Medicines & Healthcare products Regulatory Agency

AGENDA FOR BOARD MEETING HELD IN PUBLIC

10:00 – 12:30 on Tuesday 18 January 2022

Chair: Stephen Lightfoot

	AGENDA ITEM	**PURPOSE**	**PRESENTER**
10:00	INTRODUCTION 1. What are the priorities for this meeting, how will the meeting run and who are the Board Directors?	Information	Chair
	2. Are there any Apologies or Declarations of Interest?	Information	All
	3. What were the minutes & actions from last meeting?	Approval	Chair
10:15	AGENCY PERFORMANCE 4. What are the current issues from the CEO's point of view?	Context	June Raine
10:35	5. What is the performance of the MHRA on the Balanced Scorecard in Month 8?	Assurance	Jon Fundrey
10:55	PATIENT SAFETY 6. How will the outcomes and short, medium and long term benefits arising from activities being undertaken to address the recommendations of the Cumberlege Review be measured?	Assurance	Alison Cave
11:15	7. What assurance can be provided by the Patient Safety & Engagement Committee?	Assurance	Mercy Jeyasingham
11:30	8. What are the updated Terms of Reference for the Patient Safety & Engagement Committee?	Approval	Mercy Jeyasingham
11:40	HEALTHCARE ACCESS 9. What are the strategic priorities for the regulation of Artificial Intelligence as a Medical Device and how can this be developed effectively?	Strategic Direction	Laura Squire and Johan Ordish
12:05	EXTERNAL PERSPECTIVE 10. What questions do members of the public have for the MHRA Board?	Public Engagement	Chair
12:30	CLOSE OF MEETING	-	Chair

MHRA Agency Board Declarations of Interest – January 2022

Name and MHRA Role	Name of Other Company or Organisation	Nature of interest	Paid	Current
Stephen Lightfoot Chair of Board	NHS Sussex Integrated Care Board	Chair Designate	Yes	Yes
	Sussex Community NHS Foundation Trust	Deputy Chair and Non-Executive Director	Yes	No
	Sussex Primary Care Limited	Chair and Director	No	No
	Gainsborough Property Development UK Limited	Director	No	No
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
	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
Amanda Calvert Non-Executive Director	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.	Yes	Yes
	University of Manchester digital Experimental Cancer Medicine Team	Quince Consultancy providing strategy and data protection consultancy	Yes	No
	Cambridge Judge Business School	Member of Advisory Board	No	Yes
	The Guinness Partnership Limited – Housing Association	Non-executive Director, member of Audit Committee and Chair of Health and Safety Committee	Yes	Yes
Dr Alison Cave Chief Safety Officer	None	N/A	N/A	N/A
Jon Fundrey Chief Operating Officer	None	N/A	N/A	N/A

Name and MHRA Role	Name of Other Company or Organisation	Nature of interest	Paid	Current
Dr Paul Goldsmith Non-Executive Director	Closed Loop Medicine Ltd	Shareholder, director & employee	Yes	Yes
	Summit Inc	Shareholder	No	Yes
	Ieso Digital Health	Shareholder	No	Yes
	MDU Ltd	Director	Yes	Yes
	MDU Investments Ltd	Director	Yes	Yes
	NHS	Consultant Neurologist	Yes	Yes
	NHS	Clinical Senate Member	No	Yes
	Big Tent Foundation	Trustee	No	Yes
	Radix Group Limited	Trustee	No	Yes
	Sleepstation	Co-founder of original programme, 2012-2014	No	No
Professor Graham Cooke Non-Executive Director and Deputy Chair	30 Technology Ltd	Consultant/Advisor	Yes	Yes
	DNAnudge Ltd	Consultant/Advisor	No	Yes
	Seventh Sense Biosystems	Consultant/Advisor	Yes	Yes
	Debevoise and Plimpton LLP	Consultant/Advisor in relation to COVID protocols	Yes	Yes
	Sanofi CoV	Chair of End Point Review Committee for vaccine trial	Yes	Yes
	WHO	Chair of Committee for Selection and Use of Essential Medicines	No	Yes
	NIHR	NIHR Research Professor	Yes	Yes
Claire Harrison Chief Technology Officer	Detail of declarations awaited			
Haider Husain Associate Non-Executive Director	Healthinnova Limited	Chief Operating Officer	Yes	Yes
	Milton Keynes University Hospital NHS Foundation Trust	Non-Executive Director	Yes	Yes
	British Standards Institute	Panel Chair BS30440 – Use of AI within Healthcare	No	Yes
	Dementia Carers Count	Trustee	No	Yes
	World Ward Muslim Memorial Trust	Trustee	No	Yes
	Microsoft Corp	Shareholder	Yes	Yes
	BBC	Family Member	No	Yes
Mercy Jeyasingham MBE Non-Executive Director	Royal College of Podiatry	Consultancy	Yes	No

Name and MHRA Role	Name of Other Company or Organisation	Nature of interest	Paid	Current
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
	EC IMI NEURONET EC Innovative Medicines Initiative (IMI) Non-Product	Scientist Advisory Board	No	Yes
	Gates Venture – EC Innovative Medicines Initiative (IMI) Non-Product – IMI European platform for Neurodegenerative Disorders	Advisory	Yes	Yes
	HUYA Bio	Access Advisory	Yes	Yes
	PAVIA – PV Africa Board (EC Funded)	Advisory Board	No	Yes
	WHO – Sustainable COVAX Manufacturing Strategy for Regional Health Security	Advisory Expert	No	Yes
Laura Squire OBE Chief Healthcare Quality & Access Officer	None	N/A	N/A	N/A
Michael Whitehouse OBE Non-Executive Director	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	Yes
	Republic of Ireland Audit Office	Member of Audit Committee	No	Yes
	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 of 16 November 2021

(10:00am – 12:30pm)

at the National Institute of Biological Standards and Control, South Mimms
and by Zoom Webinar

Present:

The Board

Stephen Lightfoot	Chair
Dr June Raine CBE	Chief Executive
Dr Marc Bailey	Chief Science, Research and Innovation Officer
Dr Junaid Bajwa	Non-Executive Director
Dr Alison Cave	Chief Safety Officer
Amanda Calvert	Non-Executive Director
Professor Graham Cooke	Non-Executive Director and Deputy Chair
Jon Fundrey	Chief Operating Officer
Dr Paul Goldsmith	Non-Executive Director
Claire Harrison	Chief Technology Officer
Haider Husain	Associate Non-Executive Director
Mercy Jeyasingham MBE	Non-Executive Director
Raj Long	Non-Executive Director
Dr Laura Squire OBE	Chief Healthcare Quality and Access Officer
Michael Whitehouse OBE	Non-Executive Director

Others in attendance

Rachel Bosworth	Director of Communications *(via Zoom)*
Carly McGurry	Director of Governance
Natalie Richards	Head of the Executive Office
Jude Thompson	Executive Assistant to the Chair
Dr Dan O'Connor	Expert Medical Assessor *(via Zoom)*
Kathryn Glover	Deputy Director, Medicines Regulation and Prescribing, DHSC *(via Zoom)*

INTRODUCTION

Item 1: What are the priorities for this meeting, how will the meeting run and who are the new Board Directors?

1.1 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.

1.2 The Chair welcomed everyone to the meeting, including a broad range of observers representing a range of patient groups, other health bodies, UK government, MHRA staff, industry and the media.

1.3 The Chair also welcomed Claire Harrison who has joined the MHRA as Chief Technology Officer, and Dr Laura Squire who has joined the MHRA as Chief Healthcare Quality and Access Officer.

Item 2: Are there any Apologies or Declarations of Interest

2.1 Apologies were received from Greig Chalmers, Head of Chief Medical Officer's Policy Division at the Scottish Government; Alison Strath, Interim Chief Pharmaceutical Officer and Deputy Director at the Scottish Government, and Cathy Harrison, Chief Pharmaceutical Officer for Northern Ireland.

2.3 The Board noted that there is a paper on the Innovative Licensing and Access Pathway (ILAP) on the agenda of this meeting. The Board also noted that Amanda Calvert provides consultancy services to a company who has made an ILAP application in the past, and a company of which Paul Goldsmith' is a Director is planning on making an ILAP application at a future date. The Chair confirmed that as the Board is being asked to comment on the strategic direction of ILAP at this meeting and not make any regulatory decisions associated with this pathway, he was satisfied that Amanda and Paul's involvement would does not amount to a conflict of interest on this occasion.

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 and updates were provided.

AGENCY PERFORMANCE

Item 4: What are the current issues from the CEO's point of view?

