different aspect of behaviour, can have a material diminishing effect on the overall level of the criminal threat.

3.14 The overall threat reduction impact is often spread across multiple linked TRIs. These elements can be either concurrent or consecutive. In a tactical operational scenario, for example, the arrest of a suspect, the seizure of illegally traded medicines in their possession, the imposition of a custodial sentence upon conviction, and the confiscation of financial assets can all contribute to the overall threat reduction outcome.

3.15 TRIs often involve activity not targeted at achieving a criminal justice disposal. The unit's online enforcement capabilities are especially productive in this area. The removal of online marketplace listings for ITM and the taking down of illegally trading websites can have a valuable disruptive impact. Although online recidivism is common, sustained interventions of this kind that reduce the means to offend in the short-term can, over time, also remove longer-term motivation.

3.16 The CEU measures and reports on its performance using a bespoke methodology based on the number and assessed impact of TRIs completed. A TRI is included in reporting when an identified criminal threat is adjudged to have been diminished or degraded as a direct consequence of activity led, supported, or coordinated by the CEU.

3.17 Each TRI is assessed as minor, moderate or major for the extent of its positive impact on the threat and the likely duration of that impact. By way of example, an intervention assessed to have reduced a threat by more than two thirds for more than twelve months will generally be scored as ‘major’, a one-third reduction for between six and twelve months as ‘moderate’, and by less than a third for fewer than six months as ‘minor’. Although informed by professional judgement and intelligence, the process of assessing threat reduction impact is necessarily a subjective one. To provide additional rigour, therefore, each preliminary assessment is subject to a process of moderation by an independently chaired panel within the Agency.

3.18 After moderation, a nominal value is applied each TRI by reference to its impact category (major, moderate or minor), giving an aggregate threat reduction ‘score’. Each quarter, to assist in both the presentation and understanding of this measure (and to better align with the rhythm of the unit’s delivery), the CEU reports this score for a rolling twelve-month period as the Threat Reduction Index.

3.19 Reflecting delivery during the pilot for the new measure, the first-year baseline for the Threat Reduction Index was set at 7941. The CEU closed the 2023/24 performance year with the index standing at 8730 - up from 7390 in the first quarter of the year and 10% above baseline. A total of 1334 moderated TRIs were completed, including seven assessed as resulting in major threat reduction impact. Criminal profits of £2.1m were denied to suspected offenders and, working in partnership with colleagues in Border Force, a total of 17.9m doses of illegally traded medicines was removed from circulation throughout the year.

3.20 Since its inception, law enforcement has been a profession in which the perfect outcome-focused performance measure has remained elusive. Measures such as investigations conducted, and arrests, convictions and seizures made, whilst superficially informative and readily available, say little about the overall strategic purpose of law enforcement effort. Although not without its limitations, the CEU’s unique threat reduction index links all unit activity to its core threat reduction objective and offers a valuable proxy indicator for public facing outcomes.

3.21 Given the relatively static nature of the criminal business model, the threat reduction tools, tactics, powers and resources available to the CEU are likely to remain fully effective in the short to medium term. The CEU recently completed a project to replace its core intelligence and case management IT solution. Significant deficiencies in the outgoing solution led to the development of multiple workarounds and the use of a variety of disparate systems, spreadsheets, and databases to deliver critical services. The replacement system seamlessly integrates working processes to maximise the use made of intelligence and other data and remove inefficiencies.

4. Recommendation

The Board is asked to consider the information provided in this paper and to support the Criminal Enforcement Unit's approach to the identification, prioritisation and reduction of the threat posed by the illegal trade in human medicines.

Andy Morling
Deputy Director (Criminal Enforcement)
May 2024

Medicines & Healthcare products Regulatory Agency

BOARD MEETING HELD IN PUBLIC

21 May 2024

Title	How will the new Post Market Surveillance regulations improve patient safety whilst enabling access and innovation?
Board Sponsor	Alison Cave/Laura Squire
Purpose of Paper	Strategic Direction

How will the new Post Market Surveillance regulations improve patient safety, whilst enabling access and innovation?

1. Executive Summary

1.1. The MHRA is delivering a programme of changes to the Medical Device Regulations of 2002. This will take the form of a series of statutory instruments, in parallel with stakeholder engagement, as set out in our recently published Roadmap.

1.2. The primary aim of this regulatory change is improving patient safety, although it is also acknowledged that maintaining the supply of medical devices to the NHS and making the UK an attractive place for innovators, will also benefit patients and the public provided it can be done without compromising safety.

1.3. This paper sets out how the new regulations will strengthen the power of the MHRA to act to keep patients safe, as well as exploring how stronger post market controls can enable access and innovation.

1.4. In our Roadmap we set out our intention to consult further to refine measures beyond our planned core regulations. This paper seeks a strategic steer from the Board on measures to consider for that consultation, taking account of the learning since 2021, to ensure that the UK has a regulatory framework which is safe and enables UK based innovation.

2. Introduction

2.1. The Medical Device Regulations 2002 (UK MDR 2002) form the legislative basis of the current GB framework for medical device regulation. Since 2002, the EU has updated their regulations on medical devices, introducing EU MDR 2017/745 and IVDR 2017/746. MHRA was involved in the creation of that regulatory framework, however following the UK exit from the EU, the opportunity for the MHRA, as an independent sovereign regulator, to create our own framework, protecting patients whilst enabling innovation, was recognised.

2.2. The power to make amendments to the UK MDR 2002 comes from the Medicines and Medical Devices Act 2021. It is a requirement of that Act that any changes can only be made following public consultation. We undertook a consultation on all aspects of the proposed amendments in 2021 and published the government response in June 2022.