4.1 Dr June Raine presented the Chief Executive's monthly report, which covered topics within the four strategic priorities:

(i) Healthcare Access – including latest updates on COVID-19 antivirals; ILAP; Clinical Trials legislation; medicines approvals; COVID-19 vaccines; Validation for NHS testing of SARS-CoV-2 infection; the NIBSC polio vaccine nOPV2 which has been recommended for wider use; NIBSC's redesignation as a WHO Collaborating Centre for Biological Standards; WHO international standards produced by NIBSC; published guidance on electronic cigarettes as a licensed medical device; the MHRA consultation on UK legislation for medical devices; partnerships including with NICE; the Access Consortium; international engagement on COVID-19 diagnostic tests; NIBSC international meetings and workshops; partnership working on artificial intelligence and software as a medical device; and pharmaceutical inspection cooperation scheme;

(ii) Patient Safety – including updates on the safety of COVID-19 vaccines; provision of safety information on sodium valproate; the safety review of isotretinoin; safe use of tofacitinib; restriction of the paediatric indication for chloral hydrate; safety of breast implants; and enforcement;

(iii) Dynamic Organisation – including an update on the Transformation Programme; and

(iv) Financial Sustainability – including updates on the Spending Review (SR); and the financial forecast.

4.2 The Board thanked Dr Raine for her report and provided comments. These included congratulations on the MHRA's continued work tackling the COVID-19 pandemic; how international collaboration and partnerships are key to being an effective regulator; how to work towards regulatory alignment on a global scale and the work the MHRA currently does on regulatory harmonisation with collaborative groups such as ICMRA and IMDRF. It was agreed that the Board should consider international healthcare systems and regulatory frameworks at a future meeting.

Action 64: Review opportunities for more partnership working with other regulators as part of the MHRA International Strategy

Glenn Wells

4.3 The Board provided further comments regarding the safety of breast implants and research on patient and public perception of risk; it was noted that patient perception may be different to the risk perception by healthcare professionals. It was agreed this should be reviewed by the Patient Safety and Engagement Committee (PSEC). Further comments were provided covering machine learning and good practice guidelines; outreach and education; the upcoming consultation on updates to the clinical trials legislation and engagement with stakeholders; how to develop underpinning guidance to legislation; and development of key partnerships in relation to clinical trials to allow the system to adapt and function effectively. The Board thanked Dr Raine for her comprehensive report.

Action 65: PSEC to seek assurance on how safety risks are considered by the MHRA in those situations where patients are willing to accept more risk than healthcare professionals ***Mercy Jeyasingham***

Item 5: What is the current performance of the MHRA on the Balanced Scorecard in Quarter 2?

5.1 The Board discussed the current performance of the MHRA, presented via the quarterly Balanced Scorecard. The Board considered whether the metrics and the commentary provided appropriate assurance that current performance is on track and aligned to the Agency's strategic objectives. The Board provided comments on the public's awareness of the MHRA, and any demographic breakdowns that can be provided, and noted procurement is underway for a reputation index to review public

perception of the MHRA; reviewing reputation, branding and communication; and the importance of reviewing outcomes rather than inputs.

5.2 The Board provided further comments regarding the Equality, Diversity and Inclusion (ED&I) metrics in the scorecard and whether a deeper dive in to ED&I should be undertaken; how to improve the results on effectiveness of senior leadership in the balanced scorecard; undertaking benchmarking with other Arms' Length Bodies to understand and identify areas where the MHRA can improve. It was agreed that the Organisational Development and Remuneration Committee (ODRC) should review the results on effectiveness of senior leadership from the balanced scorecard, and provide recommendations of specific actions to address this issue.

Action 66: Assurance to be provided to ODRC on actions being taken to improve culture survey scores (i.e. walking the talk and taking timely decisions) in the Balanced Scorecard ***Executive Committee***

5.3 The Board provided comments on the work on productivity indexes and the importance of using external benchmarks to set productivity levels, for example how to reduce timescales of delivery of generic products to the NHS; how to broaden the scientific agenda within the balanced scorecard to provide assurance on the impact of science; a request to include more context and explanatory notes as necessary within the scorecard; how to appropriately prioritise the technology roadmap in collaboration with other areas of the Agency. The Board noted that corporate overheads have increased which must be carefully monitored.

Further addition to Action 51: Broaden the measures to include the impact and quality of our scientific work rather than volumes. Seek input from our customers on what MHRA services they value for inclusion in the Balanced Scorecard.
Jon Fundrey

Item 6: What has the MHRA achieved compared to each Quarter 2 deliverable in the Delivery Plan and how will any under-performance be recovered to avoid any impact on the overall two year Plan?

6.1 The Board considered a report describing what the MHRA has achieved compared to each Quarter 2 deliverable in the Delivery Plan. The Board noted that all but one of the nine items due this quarter were delivered on time. The RAG ratings were reviewed and for the 2 new Red, 2 new Amber/Red and 4 new Amber items remedial action has been agreed and will be implemented and monitored. The Board agreed there has been good progress in the last six months, however commented that the rating on the cash reserves spend should be downgraded to red as it is vital that this is achieved.

6.2 The Board provided further comments regarding the possibility of utilising the cash reserves on cultural work and management training for staff; investing in staff to develop the level of leadership the Agency needs and expects; and migration of data from legacy systems. The Board were content the MHRA is delivering on key objectives.

Action 67: Delivery Plan – update the RAG rating on the reserves spend to red ***Jon Fundrey***

HEALTHCARE ACCESS

Item 7: What has the Innovative Licencing and Access Pathway delivered and how will it be developed?

7.1 The Board considered a paper describing what the Innovative Licensing and Access Pathway (ILAP) has delivered; Dr Dan O'Connor, Expert Medical Assessor, joined for the discussion. Following the UK leaving the European Union, the MHRA became a sovereign regulator which was a change that has opened up significant opportunities. These opportunities have been capitalised on through the creation of a new ambitious expedited route to market for medicines, the ILAP. The Board reviewed the ILAP activity to date and commented on the proposed direction of travel and other areas for development.

7.2 The Board provided comments regarding the importance of ensuring patients are able to input at all appropriate points in the ILAP process and use of the PSEC was commended to provide a critical review of the process; ensuring the fee structure is adequate to resource the process; how the ILAP creates a different way of working with a degree of cultural change working with partners and patient representatives; how to move from a new process to embedding ILAP as business as usual; and how delivery of the Target Development Profile relies on other partners.

7.3 The Board noted that moving forward, ILAP should be embedded in the Agency's process as a normal regulatory pathway. The Board discussed utilisation of the ILAP process for medical devices noting the timing is ideal as the medical devices legislation is currently being revised; it was agreed a medical device should be piloted through the ILAP process to develop this pathway. The ILAP pathways for medicines and medical devices and companion diagnostics must not be separate as there may be products which intersect the two.

7.4 The Board agreed this process should not be undervalued; a dedicated patient engagement tool and best practice guidance will enable industry sponsors to understand what 'good' looks like from a patient perspective. The Board provided further comments relating to measures of success and understanding performance; the importance of marrying up early access with robust vigilance risk management systems; development of a continuous benefit risk tool to generate lifecycle information; opportunities to engage in the area of medical research; and exploring a role for NIBSC in companion diagnostics and biomarkers. The Board congratulated everyone involved in developing this programme of work.

Further addition to Action 46: Consider if ILAP should be rebranded as an "Innovative Therapy Pathway" and conduct a pilot with a medical device through this innovative regulatory route. ***Laura Squire / Marc Bailey***

DYNAMIC ORGANISATION

Item 8: What assurance can be provided by the Organisation Development & Remuneration Committee?

8.1 The Board considered the assurance report from the Organisational Development and Remuneration Committee (ODRC). The ODRC had reviewed the ODRC role and Terms of Reference; a review of the Services which will be provided by the Agency in the future and how they will be implemented as part of the Transformation Programme; a review of the HR Deliverables within the Transformation Programme; and a review of the HR Balanced Scorecard Metrics.

8.2 The Board provided comments regarding the importance of setting the Services for the future Agency; ensuring closer collaboration with transformation and processes affecting staff; and the importance of timescales of the transformation and ensuring there is due process to ensure staff morale and motivation is retained. The Board were content with the assurance provided from the ODRC.

FINANCIAL SUSTAINABILITY

Item 9: What assurance can be provided by the Audit & Risk Assurance Committee?

9.1 The Board considered the assurance report from the Audit & Risk Assurance Committee (ARAC). ARAC reviewed the Agency's financial performance in the first six months of 2021/22 together with the cost-effective utilisation of the Agency's reserves; the risk ratings on the implementation of the new Device Regulations and the implementation of the Future Operating Model; the risk in relation to Digital Implementation; preparation for change in Trading Fund status; the corporate risk register; external and internal audits; and a lessons learned review of the MHRA Annual Report.

9.2 The Board provided comments relating to the speed of the transformation and appropriate sequencing of activities; the uncertainty in relation to digital spend; and the Spending Review. The Board were content with the assurance provided from the ARAC however noted that progress must continue to be closely monitored.

EXTERNAL PERSPECTIVE

Item 10: What questions do members of the public have for the MHRA Board?