2.3. The scale of the work to implement the response to the consultation is substantial, with changes needed across all aspects of the 2002 regulations from pre-market requirements through registration and traceability, through to post market vigilance and surveillance. To manage the scale of change, we are therefore implementing the changes through a series of statutory instruments (SIs).

2.4. In determining the content of these SIs we have prioritised patient safety. In addition to the transition SI enacted in 2023, and an SI for how EU IVDR will operate in Northern Ireland in force from 21 March 2024, we will have 3 further SIs; one for Post Market Surveillance (PMS), one covering the core elements of the new Regime, and one covering enhancements, which will require further consultation. We expect the new PMS regulations to be debated in both Houses in the coming weeks, subject to Parliamentary time.

3. How the new regulations will improve patient safety.

3.1. The new regulations will improve patient safety in a number of ways. Set out below are the key highlights.

3.2. *Post-market surveillance (PMS)* is a set of activities conducted by manufacturers, to collect and evaluate experience gained from medical devices that have been placed on the market, and to identify the need to take any action. It is crucial to ensuring that medical devices continue to be safe and well-performing and that actions are undertaken if the benefits of continued use of the medical device become outweighed by the risks. The evaluation of PMS experiences can also highlight opportunities to improve the safety and efficacy of the medical device.

3.3. Under the UK MDR 2002 there are limited high-level provisions for PMS. The detail on how a manufacturer conducts and reports PMS is covered in guidance creating inconsistencies that make recognising safety issues difficult. The new regulations will introduce clearer and more stringent PMS requirements for medical devices in Great Britain (GB) that are risk proportionate, with improved regulatory oversight. PMS requirements will be reflective of the risk classification of the device in question and will include;

3.3.1. On vigilance, manufacturers will:

- be expected to investigate and report serious incidents within specific timelines.
- be required to carry out preventive and corrective actions to mitigate device safety-risks and non-conformities.
- produce and submit a risk assessment of any field safety corrective actions (FSCA) and an initial report on the proposed actions.
- undertake trend reporting to recognise adverse safety trends or signals in their data earlier.

3.3.2. On surveillance, manufacturers will be required to:

- maintain a PMS system.
- implement a PMS plan linked to the lifetime of the device.
- produce a PMS report (PMSR) for low-risk devices.
- produce and submit a Periodic Safety Update Report (PSUR) to their UK Approved Body for medium and high-risk devices.
- use the output of the PMS system to update technical documentation required by the conformity assessment procedure carried out in respect of the device.

3.4. A field safety corrective action (FSCA) is an action taken by a manufacturer to reduce a risk of death or serious deterioration in the state of health associated with the use of a medical device. A Field Safety Notice (FSN) is a communication sent by medical device manufacturers, or their representatives, in connection with an FSCA. These are internationally harmonised terms, in line with International Medical Device Regulators Forum (IMDRF) guidance. Manufacturers should take all reasonable steps to ensure their FSNs reach their customer base and provide a copy of the FSNs to MHRA. We continue to consider how further requirements for manufacturers to ensure there is a future proof mechanism for improving the visibility of these notices for example by publishing them on their own websites, could be introduced in a proportionate way in the future.

3.5. We are also continuing to examine how we can ensure that obligations for PMS continue until a device is no longer used. Manufacturers test their devices and assign them a “device lifetime”, however in practice, we know that many devices, especially implantable devices, are used for longer than that. Again, further consultation may be a route to ensuring this can be introduced in a proportionate way. Initially we will do this through guidance.

3.6. *Up-classification - implantables and SaMD* - The existing classification rules in the UK MDR 2002 (as amended) have fallen out of step with best international practice, particularly for implantable devices and software as a medical device. The changes being brought in as part of the future core regulations, will bring the classification of devices in line with best international practice, and as recommended by the Cumberledge report (Independent Medicines and Medical Devices Safety review) and ensure that the regulatory scrutiny of a device is commensurate with the level of risk it may pose to the patient. Thus, devices such as those implanted into the body or those that diagnose, treat or measure life threatening disease or conditions will undergo the highest level of inspection and regulation.

3.7. Software as a medical device (SaMD), either as stand-alone software or software that has been integrated into other medical devices (example software used to assist in x-ray or MRI imaging and analysis), has grown in market share and complexity since the UK MDR was written in the early 21st century. The UK MDR 2002 currently contains no definition of software or specific classification of SaMD, making it difficult for the developers of these devices to determine to which category their device belongs, and therefore which regulations they must adhere to. Artificial Intelligence technologies are a subset of SaMD.

3.8. The updates to the regulations we are bringing in will clearly define software and will have a clear classification matrix of software in line with current international best practice, as defined by the IMDRF. These steps alone will go far in improving patient safety of SaMD and software in medical devices and will place the UK among the most advanced regulators of software in or as a medical device in the world.

3.9. *Changes to the classification framework of IVDs* - The classification of *In Vitro* diagnostic medical devices (IVDs) is currently loosely based on risk, however only a

selection of what could be considered the highest risk devices are required to undergo the tightest regulation. The updates to the UK MDR 2002 will overhaul the classification of IVDs, clearly grouping devices according to increasing risk of erroneous result to the patient. Again, this classification framework will bring the UK in line with best international practice and is based on the Principles of IVD Medical Device Classification ((IMDRF/IVD WG/N64FINAL:2021) published by the IMDRF IVD working group on 21 January 2021. Software as an IVD will be classified according to the IVD classification matrix.

3.10. *Implant cards* - Between 2001 – 2010, breast implants from the manufacturer Poly Implant Prosthèse (PIP) used a low-grade industrial silicone which was a different composition to the one that had been approved. Many of these implants ruptured with no traceability to affected patients. Patients didn't know what implants they had, rendering a meaningful recall or follow-up clinical care problematic.