9.1 The Board answered a range of questions from members of the public. One specific question related to rectopexy mesh and hernia mesh complications, and the Mesh UK patient group was invited for a meeting to discuss this issue with the MHRA. A large number of questions were submitted by members of the public and although most of them were answered, it was not possible to address every question in the available time. An action was taken to answer all of the remaining questions directly to the people who raised them.

Action 68: Meet with Mesh UK patient group to discuss rectopexy mesh and hernia mesh complications ***Alison Cave***

Action 69: Send written responses to observers whose questions were not answered during the November Board Meeting ***June Raine***

ANY OTHER BUSINESS

10.1 No additional business was raised and the Chair closed the meeting with thanks to all of the contributors and members of the public observing the meeting.

ACTIONS FROM MHRA BOARD MEETING IN PUBLIC – 16 NOVEMBER 2021

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 Laboratory Strategy to the Board as part of the Agency Science Strategy.	Marc Bailey	~~21/09/21~~ ~~16/11/21~~ 15/03/22	
34	20/4/21: The MHRA had a commitment in the Life Sciences Sector Deal 2 to publish a new regulatory pathway for genomic medicines and genomic tests by March 2021. Provide an update on progress of this commitment. 21/09/21: Publish communication on GOV.UK on the MHRA work to develop a pathway for new genomic products	June Raine	~~18/05/21~~ ~~21/09/21~~ ~~19/10/21~~ ~~16/11/21~~ 18/01/22	Verbal Update
38	18/05/21: PSEC and ARAC to agree how to provide assurance to the Board on the development, governance and data standards of SafetyConnect	Mercy Jeyasingham & Michael Whitehouse	~~20/07/21~~ 15/03/22	
39	18/05/21: Implement the approved Communications Strategy with particular focus on measuring trust &communication with HCPs	Rachel Bosworth	~~16/11/21~~ 18/01/22	Verbal Update
43	15/06/21: A revised assurance and governance framework for the new MHRA organisation should be presented to the Board.	Carly McGurry	15/02/22	
46	15/06/21: The Board's comments on the future development &branding of ILAP, including its potential use for medical devices, should be considered so that a definitive proposal can be presented to the Board for approval. 16/11/21: Consider if ILAP should be rebranded as an "Innovative Therapy Pathway" and conduct a pilot with a medical device through this innovative regulatory route.	Laura Squire	~~19/10/21~~ ~~16/11/21~~ 19/04/22	

50	20/07/21: ARAC to review the Agency's financial performance in the first six months of 2021/22 21/09/21: Review spending of financial reserves at next ARAC	Michael Whitehouse	16/11/21	Completed
51	20/07/21: Review Balanced Scorecard metrics and targets to provide more focus on outcomes, greater links to the Delivery Plan and (especially on innovation) and assurance that resources are available to deliver priorities 21/09/21: Review the outcome measures in the Balanced Scorecard and the RAG Ratings in the quarterly Delivery Plan reports before considering if the targets are ambitious enough. 19/10/21: Continue to evolve the Balanced Scorecard metrics to include more outcome measures. Update the data set for Clinical Trials in the balanced scorecard. 16/11/21: Broaden the measures to include the impact and quality of our scientific work rather than volumes. Seek input from our customers on what MHRA services they value for inclusion in the Balanced Scorecard.	Jon Fundrey	~~19/10/21~~ ~~16/11/21~~ 18/01/22	Balanced Scorecard Paper on Agenda
52	20/07/21: Review how multiple data sources including Unique Device Identifiers, Registries, NHS data and real world data can be captured and used to strengthen safety surveillance. Incorporate this into the planned review of SafetyConnect	Alison Cave	~~16/11/21~~ 18/01/22	Cumberlege Review Paper on Agenda
54	20/07/21: Review the progress and impact of the short, medium and long term deliverables of the agreed Culture, Equality, Diversity and Inclusion plans	Jon Fundrey	~~18/01/22~~ 15/02/22	
58	21/09/21: Update MHRA/DHSC Framework Agreement to coincide with the change in Trading Fund status.	Carly McGurry	31/03/22	

59	21/09/21: Board assurance committees to review their combined effectiveness and hold a board discussion on this topic.	Michael Whitehouse, Mercy Jeyasingham, & Mandy Calvert	15/03/22	
61	19/10/21: Prioritise the national and international initiatives to accelerate the diversification of patient recruitment for clinical trials, exploring options to maintain diversification of representation (eg gender balance). Consider development of a public dashboard of metrics for trial recruitment.	Marc Bailey	19/04/22	
62	19/10/21: Review the Corporate Risk Register to consider whether all strategic risks to Agency outcomes are accurately captured.	Carly McGurry	19/04/22	
63	19/10/21: Send written responses to observers whose questions were not answered during the October Board Meeting.	June Raine	16/11/21	Completed
New Actions				
64	16/11/21: Review opportunities for more partnership working with other regulators as part of the MHRA International Strategy	Glenn Wells	15/02/22	
65	16/11/21: PSEC to seek assurance on how safety risks are considered by the MHRA in those situations where patients are willing to accept more risk than healthcare professionals.	Mercy Jeyasingham	19/04/22	
66	16/11/21: Assurance to be provided to ODRC on actions being taken to improve culture survey scores (ie walking the talk and taking timely decisions) in the Balanced Scorecard	Executive Committee	15/02/22	
67	16/11/21: Update the RAG rating on the use of financial reserves in the Delivery Plan	Jon Fundrey	15/02/22	
68	Meet with the Mesh UK patient group to discuss rectopexy mesh and hernia mesh complications	Alison Cave	15/02/22	
69	Send written responses to observers whose questions were not answered during the November Board Meeting.	June Raine	18/01/22	Verbal Update

Medicines & Healthcare products Regulatory Agency

BOARD MEETING HELD IN PUBLIC

18 January 2022

Title	What are the current issues from the CEO's point of view?
Board Sponsor	June Raine
Purpose of Paper	Context

Medicines & Healthcare products Regulatory Agency

Chief Executive's Report to the Board
18 January 2022

This report gives a brief overview of the Agency's current issues since the November Board meeting. The Board is asked to consider and agree the priorities.

HEADLINES

- The MHRA transformation is moving forward and an All Staff Meeting was held to present the outcome of staff consultation and the next steps for staff
- We authorised the oral antiviral agent PF-07321332/ritonavir (Paxlovid) and the monoclonal antibody sotrovimab (Xevudy), for treatment of COVID-19 infection
- The new antiviral molnupiravir is being deployed through the trial PANORAMIC, and as it not recommended in pregnancy we have set up a pregnancy registry.
- The Pfizer/BioNTech vaccine was approved for children aged 5 to 11 in a new formulation as well as approving a new dose of the adult vaccine for children
- The Innovative Licensing and Access Pathway received 76 Innovation Passport applications in 2021, and the first target development profiles have been issued
- Proposals to reform the Clinical Trial Regulations, positioning UK as the best place to develop safe, innovative medicines, have been agreed for public consultation.
- We have published new guidance outlining how to use real-world evidence in clinical studies to support and facilitate robust regulatory decisions
- CPRD has been supporting two NIHR-funded clinical trials through its Clinical Trial Management Service, and a further study on Long COVID is about to commence
- The Commission on Human Medicines has considered the Report of its Isotretinoin Expert Working Group on the link with psychiatric and sexual side effects
- The Enforcement Group has introduced new "landing pages" for domains suspended for criminal activity, redirecting to safe medicines purchasing guidance.

HEALTHCARE ACCESS

COVID-19 antivirals

1. In December 2021, the MHRA approved a second oral antiviral medicine Paxlovid (PF-07321332/ritonavir) for the treatment of COVID-19 in adults who do not require supplementary oxygen and who are at increased risk for progression to severe COVID-19. The MHRA also approved Xevudy (sotrovimab), a monoclonal antibody for the treatment of symptomatic adults with acute COVID-19 infection who do not require oxygen supplementation and who are at increased risk of progressing to severe COVID-19 infection. The rolling review approach was used in order to reach a regulatory decision on benefit risk in the shortest time possible, with advice provided by the COVID-19 Therapeutics Expert Working Group. The Commission on Human Medicines recommended grant of a conditional marketing authorisation and that a pregnancy registry should be established.

COVID-19 vaccines

2. Following the extension of the approval of the Pfizer/BioNTech vaccine to 11 to 15 year olds earlier in 2021, at the end of November the approval was further extended to children aged 5 to 11 years. The paediatric vaccine is a new formulation and approval was also given to a new paediatric-appropriate dose of the adult vaccine. Rolling submission of data for several new COVID-19 vaccines has continued and during December the MHRA started discussions with companies concerning the approval of new, Omicron-specific version of vaccines. This follows the agreement with Access countries (Australia, Canada, Singapore and Switzerland) in 2021 of a guideline on evidence requirements for variant-adapted COVID-19 vaccines.