3.11. The Independent Medicines and Medical devices safety review focused on women who had been affected by implantable pelvic mesh. Strengthening the regulatory framework for medical devices is part of the government response to that report, with a commitment made in the 2022 update report to deliver on the need for improved regulation of implantable devices highlighted by the review. One way in which we are strengthening the regulatory framework is through the introduction of Implant Cards.

3.12. Implant Cards have already been introduced in the EU Medical Device Regulations to:

- Enable the patient to identify the implanted devices and to get access to other information related to the implanted device.
- Enable patients to identify themselves as persons requiring special care in relevant situations e.g., security checks.
- Enable emergency clinical staff or first responders to be informed about special care/needs for relevant patients in case of emergency situations.

3.13. The rules we will introduce in the new regulations will be similar. Implant cards will be provided to patients at the point of seeking informed consent to introduce the implant, and/or after the implant procedure. The implant cards will be required to contain the following information:

- information allowing the identification of the device, including the device name, serial number, lot number, the UDI, the device model, as well as the name, address and the website of the manufacturer.
- any warnings, precautions or measures to be taken by the patient or a healthcare professional with regard to reciprocal interference with reasonably foreseeable external influences, medical examinations or environmental conditions.
- any information about the expected lifetime of the device and any necessary follow-up

- any other information to ensure safe use of the device by the patient, including the overall qualitative and quantitative information on the materials and substances to which patients can be exposed.
- The identity of the patient.

3.14. *Unique Device Identifier (UDI)* – Another recommendation of the review was to improve traceability of devices, introducing UDIs on every medical device. UDIs are a series of numbers and / or letters that are created through internationally accepted device identification and coding standards. They allow for clear and unambiguous identification of specific devices on the market and facilitate their traceability.

3.15. UDIs allow devices to be identified from point of manufacture, through supply chain and to use or delivery to the patient. Being able to track devices in this way facilitates and strengthens patient safety by enabling easier recall of devices, combating counterfeiting, and ensuring quicker responses to any safety issues that may arise with devices. Once Regulatory Connect has been delivered we intend to mandate the recording of UDI as part of registration but it's requirement on all products will be introduced earlier, in the future core regulations.

3.16. *Increased scrutiny as part of the conformity assessment* is a further measure to increase patient safety in the new regulations. Approved Bodies will be required to examine 100% of the technical files for class IIb and above implantable medical devices. Under current rules they only need carry out a sample check.

4. Post Market Surveillance as an enabler of access and innovation.

4.1. All regulatory requirements represent a cost to industry. Although arguably an investment to prevent future costs that might result from harm to patients arising from poor quality devices, with the UK as only 2.7% of the global device market, those costs can be a barrier to supplying products to the UK.

4.2. The solution to this cannot be to reduce the standards a product must achieve before being able to register with MHRA and placed on the UK market. What we can do however, is remove duplication from that process, through a framework of international recognition. For companies for whom the UK is a follow-on market, this framework will take into account the work already done pre-market by comparable regulators, to establish the safety, quality and effectiveness of a medical device or IVD, already approved for use in their country.

4.3. Having a strong framework for post market surveillance and vigilance, is an enabler of such an approach. Later this month we intend to publish a policy paper setting out our plans for international recognition, and the intention will be that however products reach UK patients, they will be subject to clear obligations to provide post market reporting to the MHRA, enabling us to take swift action should a concern arise.

4.4. For manufacturers for whom the UK is a first launch market, strong post market controls offer the potential to developed pathways for earlier market access in

controlled circumstances. The Innovative Devices Access Pathway (IDAP) pilot is an initiative to bring new technologies and solutions to the National Health Service (NHS) to help with medical needs that are not currently being met.

4.5. The aim of IDAP is to enable and improve patient access to innovative and transformative medical devices by providing an integrated and enhanced regulatory and access pathway to developers. The aim of the pilot is to test the main elements of the pathway and to provide informative learning and feedback that helps to build the future access route for innovative devices in the UK.

5. Recommendations

5.1. The Post Market Surveillance Rules will be the first of three statutory instruments to implement the new Medical Devices regulatory framework. A statutory instrument to put in place further core elements of the new framework will be put in place in 2025, with a plan to consult further, ahead of a further statutory instrument to complete the delivery of the framework.

5.2. This paper focuses on how our current plans enhance patient safety whilst supporting access and innovation, which will be achieved through a combination of these statutory instruments through pre and post market measures.

5.1. The Board is asked to consider:

5.1.1. Is the Board assured that these measures will improve safety for patients and the public?

5.1.2. With the opportunity to consult further, as set out in our roadmap, does the Board see opportunities for further improvements in that consultation?

Alison Cave and Laura Squire
21 May 2024

Medicines & Healthcare products Regulatory Agency

BOARD MEETING HELD IN PUBLIC

21 May 2024

Title	How are we addressing the challenges of regulating *In Vitro* Diagnostics?
Board Sponsor	Laura Squire
Purpose of Paper	Strategic Direction

How are we addressing the challenges of regulating *In Vitro* diagnostics?

1. Executive Summary

1.1. The MHRA as a standalone sovereign regulator has presented opportunities for regulatory reform to strengthen patient safety and adapt to the future needs of innovative medical technologies. It has also highlighted the importance of working in partnership with other regulators both nationally and internationally.

1.2. Our future regulatory framework aims to protect patients and the public while providing an attractive environment for the life sciences industry, particularly in supporting domestic and international innovators of medicines, medical devices and *In Vitro* Diagnostic devices (IVDs).

1.3. The MHRA's programme of regulatory reform for medical devices will impact on all medical devices and IVDs on the market in the UK. This paper focuses on how the Agency is addressing the particular challenges of regulating IVDs. It also introduces our IVD Strategy, which describes our approach to exploiting the strengths of the UK diagnostics sector to facilitate access to high quality IVDs for patients and the public.

1.4. Creating a risk proportionate regulatory framework is one of five strategic themes of the IVD Strategy which sets out our approach to exploiting the strengths of the UK diagnostics sector to facilitate access to high quality IVDs. The other four themes; regulatory science, research and training, pre-market support for innovators, patient safety and surveillance, and pandemic preparedness and resilience, will be explored in detail in a fuller strategy to be published in the coming weeks.

1.5. In this paper we consider the impacts of advancements in Artificial Intelligence supporting clinical diagnosis, greater adoption and acceptance of diagnostic test results on UK patient samples with tests being performed outside the UK, the need for education during the implementation of digital tools in diagnostics and requirement for independent verification testing, all topical challenges that must be overcome to ensure patient safety.

2. Introduction

2.1. Diagnostic devices play a vital role not only in the treatment of conditions and diseases, but in enabling people to have longer symptom free lives as well as being seen as a tool in the recovery of healthcare systems from the pandemic, reducing waiting times and improving health outcomes.[1]

2.2. IVDs are tests which are essential for patient management. They ensure that clinical and treatment decisions provide accurate and safe patient care. IVDs examine

[1] Why do diagnostics matter – Maximising the potential of diagnostic services, Charlotte Wickens, Oct 2022

specimens (e.g. blood, urine, tissue, etc.) or bioinformatics data to identify a disease or medical condition.

2.3. Diagnostic test results have been historically presented in analogue formats, where a trained healthcare professional reads and interprets the results to provide a clinical diagnosis. Examples include:

- X-ray shadows on a film or fluorescent screen where bones appear white, while shadows of soft tissue appear in shades of grey to identify abnormalities.
- Lateral flow tests presenting a coloured line on a white background to indicate a positive or negative result for pathogens.
- Electrocardiogram (ECG) traces on a voltage over time graph printed on lined paper from a 12-lead ECG machine to show sinus rhythm.

2.4. The conversion of test results into digital formats has transformed diagnostics, treatments and the approaches in delivering healthcare. It has enabled diverse and unconventional disciplines to collaborate and discover novel methods in molecular diagnostics, particularly in proteomics and genomics.

2.5. Digitisation has advanced diagnostics and Artificial Intelligence (AI) much closer together with digital diagnostic devices emerging and transforming healthcare practices and access to diagnostics (particularly in early diagnosis) more broadly. Examples include:

- Digital mammography using digital receptors and AI to examine breast tissue for cancer, with comparable diagnosis outcomes to traditional X-ray methods.
- Digital readers of lateral flow tests incorporating AI functions to interpret the presence of a line irrespective of the luminosity of the line, eliminating human reading errors.
- Digital ECGs that scan or read tracers to detect or predict heart conditions such as AF or MI using AI advanced models.

2.6. Artificial Intelligence will continue to evolve and develop in diagnostic devices, complementing and potentially superseding established practices as it matures. The MHRA is in regulatory and scientific advisory dialogue, brought forward by precision medicine innovators, to design immunotherapies that use diagnostics and AI to select neoantigens in targeted cancer therapies.

3. Key challenges for regulating diagnostic devices

Challenge 1 - Applying the current regulations impedes the assessment of diagnostic devices that combine AI functions.

3.1. Under current UK regulations, manufacturers of diagnostic devices are required to align their device with specific regulatory requirements on the type of the device - i.e. as general medical devices, active implantable devices or in vitro diagnostic devices. These regulatory requirements were transposed into UK law from EU Directives in 2002 and over the past 22 years, they have not kept pace with the advancement of

medical device and diagnostics technologies including the advent of AI as a medical device.

3.2. Manufacturers are required to identify the type of device (i.e. a general medical device or IVD device) and to comply with the specific regulatory requirements for the type of device. Manufacturers of diagnostic devices are applying the general medical device regulatory requirements because software is described as such in the current regulations.

3.2.1. Once the medical purpose is established for the device, manufacturers must identify the type of device as a general medical device or an IVD device but not both.

3.2.2. Subsequently, manufacturers and Approved Bodies[2] would need to assess their device against a set of regulatory requirements specific for the type of device. It means the diagnostic devices combining AI functions could meet some – but not all – of the requirements for the type of device. In certain instances, the device would have to meet both general medical device and IVD device regulatory requirements, which introduces duplicative regulatory burdens.

3.2.3. Using the principles of AI (i.e. values that aim to ensure the ethical an beneficial use of AI such as testing for safety and security) and placing appropriate controls into future regulations is an opportunity for the MHRA to break with legacy siloes of regulating individually for a general medical device, a software and AI device and an IVD device.

MHRA Response

3.3. The future UK medical device regulations will build proportionate regulatory controls that ensures the device lifecycle yields a diagnostic result that is dependable and safe for patients and the public. Unlike the EU, we intend to do this through a single set of regulations that can apply to all medical devices, including diagnostic devices combining an AI function.

3.4. Future regulations will include classification rules that stratify the risk category of devices. The risk category will determine the requirements that the device will need to adopt. The MHRA will publish guidance that stratifies diagnostic devices based on the intended purpose as defined by the manufacturer. Devices that combine an AI function must adopt regulatory requirements that comply with the requirements for IVDs and Software as a Medical Device. Devices that do not have a diagnostic intended purpose may continue to comply with Software as a Medical Device (SaMD), for which AI as a Medical Device is a subset.