One-year anniversary of approving the first COVID-19 vaccine

3. On 2nd December 2021, NIBSC marked the one-year anniversary of issuing the first National Control Laboratory (NCL) certificate for the first authorised COVID-19 vaccine, Pfizer/BioNTech on the same day that it was given regulatory approval. On the 29th December 2020, NIBSC had certificated the first AstraZeneca/Oxford batch, again on the same day the product was authorised. Since then, two more authorised products have been added to the portfolio of certificated COVID-19 vaccines (Moderna, Janssen), and work is continuing to establish study areas for another four vaccines. By 2nd December 2021, NIBSC had certificated 179 batches totalling more than 176 million doses for UK and overseas vaccination programmes.

Innovative Licensing and Access Pathway

4. We have received a further six applications for the Innovation Passport designation covering both common and rare diseases. There has now been a total of 76 applications for Innovation Passports in 2021. We have received thirteen requests for a Target Development Profile and the first roadmaps have been issued to Innovation Passport Holders. Progress on a new applications portal is on track and due to launch end of January 2022. The Innovative Licensing and Access Pathway was the main topic of interest at the joint MHRA & BioIndustry Association conference in December.

Clinical trials legislation and process

5. From 1st January 2022, all applications for new Clinical Trials of Investigational Medicinal Products (CTIMPs) and combined IMP/device trials will be handled via combined review. This offers a joint regulatory and ethics review thus facilitating applications, halving the time to approval and cutting the time from application to recruiting the first patient by 40 days. Work to strengthen international co-operation on clinical trials has commenced via a working group of the International Coalition of Medicines Regulatory Authorities (ICMRA) and also via the Access consortium. Proposals for public consultation on revised UK clinical trials legislation were agreed by a short-life working group and will be launched in mid-January. A communication plan is in place to ensure a wide range of stakeholders are aware of the consultation.

Innovation in clinical trials supported by Clinical Practice Research Datalink (CPRD)

6. Following a workshop on data enabled clinical trials co-hosted by CPRD, National Institute of Health Research (NIHR) and Health Data Research UK in 2018, CPRD has been supporting two NIHR-funded clinical trials through its Clinical Trial Management service. Over 100 patients have already been recruited for the DaRe2THINK trial and the ASYMPTOMATIC trial, which has only recently gone live with one pilot practice, is expecting the first patient to be recruited in the first half of January 2022. The use of electronic health records data and patient reported

outcomes to determine outcomes and employ a risk-adjusted and pragmatic approach to safety reporting represents a cost- effective approach to clinical effectiveness trials. Furthermore, use of a widespread GP network helps democratise participation. A further NIHR-funded study into non-hospitalised community Long COVID cases is also about to commence recruitment using a CPRD-based patient referral model.

Use of real-world data for clinical trials

7. On 16 December, following a 6-week consultation and analysis of the responses, we published guidance on the use of real-world data (RWD) in clinical studies to support regulatory decisions. The guidelines provide general points to consider for sponsors planning to conduct clinical research using RWD and information to aid the design of studies aiming to provide evidence suitable for supporting regulatory decisions. Guidance is also given on requirements for gaining approval for studies to be run in the UK. Use of such data sources for this purpose in clinical studies has the potential to increase the speed and reduce the cost of development, which would see effective medicines being approved more quickly.

Innovative devices

8. The public consultation on the future regulation for medical devices closed on 25 November 2021 with over 900 responses. We are currently reviewing the responses to assess how we might amend our legal framework, ahead of the publication of a Government response in the first quarter of 2022 and new legislation to follow later in the year. We are setting up a series of focus groups with our stakeholders, including patient groups, to continue engagement with them throughout the coming months. The intention of the focus groups is to seek their input into guidance and other support systems necessary to ease transition to the new regulatory system.

Best practice guidance for Advanced Therapy Medicinal Products

9. A new best practice guidance has been published by the British Pharmacopeia (BP) on the application of flow cytometry to Advanced Therapy Medicinal Products (ATMPs). ATMPs provide an unprecedented opportunity to manage or treat diseases, and their effectiveness is underpinned by suitable characterisation techniques for quality assessment. Working with colleagues across the Agency, the BP has engaged with the ATMP community to develop guidance for key analytical technologies to support quality, safety, and efficacy throughout the product lifecycle. This is the first guidance to be published and is a key outcome from the strategy for pharmacopoeial biological quality standards to enable innovation.

Neurovirulence of Polio vaccine

10. A Transgenic Mouse Neurovirulence Test (TgMNVT) is used to assess the neurovirulence of poliovirus monovalent bulks for the batch release of oral polio vaccines. This is in accordance with the current World Health Organisation/Official Medicines Control Laboratory (WHO/OMCL) guidelines following a protocol laid down by WHO. It has also been adopted for research and developmental purposes using 2 unique strains of mice carrying the poliovirus receptor bred at NIBSC. Scientists at South Mimms worked to develop an improved competency assessment tool which demonstrates our commitment to the 3Rs (Refinement, Reduction, Replacement) and the highest standards of animal welfare.

PATIENT SAFETY

Safety of COVID-19 vaccines

11. The overall reporting rate of suspected adverse reactions associated with the Pfizer/BioNTech, COVID-19 Vaccine AstraZeneca, COVID-19 Vaccine Moderna and unspecified brands of COVID-19 vaccine has increased by December 2021 to around 3 to 7 Yellow Cards per 1,000 doses. The overwhelming majority of reports continue to relate to injection-site reactions (sore arm for example) and generalised symptoms such as 'flu-like' illness, headache, chills, fatigue (tiredness), nausea (feeling sick), fever, dizziness, weakness, aching muscles, and rapid heartbeat. Generally, these happen shortly after the vaccination and are not associated with more serious or lasting illness. These types of reactions reflect the normal immune response triggered by the body to the vaccines and are typically seen with most types of vaccine. We continue to publish a weekly summary with commentary of reporting trends of interest.

Antiviral safety surveillance

12. The new antiviral molnupiravir is now being deployed through PANORAMIC, a national trial, to targeted pre-identified patients at highest-risk of developing severe COVID-19 disease. Molnupiravir is not recommended for use in pregnancy until further studies have established its effectiveness and safety in pregnancy. We have been working with the UK Teratology Information Service and other stakeholders, to set up a pregnancy registry to capture data on exposed pregnancies, the core of which is now up and running. An alert via the Central Alerting System was sent to healthcare professionals to encourage reporting to the registry and a patient leaflet was developed to be distributed to patients along with their molnupiravir prescription. We are working on a communications plan to prepare for wider deployment and broadening the registry to include pregnancy exposure to other COVID-19 antivirals.

Safety review of Isotretinoin

13. The Isotretinoin Expert Working Group's review of psychiatric and sexual side effects was considered by the CHM in December. Patients, their families and other stakeholders have been an integral part of the review of the safety of isotretinoin. The perspectives provided by patients and families and the views and experiences shared with the Isotretinoin Expert Working Group through the call for information and the series of meetings has provided valuable information to the Review. The report of the isotretinoin review will be published once the full process has been completed. Patients and stakeholders will be kept up-to-date and involved in the process.

Medicines recalls

14. A recall to patient level was undertaken for a skin cream found to contain a steroid. Dermaved Sensitive Cream is not a licensed medicine and following investigation by the medicines borderline team, analysis confirmed the presence of clobetasol proportionate, a prescription only medicine for conditions such as psoriasis and eczema. In view of the risks associated with prolonged use of strong steroids, particularly in children, this recall was expedited. In addition, there was a further pharmacy level precautionary recall of irbesartan products due to the presence of an azido (AZBT) impurity which has mutagenic potential. Laboratory testing has found that long-term exposure to AZBT above acceptable limits may potentially increase the risk of cancer, but there is no UK or international evidence that this substance has caused any harm to patients. In collaboration with other regulators we have set acceptable daily intake limits for AZBT. If medicines contain levels of AZBT above this limit, these need to be recalled by the manufacturer as a precaution.

Enforcement activities

15. Collaboration with internet domain name service providers has resulted in suspension of websites promoting the sale of medicines contrary to Human Medicines Regulations 2012. In addition, the Enforcement Group's (EG) ongoing partnership with Nominet has resulted in the introduction of law enforcement "landing pages" for domains suspended for criminal activity involving medicines and medical devices. Users attempting to access these suspended domains will be redirected to guidance on purchasing medicines online safely. The Group's financial investigators continue to make effective use of Account Freezing Orders (AFOs) to disrupt those suspected of laundering the proceeds of medicines-related crime. Collaborative investigative work with the Inspectorate led to a wholesaler suspected of supplying falsified medicines having their licence suspended until measures and appropriate practices are implemented. These interventions will have a deterrent impact on offending.

PARTNERSHIPS

Access Consortium

16. In December, the Access Consortium COVID-19 Vaccines and Therapeutics Working Group published a consensus statement on authorising new COVID-19 therapeutics. The statement sets out the continued commitment to robust processes for authorisation of COVID-19 medicines, and continued collaboration between Access Consortium partners in pharmacovigilance. The New Active Substance Working group continues to oversee work-sharing procedures. We have led collaborative discussions with Access partners on the creation of a new Clinical Trials Discussion group and a Joint Scientific Advice Discussion group.