[2] An Approved Body is an organisation that has been designated by the MHRA to assess whether manufacturers and their medical devices meet the requirements set out in the Medical Devices Regulations.

3.5. The AI-Airlock, launched earlier this month, will translate learnings for diagnostic devices combining and AI function too, ensuring the diagnostic performance and outputs improve the quality and safety of diagnostic devices.

3.6. Our approach recognises that the devices are not intended to replace the healthcare professionals in providing a clinical diagnosis but rather to augment their capabilities and expertise. Therefore, future regulations will be design with appropriate controls, so the device offers results that are used as a valuable diagnostic decision support tool for healthcare professionals.

Challenge 2 - Changes in the way the USA plans to regulate Lab Developed Tests will impact significantly on the UK and is happening in parallel to our regulatory changes.

3.7. The US FDA is taking greater responsibility of regulating Lab Developed Tests (LDTs). The future international recognition of medical devices in the UK, including LDTs cleared by the US FDA, coupled with the industry trend towards more centralised testing services with specialist laboratories that process test samples from different geographies, will mean that diagnostic test results generated in the USA will increasingly become commonplace in the UK. The diagnostic test results must be dependable and safe for patients and the public.

3.7.1. Laboratory Developed Tests (LDTs) are *In Vitro* diagnostic products intended for clinical use within a specific laboratory typically located in the United States and with high throughput. A specimen (such as blood, urine, tissue, etc.) from UK patients may be dispatched to the laboratory where the sample is processed by the US laboratory hosting the LDT. The diagnostic test results are digitised with the test results and diagnosis communicated to UK patients or healthcare professionals. The test results may be translated into a clinical diagnosis using AI.

3.7.2. Regulations on the transparency of the diagnostic algorithms must ensure the outputs of such tests provide valuable diagnostic decision support information for healthcare professionals and patients, especially in identifying diagnostic scenarios for rare and complex conditions such as in genetic diseases or when used with a medicine such as in a companion diagnostic or a device for drug therapeutic monitoring.

MHRA Response

3.8. We have been working with the US FDA over recent months to understand their plans, including sessions on Lab Developed Tests and their 510(k) access routes as part of our work on International Recognition. We will shortly publish details of our proposed policy approach to Diagnostic tests that have already passed regulatory requirements through comparable regulators, including the US FDA.

3.9. The US FDA work on LDTs culminated on 29 April 2024, with an announcement of a final rule, aimed at helping to ensure the safety and effectiveness of laboratory developed tests. The rule amends the FDA's enforcement and to make explicit that

IVDs are devices under the Federal Food, Drug, and Cosmetic Act (FD&C Act) including when the manufacturer of the IVD is a laboratory. Along with this amendment, the FDA is finalising a policy under which the FDA will provide greater oversight of IVDs offered as LDTs through a phaseout of its general enforcement discretion approach for LDTs over the course of four years, as well as targeted enforcement discretion policies for certain categories of IVDs manufactured by laboratories.

3.10. We welcome this announcement, which also brings greater alignment internationally to the approach of laboratory-based testing, more closely aligned than previously to UK and EU approaches to ensuring appropriate controls over tests developed and used in health institutions.

Challenge 3 - Education and awareness of the regulatory requirements of digital diagnostic tests is critical to ensuring patient safety

3.11. Diagnostic devices combining traditional methods, software and AI functions will become more sophisticated and commonplace and the pace of change is accelerating. The future regulations must be capable of regulating such devices whilst maintaining the tenets of patient safety and ensure continued supply of safe and reliable diagnostic devices to the UK market. There also needs to be a wide understanding of what those regulations are. The attractiveness of the notion of removing the 'human in the loop' to meet efficiency challenges must be balanced against an understanding that the addition of a digital element to a diagnostic device brings with it additional regulatory requirements to protect patients and the public versus ensuring any efficiency benefits are real.

MHRA Response

3.12. We continue to work across the Healthcare System and central and devolved governments, to improve the breadth and depth of understanding of how adding digital elements can impact on the regulatory requirements a diagnostic device must meet. This includes inputting into cross government reviews, proposed changes to linked regulations – for instance inputting into work on the Ionising Radiation (Medical Exposures) Regulations (IRMER) 2017 and it's handling of 'autonomous' AI use. Health Care professional awareness is critical to ensuring regulatory compliance and we have recently agreed with NHS England that we will provide input into their Clinical Entrepreneurs Programme.

Challenge 4 – Independent verification testing of IVD devices

3.13. IVDs for ABO blood typing and to detect HIV, Hepatitis and Human T-lymphotropic viruses (HTLV) are high risk devices that require greater oversight of manufactured batches. Current regulations require manufacturers to meet common technical specifications and to submit batch samples to be independently verified by reference laboratories prior to final release and use. Provision for this sort of testing in Europe is limited to the Paul-Ehrich Institute and Robert Koch Institute, which have

historically provided independent verification testing services for the UK using standardised reference methods and control materials. As a sovereign regulator outside the EU, we are keen to ensure UK independent verification testing does not have to rely exclusively on capacity outside the UK and that there is resilience in the system in response to demand spikes.

MHRA Response

3.14. The requirement to batch test certain devices is an existing UK regulatory requirement and one we plan to retain in our new regulations. In our MedTech Regulatory Roadmap, published this month, we have included our plans for an additional consultation later in 2024, which could provide an opportunity to revisit *how* that requirement could be met. Ahead of that, we are starting work now, including establishing a Trusted Advisor Group, to explore what a sustainable and resilient UK solution could be.

4. International Engagement

4.1. The challenges presented above are primarily domestic challenges, however the regulation of IVDs also presents shared global challenges which are working on through international fora and collaborations.

4.2. The International Medical Devices Regulators Forum (IMDRF) working group on IVDs was previously paused. In March 2024, a joint proposal between the UK and European Commission, to set up a new IVD working group initially looking at clinical evidence for IVDs was supported by the IMDRF Management Committee and is being worked by the group to be re-started, co-chaired by the MHRA and European Commission.

4.3. The group could then tackle a number of global issues where there is a need for international harmonisation including on performance evaluations and IVD classifications. Whilst the future UK IVD regulations will align to IMDRF classifications and rules as committed in the government response, those classifications and rules are already out of date and need to be revised.

4.4. Another area where regulations globally are not keeping up with developments is that of genetic testing. The EU and other regulators are keen to partner with us bilaterally on this topic with a view to taking proposals to the IMDRF in the future.

4.5. Wellness products, for example continuous glucose monitors for health management purposes (not for medical purposes), do not come within the remit of UK Medical Device regulations. We do not currently intend to bring them into scope of the new regulations. They are excluded because they do not make medical or diagnostic claims. Expanding into this are risks disproportionate regulation and a diversion of resources away from more critical areas. There is limited international consistency on this issue and limited appetite to consider this at the IMDRF. The EU is considering expanding their regulations to wellness products. In the US, products

are based on a predicate, the FDA will accept applications for registration as a medical device.

4.6. We continue to learn the lessons of the pandemic and a key international activity for us is as UK rep, alongside UKHSA, to the G7 100-day mission group for preparedness for the next pandemic, an important strand of our IVD Strategy.

5. Questions for the Board

5.1. Is the Board content that the key challenges have been identified and with the MHRA responses for each challenge?

Laura Squire
21 May 2024

Medicines & Healthcare products Regulatory Agency

BOARD MEETING HELD IN PUBLIC

21 May 2024

Title	What assurance can be provided by the Patient Safety and Engagement Committee (PSEC)?
Board Sponsor	Mercy Jeyasingham
Purpose of Paper	Assurance

What assurance can be provided by the Patient Safety and Engagement Committee (PSEC)?

1. Executive Summary

1.1 PSEC discussed two substantive items which were: “What are the findings from the evaluation of the Patient Involvement Strategy?” and “How is the Agency going to effectively contribute to the UK Electronic Patient Information (ePI) Task Force?”

1.2 The evaluation of the Patient Involvement Strategy took place during June 2023 and March 2024. A model developed by Gibson et al (2017)[1] was used to guide the evaluation. This model provides a theoretical framework for use as a mapping tool to evaluate the experience of patient involvement in health research. The results were summarised as:

Are there multiple ways for patients to be involved?
Yes. Although not all staff nor patients are aware of these.

Who sets the agenda? Whose concerns?
MHRA patient involvement has mainly focused on immediate business needs although concerns as expressed by public and patient continue to be picked up through direct liaison and the Customer Experience Centre.

Is the patient “heard”?
Patients feel that the Agency is on a journey and moving in the right direction; they understand the drive for improvement. However, participants in the study said that they do not necessarily feel that their contributions are heard nor have impact.

1.3 PSEC explored several areas of possible improvement including explaining to patients how their views are used, and how the MHRA fits in with the rest of the health care system. The website was a key communication channel but there are currently limitations, and this will be considered by the board. PSEC felt that the evaluation should be presented to the board with a focus on what needs to be achieved and how it will be achieved in the refreshed strategy.

1.4 The UK ePI Task Force is a group of UK medicines manufacturers, NHS organisations and the MHRA working together to explore the provision of patient information in a digital format. The proposed pilot commencing in May 2024 is limited to working with a few products and not changing what is in the current patient information leaflet. The committee considered the potential of changing the patient information leaflet. It was asked to consider the capacity of different companies, the legal position of who owned the information, the need for a secure holding facility for all information, interaction with the yellow card scheme and opportunities to support the

[1] Gibson A, Welsman J, Britten N. Evaluating patient and public involvement in health research: from theoretical model to practical workshop. Health Expect. 2017 Oct;20(5):826-835. doi: 10.1111/hex.12486. Epub 2017 Jun 30. PMID: 28664563; PMCID: PMC5600246.

digitally excluded (given that many people are not able to read the Patient Information Leaflet currently). PSEC recommended that ePIL should be discussed at the board in July for the board to discuss its business case and potential costings considering the legal issue on information ownership and the need to host information on one platform.

2. Introduction

2.1 The Patient Safety and Engagement Committee met on the 9th of May 2024.

3. PSEC discussed each of the following items at the meeting

3.1 "What are the findings from the evaluation of the Patient Involvement Strategy?"

On 12 May 2023, PSEC considered a paper that set out key principles for the evaluation of the Patient Involvement Strategy. Work started on the evaluation in September2023 and was completed in March 2024, with fieldwork carried out between November 2023 and February 2024. The MHRA's Patient Involvement Strategy 2021-25 was published in September 2021 and is an important element of the response to Recommendation 6 of *First Do No Harm* ("the Cumberlege Review"). An evaluation during the life of the strategy was implemented to provide information on progress with a view to improvement rather than summative outcomes. Staff and patient interviews were conducted by an external contractor. The Patient Public Stakeholder Engagement team reviewed and assessed examples of patient involvement across the organisation over the past year.

The theory used to evaluate the strategy was the Griffin model. The results were summarised as:

- *Are there multiple ways for patients to be involved?*

Yes. Although not all staff nor patients are aware of these.

- *Who sets the agenda?*

The MHRA patient involvement has mainly focused on immediate business need although concerns as expressed by public and patient continue to be picked up through direct liaison and the Customer Experience Centre.