International collaboration on remote Inspections

17. We chaired a working group of ICMRA to look at the move to remote inspections for Good Clinical Practice and Good Manufacturing Practice during the pandemic. This working group included regulatory authority representatives from the US, EMA, Canada, Switzerland, Ireland, Spain, France, Germany, Japan, Australia, Brazil, Singapore, Saudi and WHO. A reflection paper on this topic has now been published which includes discussion on the various types of remote inspections (e.g. digital and desk-based, risk management and the adoption of hybrid approaches). The outcome of this work reflects the importance of joined up global approaches to regulation and whilst not formal guidance it will help inform the future role of remote inspections.

Scientific speaking and training engagements

18. External speaking engagements have been undertaken by Agency scientists on:
    - development of microbiome standards and research in the microbiome field
    - antimicrobial resistance in the UK and the UK's role on the global stage
    - STEM (Science, Technology, Engineering, and Mathematics) activities for students at schools and colleges

DYNAMIC ORGANISATION

Transformation Programme

19. On 30th November an All Staff Meeting was held to present the response to the staff consultation and outline the next phase in the transformation process for staff. Further engagement with staff followed via open group sessions for all staff, as well as local teams and individual meetings. Key to the design of the Agency's future operating

model is to fully capture the benefits of operating as One Agency along the product lifecycle. We have been working extensively with key stakeholders to clarify our services profile, redesign critical services and optimise processes with the primary objective of delivering the best health outcomes for patients and the public. The Agency will begin to realise the benefits of transformation in improving public health and safety as we implement more efficient and effective safety systems and deliver patient outcome-centred services, enhanced by streamlined and standardised processes enabled by modernised technology.

Applications Outsourcing Transition

20. The Applications Outsourcing Transition Project to secure a provider for the maintenance of IT systems undertook a successful procurement exercise. The next step is Full Business Case approval. The transition activities will move the Agency from its current support contract for a range of Agency regulatory systems, to a fresh contract and service. This also potentially provides substantial capability and capacity to develop the Agency's next generation of regulatory systems, subject to separate business cases. As such, the award of this contract will signal the commencement of the delivery of a foundational component of the Agency's Digital, Data and Technology Strategy, which itself is critical to the success of the Agency's Transformation agenda.

External Audits

21. Following its recertification audit on 9-10 November 2021 by a global safety certification company (UL), including in-vitro diagnostic (IVD)-related Quality Management System activities, NIBSC has maintained its ISO 13485:2016 certification subject to review by the Notified Body panel. On the 9 November 2021, the Health and Safety Executive carried out a routine inspection of NIBSC high containment facilities. The outcome of the inspection was positive, with the HSE confirming that a suitable competence management system was in place and the process for developing, implementing, and revising standard operating procedures was also satisfactory. Following a 2 day audit in November 2021 by the British Standards Institution, the Agency successfully achieved renewal of its certification to ISO 45001:2018 (the international standard for health and safety management systems), with no non-conformities and just two opportunities for improvement. This successful re-certification is an excellent result given the extra COVID-19 and Transformation-related work being carried out by many staff during the current time.

FINANCIAL SUSTAINABILITY

22. Following a survey of staff accommodation requirements, the Accommodation Board recommended a reduction in our occupancy of 10 South Colonnade, which will release £2m to contribute to achieving financial sustainability. We welcomed a new Deputy Director of Finance, Rose Braithwaite. Work will now progress on the Fees Policy Review under the leadership of the previous interim Director, Jo Passingham. We await the outcome of the Comprehensive Spending Review. With the assistance of our sponsor team, a workshop has been arranged with DHSC Finance colleagues to discuss the transition from Trading Fund status to operating withing the Departmental accounting boundary from 1 April 2022.

June Raine CEO
January 2022

Medicines & Healthcare products Regulatory Agency

BOARD MEETING HELD IN PUBLIC

18 January 2022

Title	What is the performance of the MHRA on the Balanced Scorecard in Month 8?
Board Sponsor	Jon Fundrey
Purpose of Paper	Assurance

What is the performance of the MHRA on the Balanced Scorecard in Month 8?

1. Executive Summary

1.1 This paper sets out commentary to support the Monthly Balanced scorecard detailed in the attached appendices.

1.2 The Board is asked to review the metrics and the commentary and consider whether this provides appropriate assurance that current performance is on track and aligned to our strategic objectives.

2. Introduction

2.1 This monthly balanced scorecard has been updated with data up to 30th November 2021. A list of metrics included in each area along with the current status of those metrics is included in the table at the end of this document.

3. November Metrics Commentary

3.1 Scientific Innovation

Clinical Trials

Normal and First-in-Human Clinical trial applications continue at a steady rate and are in line with expectations.

Novel trials have also been at the expected rate this quarter although this is double the rate we saw in 2020.

3.2 Healthcare Access

EAMS

Applications for the Early Access to Medicines Scheme (EAMS) remain in line with current expectations. The Promising Innovative Medicine (PIM) Designation and EAMS Scientific Opinion applications activity are currently modest but may increase over time following the future implementation of the EAMS statutory instrument in the Human Medicines Regulations.

ILAP

Applications of the Innovation Passport Designation of the Innovative Licensing and Access Pathway (ILAP) have continued to exceed expectations month on month. This reflects the attractiveness of the pathway to medicines developers. To note the outcome of the designation reflects the assessment process, and a positive outcome is not guaranteed as this is based on the quality of data and the interpretation and conclusions drawn on that data. Target Development Profile (TDP) applications are increasing as more Innovation Passport designations are issued and companies transition to the roadmap step of ILAP.

Variations

High volumes of National Applications during October and November (205) have seen the backlog increase as there have only been 103 determinations over the same period. However this is partially to be expected with applications usually seeing a seasonal spike during the autumn while the level of National determinations is usually very consistent.

The volume of European Commission Decision Reliance Procedure (ECDRP) determinations was very high at 128 in November, we expect activity to remain at a high level until March, in order to meet demand before the start of the new financial year.

3.3 **Patient Safety**

ADRs

Adverse Drug Reactions (ADRs) were 6x higher than pre Covid-19 volumes. There has been a significant reduction since June, however November was the first month since then that we have seen an increase, up by 6k to 22k. This could be an impact of the increased vaccinations administered.

3.4 **Dynamic Organisation**

Full Time Equivalents

The current pause on recruitment in order to protect displaced members of staff had previously been resulting in a fall of Full Time Equivalents (FTEs). However, this trend has stopped with FTE numbers staying flat since August.
This financial year the agency has recruited an additional 40 contractors to help fill posts vacated by leavers which has halted the decline.

3.5 **Financial Suitability**

Year to Data Operational Surplus/Deficit

Operating result at the end of November is £11.7m favourable to budget.
The majority of this is driven by £5.9m of lower staff costs (further detail below), £3.1m of lower ICT costs and £1.6m of reduced travel & training.
The ICT savings are expected to reduce throughout the rest of the year, with a yearend expected saving of £1.5m.
The budget for Travel & Training assumed we would return to pre Covid-19 activity, but this has not happened.

Available Cash Reserves

Cash reserves increased significantly in October due to receiving £31.3m of DH funding (originally expected in November and March). The balance should reduce monthly going forward, with yearend projection of £20m. This will be reviewed as part of the P9 forecasting which will begin shortly.

Staff Costs

Several factors are currently contributing to a low staff cost expenditure (despite the increase in contractors):

- Current vacancies are saving the agency £4.8m, we did however budget for £2.7m of this.
- A DHSC grant for batch testing is now being split across multiple years, reducing costs by another £1.6m.
- Average salaries have reduced in the agency, this has resulted in a YTD saving of £0.8m. This is a result of no pay increases this year combined with a high volume of staff exits where the replacements enter at a lower rate or where the employee has not been replaced but was previously earning more than the average.
- We also have a bonus underspend and a budget phasing saving of £0.9m.

4. Balanced Scorecard Development

4.1 The scorecard team are currently developing a coversheet that will define each metric. This will be included in the next quarterly version of the report.