- *Does the patient have a strong or weak voice? Are they "heard"?*

Patients feel that the Agency is on a journey and moving in the right direction; they understand the drive for improvement. However, participants in the study said that they do not necessarily feel that their contributions are heard nor have impact.

PSEC discussed the findings from staff and patients drawn from a group with knowledge of the Agency. Additional group discussions were held with members of the public with little knowledge of the Agency. Areas that were explored at committee included gaining diversity of views given sometimes limited input from some communities; the resource intensiveness of some engagement methods; some staff needing to appreciate the benefits of patient involvement given the time, expertise and resource needed to engage; and the expectations of patients. The agency has an ambition to systematically engage patients at all levels of decision making and give timely feedback on how their input is used. However, there are a number of limiting factors to achieving this including the level of awareness of the public on what the agency does in relation to the wider

health system and the resources and expertise available to staff. Awareness would be helped by a more public facing website as there are limitations. Further discussion on the website needs consideration by the board. PSEC felt that the evaluation should be presented to the board with a focus on what needs to be achieved and how this will be done.

3.2 "How is the Agency going to effectively contribute to the UK Electronic Patient Information (ePI) Task Force?"

Current legislation requires the provision of a paper leaflet in the packs of all licensed medicines, unless the relevant information can be accommodated on the outer packaging. The leaflet is intended to help patients take their medicines safely and effectively. It reflects the information set out in the approved Summary of Product Characteristics (SmPC) in lay language. The leaflet also encourages patients to report any side effects they may experience whilst taking their medicine, which helps the MHRA monitor the safety of medicines throughout their lifecycle. Patients are not a homologous population, and it is recognised that a paper leaflet presenting often complex information, will not be understood by all. This can lead to medication errors and poor adherence, which in turn can lead to further demands on NHS services. Additionally, leaflets are regularly updated with new safety information but due to lead times for printing and entry into the supply chain, are often not available in packs for at least 6 months.

The UK ePI Task Force is a group of UK medicines manufacturers, NHS organisations and the MHRA working together to explore the provision of patient information in a digital format, whilst ensuring no-one is left behind, and the legislative changes required to enable this. As the medicine's regulator in the UK, MHRA input into this programme is essential to ensure that the correct regulatory framework is put in place for the provision and updating of patient information and that the connection to the MHRA pharmacovigilance systems is maintained.

PSEC discussed the current work of the UK ePI Task Force and the influence of the MHRA on the group. The need for global harmonisation and the great opportunities digital interactions using QR codes, videos, and other ways of explaining side effects were noted. However, the proposed pilot commencing in May 20024 is limited to a few products with no change to the content of the Patient Information Leaflet. For the future development of ePI things to consider were the capacity of different companies, the legal position of who owned the information, the need for a secure holding facility for all information, interaction with the yellow card scheme and opportunities to support the digitally excluded (given that many people are not able to read the Patient Information Leaflet). It was noted that the Patient Safety Commissioner is part of the board for the ePI Task Force, but the committee would also like further patient input in development.

PSEC recommended that ePI should be discussed at the board in July for the board to discuss its business case and costings in light of the legal issue on information ownership and the need to host information on one platform. The post-pilot review will be reported back to a future meeting of PSEC.

3.3 **PSEC's Forward Plan**

The forward plan for the committee was discussed to schedule topics in a timely way and to determine what questions the committee would like addressed.

3.4 **Any other business**

The committee received the Dame Margaret Whitehead Report "Equity in Medical Devices: Independent Review" the day before it met. The report will be discussed at a future meeting, but it was recommended that all board members who have not seen the report should receive it.

4.0 Recommendations

PSEC recommended that the evaluation of the Patient Involvement Strategy, with clear steer on what needs to be achieved and how, should be presented at the July meeting of the board. It also recommended that the business case and costings for the future development of the Electronic Patient Information Leaflet should be discussed at the July board meeting. Finally, PSEC requested that the Whitehead review is circulated to all board members.

Mercy Jeyasingham
Chair Patient Safety and Engagement Committee
Non-Executive Director MHRA
May 2024

Medicines & Healthcare products Regulatory Agency

BOARD MEETING HELD IN PUBLIC

21 May 2024

Title	What assurance can be provided by the Audit and Risk Assurance Committee (ARAC)?
Board Sponsor	Michael Whitehouse
Purpose of Paper	Assurance

What assurance can be provided by the Audit, Risk and Assurance Committee?

1. Executive Summary

1.1. The Audit Risk and Assurance Committee (ARAC) met on 24 April. The key focus of the meeting was to seek assurance that all the necessary work needed to ensure that the Agency submits its annual report and financial statements to Parliament in accordance with the statutory timetable is progressing as planned.

2. Financial Statements

2.1 The Agency is on target for submitting its financial statements for final audit which will commence as planned in the week beginning 29 April. The National Audit Office and KPMG assured the Committee that they had the resources in place to ensure that the audit timetable would be met. Finance provided reciprocal assurance for the Agency's resources.

2.2 The Committee sought assurance that there were no unusual items which could put the timetable at risk including for example: any significant end of year accruals or prior year adjustments; new accounting standards; and any disclosures which would require Treasury or Cabinet Office approval. At this point in time no such risks had been identified. We discussed the disclosure of expenditure associated with the Agency's lease for its headquarters at Canary Wharf which has changed as required by new Accounting Standards and which is effected by the transfer of the lease to the Department of Health. We were assured by external audit and Finance that they were close to agreement on valuation and disclosure.

3. Internal Audit

3.1. The Committee received five reports from Internal Audit together with an update on progress in implementing prior audit recommendations. We also considered Internal Audit's draft annual opinion and their work programme for 2024-25.