4.2 The team are still looking at the addition of a Science Index metric and an Inspections metric.

4.3 Metrics Status is as follows:

Item No.	Goals	BS Metric	Quarterly	Monthly	Live Data/Sample
1	INVOLVING PATIENTS & PUBLIC	Public communications engagement	Yes	No	Sample
2	INVOLVING PATIENTS & PUBLIC	Reputational index	Yes	No	Sample
3	INVOLVING PATIENTS & PUBLIC	Positive media sentiment	Yes	No	Live
4	ENABLING INNOVATION	Clinical Trials	Yes	Yes	Live
5	ENABLING INNOVATION	Grants % success rate	Yes	No	Live
6	ENABLING INNOVATION	Research papers	Yes	No	Live
7	ENABLING INNOVATION	CPRD UK population coverage	Yes	No	Live
8	ENABLING INNOVATION	Publications using CPRD data	Yes	No	Live
9	ACCELERATING ACCESS	Variation determinations	Yes	Yes	Live
10	ACCELERATING ACCESS	Generic approvals	Yes	Yes	Live
11	ACCELERATING ACCESS	NAS determinations	Yes	Yes	Live
12	ACCELERATING ACCESS	Standards sales volumes	Yes	Yes	Live
13	ACCELERATING ACCESS	ILAP applications	Yes	Yes	Live
14	ACCELERATING ACCESS	EAM PIM applications	Yes	Yes	Live
15	ACCELERATING ACCESS	Device registrations	Yes	Yes	Live
16	ACCELERATING ACCESS	PIPS volumes	Yes	Yes	Live
17	ENSURING PATIENT SAFETY	Adverse drug reactions	Yes	Yes	Live
18	ENSURING PATIENT SAFETY	Adverse device incidents	Yes	Yes	Live
19	ENSURING PATIENT SAFETY	Adverse blood reactions	Yes	Yes	Live

20	ENSURING PATIENT SAFETY	Patient safety interventions	Yes	Yes	Live
21	DYNAMIC ORGANISATION	FTE	Yes	Yes	Live
22	DYNAMIC ORGANISATION	CS Culture Survey	Yes	No	Live
23	DYNAMIC ORGANISATION	Equality, Diversity & Inclusion	Yes	No	Live
24	DYNAMIC ORGANISATION	People engagement score	Yes	No	Live
25	DYNAMIC ORGANISATION	Key project milestones missed	Yes	No	Data Unreliable
26	DYNAMIC ORGANISATION	Indexed productivity	Yes	No	Live
27	FINANCIAL SUSTAINABILITY	Year to Date surplus	Yes	Yes	Live
28	FINANCIAL SUSTAINABILITY	Cash reserves	Yes	Yes	Live
29	FINANCIAL SUSTAINABILITY	Corporate overhead %	Yes	No	Live
30	FINANCIAL SUSTAINABILITY	Non-pay savings	Yes	No	Live
31	FINANCIAL SUSTAINABILITY	Staff costs	Yes	Yes	Live
32	FINANCIAL SUSTAINABILITY	Cashable Benefits	Yes	No	Live

5 Recommendation

5.1 The Board is asked to confirm that the Monthly Balanced Scorecard presented provides assurance that current performance is on track and aligned to strategic objectives

Jon Fundrey
January 2022

Medicines & Healthcare products Regulatory Agency

Balanced Scorecard (Monthly View) v1.0

Scientific Innovation

Clinical Trials

Normal

69

Target: 61

KPI ▲ (green) — Trend ↗

Novel

2

Target: 3

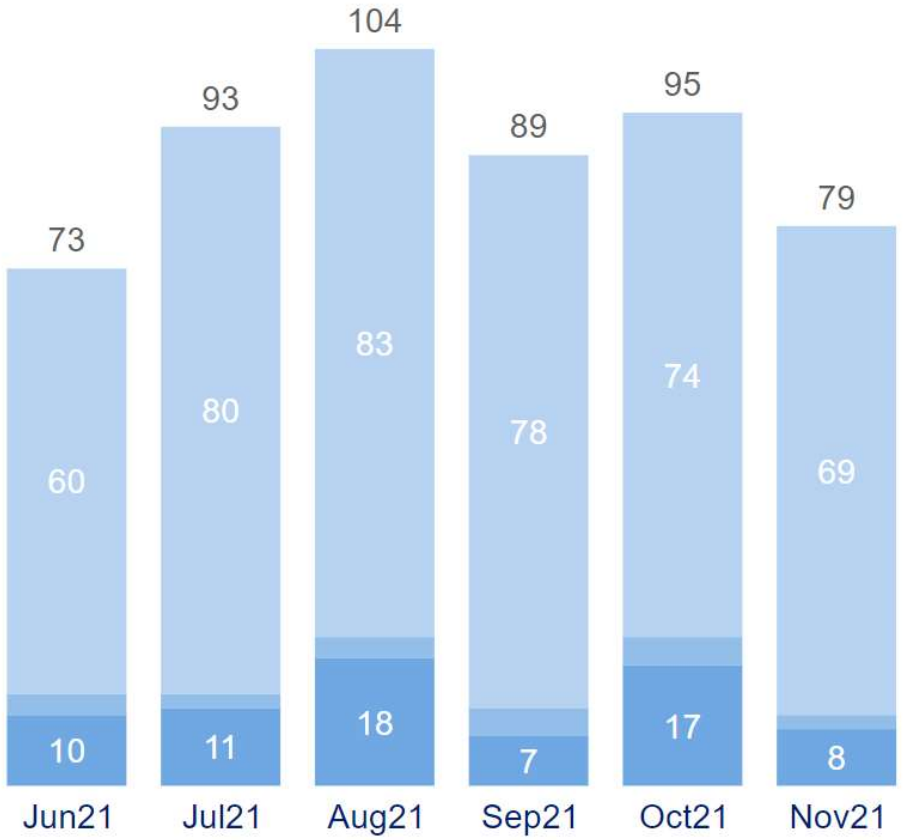
KPI ▼ (red) — Trend ↘

FIH Approvals

8

Target: 7

KPI ▲ (green) — Trend ↘



Healthcare Access

EAMs - PIM-D Applications

Received

3

Target: 2

Granted

2

% Positive

100.0%

KPI Trend

KPI Trend

KPI Trend

EAMs - EAMs SO Applications

Received

2

Target: 1

Granted

0

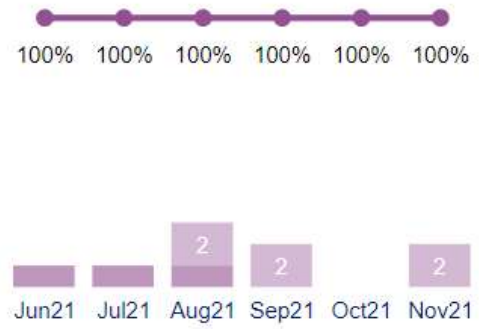
% Positive

100.0%

KPI Trend

KPI Trend

KPI Trend



Standards Sales Volume

NIBSC (Non Flu)

7,634

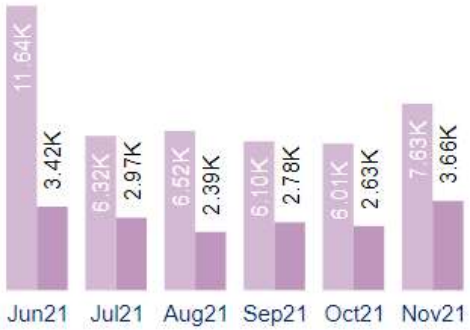
BP

3,655

Target: 2,900

KPI Trend

KPI Trend



PIPS Volume

45

KPI

Trend

Medicines & Healthcare products Regulatory Agency

Balanced Scorecard (Monthly View) v1.0

November 2021 – 3/8

Healthcare Access

NAS - Applications Received

National (PL-GB/PL UK)

4

Orbis/Access

0

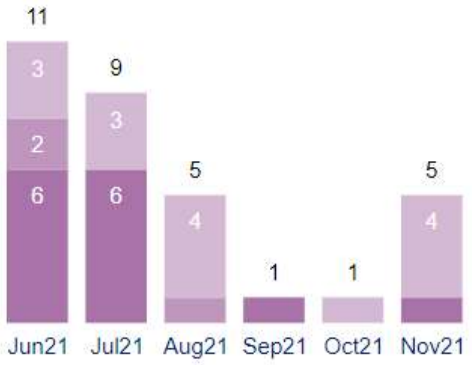
EC/MRDC Reliance

1

KPI Trend

KPI Trend

KPI Trend



NAS - Applications Determined

National (PL-GB/PL UK)

1

Orbis/Access

1

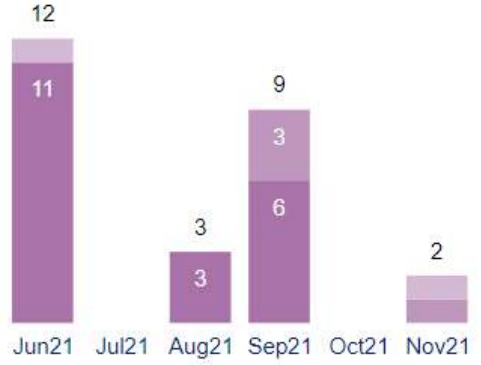
EC/MRDC Reliance

0

KPI Trend

KPI Trend

KPI Trend



ILAP Passport Applications

Apps Received

4

Target: 3

Apps Determined

4

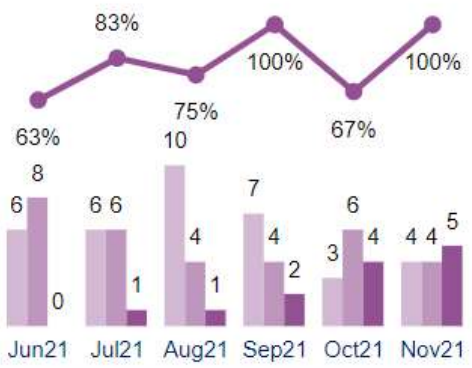
% Positive

100.0%

TDP Meeting Requests

5

Target: 2



Device Registrations

Deadline 01/05/21

617,244

Deadline 01/09/21

219,216

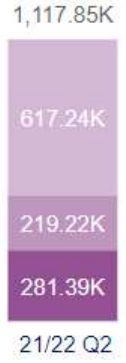
Deadline 01/01/22

281,393

KPI Trend

KPI Trend

KPI Trend



Healthcare Access

Variations - Applications Received

National (Std + Complex)

101

Target: 90

Type II Ext Complex

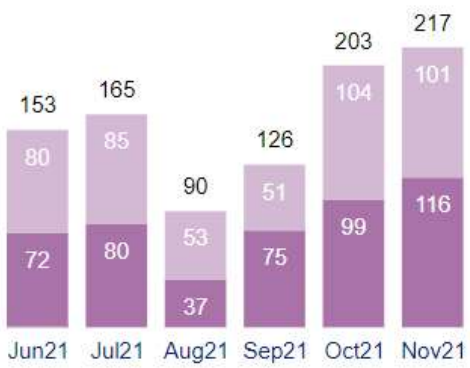
0

Type II ECDRP

116

Type II Orbis

0



Variations - Applications Determined

National (Std + Complex)

48

Target: 63

Type II Ext Complex

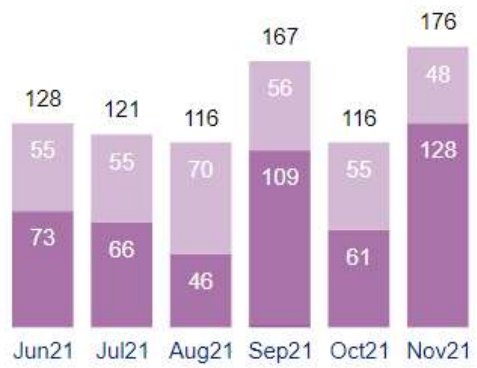
0

Type II ECDRP

128

Type II Orbis

0



Generics - Applications Received

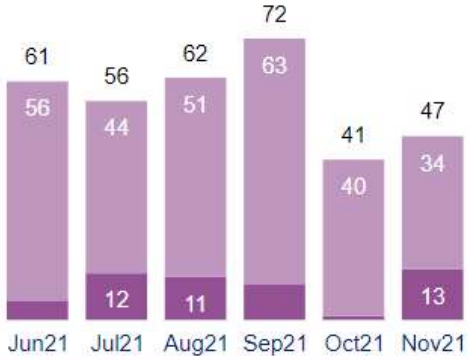
National MAs

34

Target: 56

EC/MRDC Reliance

13



Generics - Applications Determined

National MAs

43

Target: 19

EC/MRDC Reliance

4

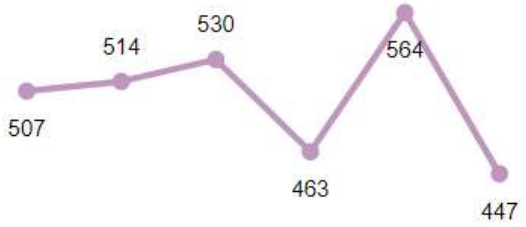
Healthcare Access

Abridged - Applications Received

Average Gross Time (Rec to Det Days)

447

KPI



Trend

Number Received

72

KPI

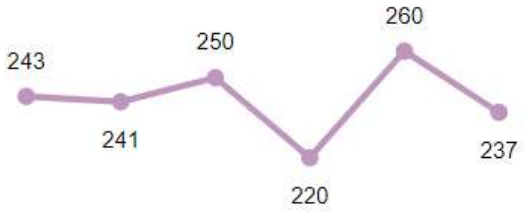
Trend

Abridged - Applications Determined

Average Net Time (Clock On Days)

237

KPI

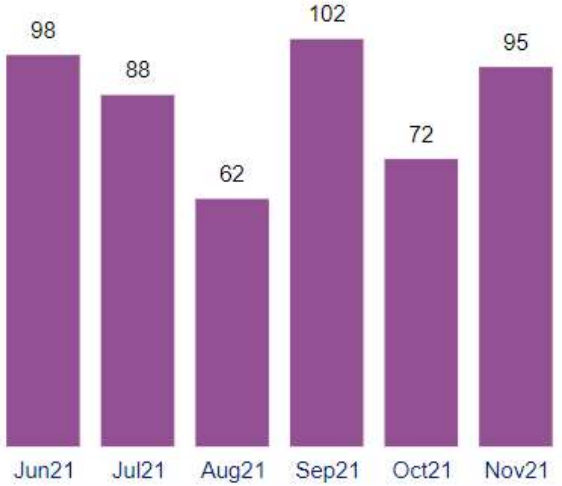


Trend

Number Determined

95

KPI



Trend

Medicines & Healthcare products Regulatory Agency

Balanced Scorecard (Monthly View) v1.0

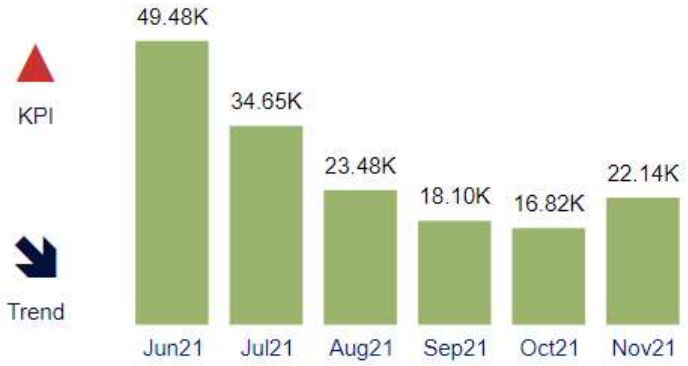
November 2021 – 6/8

Patient Safety

Adverse Drug Reactions

22,140

Nov20: 3,243 (+582.7%)



Devices - Adverse Incidents

2,084

Nov20: 1,969 (+5.84%)

Adverse Blood Reactions

64

Nov20: 55 (+16.36%)

Patient Safety Interventions

Major Signals

29,345

Manuf Safety Comms

6

MHRA Safety Comms

4

Dynamic Organisation

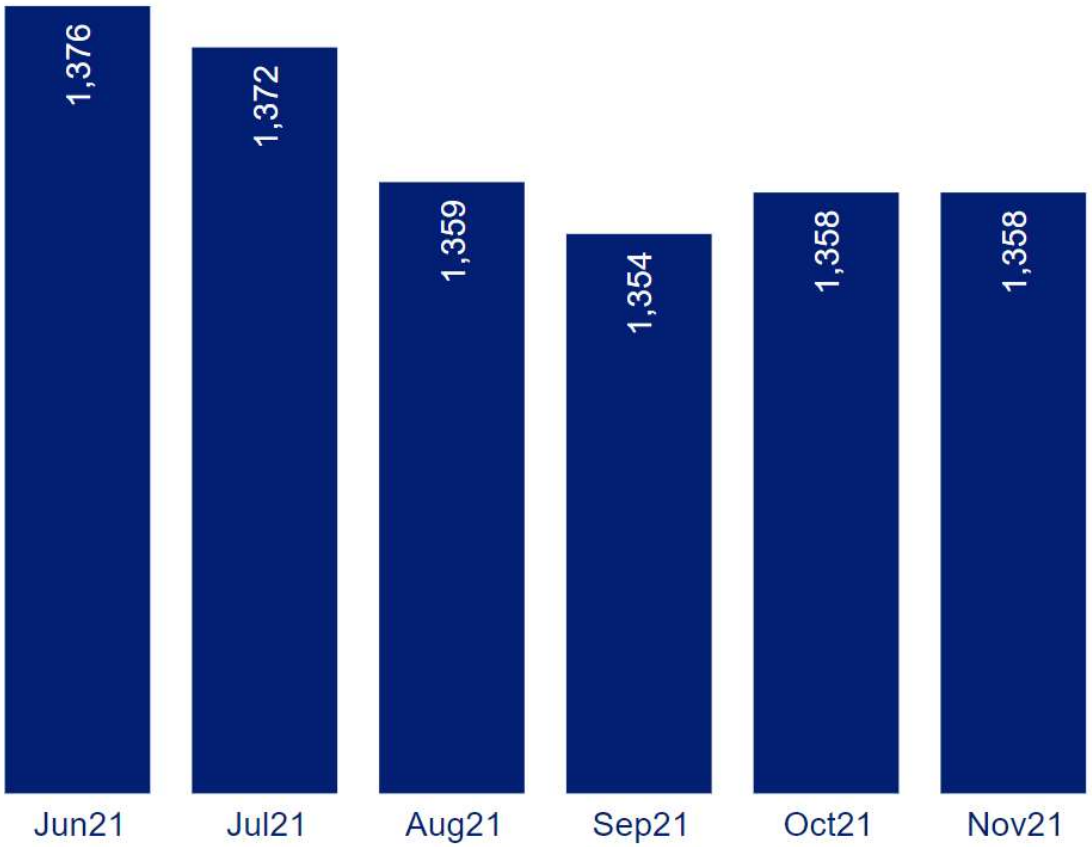
FTE

1,358

Budget: 1,458 (-6.86%)