End of life systems: Technical debt

3.2. We were pleased to note that this had received a moderate audit assessment indicating that generally sound controls were in place. To better understand the proportionality of controls and how they related to inherent risks remaining in the Agency's digital portfolio we asked for an update on the scale of remaining legacy systems and the timetable for replacing them. This is also important in providing additional assurance over the Agency's cyber resilience.

Health and Safety

3.3. We asked that this report be re submitted at ARAC's July meeting so that the report reflected the Health and Safety Executive report on South Mimms.

Business continuity

3.4. This important activity received a moderate assessment.

Risk management

3.5. This received a substantive assessment reflecting the sustained drive by the Agency to put in place a risk management approach which reflects good practice and forms the basis for enhanced decision making. This is an excellent result. The focus of the Committee's discussion was on how to continue to embed the cultural change so that all MHRA people are confident to use the tools and approaches to manage risk. This is important in helping the Agency realise its ambition to support innovation.

Backlogs

3.6. This received a substantive assessment. It is very positive to receive independent assurance that the efforts which the Agency is implementing to reduce the backlogs in delivering its regulatory responsibilities are proving to be effective. This reflects the considerable time effort invested by MHRA people. We emphasised the importance of the changes in processes and particularly the transition to a risk-based approach being sustainable and resilient so that backlogs did not accumulate again in the future.

3.7. Progress in implementing internal audit recommendations. There has been good progress. A small number of recommendations are yet to be implemented. More of these relate to digital and cyber resilience.

Internal Audit Annual Opinion

3.8. Each year Internal Audit is required to provide the Accounting Officer (Chief Executive) with a report and independent opinion on the reliability of the Agency's controls and risk management. This opinion is published as part of the MHRA's Annual Report. Internal Audit base their opinion on their programme of work which is considered by ARAC. For the last two years Internal Audit has given a limited opinion.

3.9. Over the last 18 months the Agency coordinated and led by the Governance team has invested considerable sustained effort in improving controls and risk management. This is reflected in the increase in the number of moderate and substantive assessments awarded by Internal Audit.

3.10. In forming their annual opinion Internal Audit are required to form a view on the operation of the Agency's controls over the full preceding twelve months. As well as drawing on their own work Internal Audit must also form a wider holistic assessment of the operation of controls and any other incidents which might suggest controls were not effective.

3.11. Internal Audit indicated that their overall assessment is finely balanced. It is clear that the Agency has made considerable progress most notably in risk management but also more widely. The Agency has however faced some significant performance challenges over the last 12 months and Internal Audit like the Board need to be convinced that the important remedial action which the Agency has taken is sustainable and sufficiently resilient.

3.12 Internal Audit will finalise their opinion by the time of our meeting in July. We advised that the Agency should discuss with Internal Audit how they could provide additional evidence to demonstrate the actions they had taken to strengthen controls and avoid a repetition of the performance issues which has arisen.

Internal Audit 2024-25 plan

3.13. We considered and approved Internal Audit's proposed work programme for 2024-25 which has the support of the Executive. We made two requests relating to specific proposals. We asked that the reviews covering strategic financial management and strategic work force planning be merged. The Committee consider that assurance would be enhanced by having greater transparency over how well the Agency estimates demand for regulatory activities in both the short, medium and long term and how this influences capability building and ultimately cost including the need for future investment. Merging these two reviews should ensure a more holistic approach with the potential to add more value to the Agency. We also emphasised the importance of Internal Audit's review of fees being completed as planned in time for our meeting in September.

4. Risk and assurance

4.1. The Committee considered the Agency's risk register. This was recently discussed by the Board, and we confirmed that the register covered current strategic risks. Going forward it will be important to be confident that the residual risk after mitigating actions is monitored carefully. We discussed action to embed risk management across the Agency as part of our response to Internal Audit's independent report (para 3.5 above).

Assurance Map

4.2. Strong effective governance requires organisations to map the approaches and systems they rely on to provide assurance that key controls are operating effectively. This is often done by categorising controls into three lines of defence: the first being core internal systems; the second being management oversight and the robustness and timeliness of data to exercise that oversight; and thirdly independent assurance provided by third parties such as Internal Audit. Documenting the assurance framework and having evidence of how it works in practice is a further source of evidence which Internal Audit will usually draw on in helping to form their overall opinion.

4.3. We considered a draft of the Agency's Assurance Map. We made a number of recommendations mainly around in addition amalgamating the maps to provide an integrated overview but overall this is a comprehensive and good assessment. ARAC will review annually how well the different levels of assurance are working.

5. Governance Statement

5.1. The Annual Report is required to include a governance statement which sets out the controls which the Agency has had in place over the last twelve months to manage its resources efficiently and effectively to meet its key objectives. The governance statement will include the assurance opinion provided by Internal Audit.

5.2. It was helpful to have opportunity to comment on the draft governance statement at this early stage. The draft is comprehensive and transparent. Our main recommendation was that it should be shortened and we made suggestions as to how this might be done.

6. Other Assurance

6.1. ARAC also took assurance from four other reports: Annual Raising Concerns Report; Quarterly Fraud and Error report; Update on complaints data; and an analysis of the cost of responding to complaints. There are no significant issues to bring to the Board's attention. We observed that overpayments have risen but Finance will monitor to ensure that a wider systemic issue is not developing. Complaints data is more comprehensive and we explored how this might be integrated to provide potential early warning of emerging risks.

7. Conclusion

7.1. At this point there is no indication that the Agency will not meet its statutory requirement to lay its Annual Report in Parliament before the Summer Recess. ARAC will meet again on 5 July to consider the outcome of the external audit with the intention that the Board would agree the Annual Report at its meeting on 9 July for signature by the Accounting Officer.

Michael Whitehouse
Chair, ARAC
April 2024