KPI

Trend



Medicines & Healthcare products Regulatory Agency

Balanced Scorecard (Monthly View) v1.0

November 2021 – 8/8

Financial Sustainability

Year To Date Operational Surplus/Deficit

£7.42M
Budget: -£4.30M

Cash Balance

£94.09M
Budget: £87.40M

Staff Costs

£7.50M
Budget: £8.25M

Medicines & Healthcare products Regulatory Agency

BOARD MEETING HELD IN PUBLIC

18 January 2022

Title	How will the outcomes and short, medium and long term benefits arising from activities being undertaken to address the recommendations of the Cumberlege Review be measured?
Board Sponsor	Dr Alison Cave, Chief Safety Officer
Purpose of Paper	Assurance

Medicines & Healthcare products Regulatory Agency

How will the outcomes and short, medium and long term benefits arising from activities being undertaken to address the recommendations of the Cumberlege Review be measured?

1. Executive Summary

1.1 The Board has previously endorsed the Agency's planned short, medium, and long-term deliverables in response to the Cumberlege Review, and progress has been reviewed at the Patient Safety and Engagement Committee. It was recognised that the measures to monitor the impact of the deliverables needed to be developed further and refined. This paper outlines how we propose to better measure the impact of the activities we are implementing as a direct result of the Cumberlege Report's findings and recommendations.

2. Introduction

2.1 The Cumberlege Report, '*First Do No Harm'*, sets out the evidence obtained during two years of hearings and other information gathering regarding how women who received sodium valproate, pelvic mesh implants and hormone pregnancy tests were failed by the healthcare system. The systems which should have identified risks were slow and public awareness of these systems was low, and the responses in terms of listening to and acting on women's concerns were inadequate.

2.2 Recommendation 6 of the IMMDS Review states: *The MHRA needs substantial revision, particularly in relation to adverse event reporting and medical device regulation. It needs to ensure that it engages more with patients and their outcomes. It needs to raise awareness of its public protection roles and to ensure that patients have an integral role in its work.* There are also several 'Actions for Improvement' identified in the Review report for the Agency to implement.

2.3 The Government Response included a detailed contribution on the work which the Agency is undertaking and the progress made so far in the following range of areas: to strengthen the regulatory framework for medicines and devices, improve adverse event reporting, improve patient involvement, improve the safety of medicines in pregnancy and transform our culture.

2.4 The programme of work in response to Recommendation 6 of the IMMDS Review organizes around a number of key action themes: Patient and Public Engagement and Involvement; a responsive reporting system; strengthened evidence for decision making; and conflicts of interest processes. The need to develop better measures to capture the outcomes and impact of the activities was highlighted to the Board in July and a benefits map has been developed to enable progress to be more effectively tracked.

3. Input from the IMMDSR Patient Reference Group

3.1 We were grateful to have further input from the Cumberlege Patient Reference Group when we met with them at the end of July 21. The session helped to finalise our Patient and Public Involvement Strategy and prioritise the areas of focus, and the PPI strategy has now been published. The Patient Reference Group also help inform the current considerations about how to measure the impact of what we are doing to address the concerns highlighted through the Review. We discussed the need to measure a range of impacts, from the qualitative views of patients on how well their concerns have been listened to and addressed, to quantitative measures such as the timeliness of identification of harm from a medicine or medical device (eg speed of signal detection), robustness of risk evaluation (eg comparison with views of experts and/or of other regulators), extent to which patients' input has influenced the regulatory decision-making process, and importantly monitoring the impact of regulatory action on safety issues (has the risk been eliminated or reduced to a level which patients consider acceptable?).

4. Monitoring progress and measuring impact of the actions taken so far

4.1 The Agency has made addressing the Review's concerns central to its new corporate Delivery Plan for 2021-2023 'Putting patients first - A new era for our Agency'. Involving patients in all our activities is the Agency's first priority and every member of staff will have an objective to help deliver better patient involvement. The Delivery Plan details the specific actions designed to address the Review's concerns. Staff objectives are being monitored through their progress reviews and the progress on the commitments in the Delivery Plan are been being monitored.

4.2 Government has committed to provide a further update on implementation of the Review recommendations after a twelve-month period (expected July 2022). We continue to work closely with the DHSC and wider healthcare partners and provide reports to DHSC on the progress of the implementation of the Agency's actions (a summary of these actions can be found at Annex 1).

4.3 We have carried out a benefits mapping exercise to consolidate the key activities across the Agency in response to the recommendation 6 of the Cumberlege Review, and map these activities with deliverables, indicators and potential outcomes in order to track progress against anticipated longer-term benefits. A description of the benefit map columns can be seen at Annex 2. The benefit map has been split into the following areas aligned

with key MHRA action themes: Patient and Public Engagement and Involvement (benefit map 1); a responsive reporting system (benefit map 2); strengthened evidence for decision making (benefit map 3); and conflicts of interest (benefit map 4). The maps have been developed internally with the Agency leads from the relevant areas across the Agency. It is recognised there are many interdependencies around the realisation of benefits, with many workstreams contributing to a single overarching benefit, and improvements are required to clearly show these inter-dependencies. The Agency risk register captures many of these risks and the associated controls.

4.4 Further work to develop and refine the benefits map as a tool to monitor the impact of the deliverables is being taken forward. Feedback from the Patient Safety and Engagement Committee highlighted the need for the outcomes and indicators to better reflect the patient perspective, rather than the Agency perspective.

4.5 It is noted that some of the measures are more qualitative than quantitative, and hence will be challenging to track. Targets by which to measure success are required as well as the need to establish baseline measurements, against which better to assess the impact of activities and progress made.

4.6 It will be important to consider how the evaluation of this work will be achieved and a partnership model, such as an academic partnership, or discussing options with the National Institute for Health Research (NIHR) may be of value.

4.7 The Agency will carry out a further survey to measure whether there is an improvement in the way that patients feel listened to and their views acted on.

5 Next steps

5.1 The benefits map will be further refined and used as a tool to monitor the impact of the deliverables. We will continue to work with DHSC and others in the healthcare system to progress the actions.

6 Recommendation

6.1 This paper outlines how we propose to better measure the impact of the actions we are implementing as a direct result of the Cumberlege Report's findings and recommendations. While recognising the process is iterative and will need to be continually refined, is the Board assured that the outcomes and short, medium and long-term benefits arising from activities to address the recommendations of the Cumberlege report will be measured effectively?

Dr Alison Cave
Chief Safety Officer
18 January 2022

Annex 1:

Actions to be implemented by July 2022 (when the Government progress update is due to be given)

Enhanced reporting

a. Implement new more responsive adverse event reporting system by March 22, engagement with the public directly during development via user needs sessions.

Medical devices legislation

b. Lay SIs for future medical devices legislation by end Q1, 22/23.

c. Agree and implement policy for a significantly enhanced transparency regime for medical devices by Q4, 21/22.

d. A register of all medical devices on the UK market was launched in Jan 2021 and should be fully populated by 1 Jan 2022. The above medical devices SI will mandate completion of all relevant fields (including Unique Device Identifiers (UDIs) and making the data accessible to the public.

e. MHRA will provide medical device register information to NHS Digital as reference data for the future Medical Device Information System (MDIS). NHSD will capture device and clinical performance data for all implantable medical devices via MDIS and they will inform MHRA about underperforming implants to support our regulatory decision making / safety actions (timing to be confirmed).

Medicines legislation

f. Use powers in the MMD Act 2021 to put in place new legislation to ensure safe access to innovative products and to protect public health: launch all consultations – end Q3, 21/22; publish all responses – end Q4, 21/22;

g. MHRA will work with NHS Digital and NHS X to improve the widescale capture of real world data relevant to the monitoring of the use, benefits, and safety of medicines, particularly data on medicines prescribed in secondary care linked to patient outcomes, and improve the integration of evidence from these data into regulatory decision-making to support the robustness and timeliness of actions.

h. Introduction of statutory provisions for the establishment of publicly held medicines registries through the forthcoming Health and Care Bill.

Independent expert advice for medical devices

i. Use powers in the MMD Act 2021 to put the independent advice for medical devices from the Devices Expert Advisory Committee (DEAC) and its committees onto a statutory footing

j. Implement a shadow Devices Expert Advisory Committee by Q1 2022

Greater patient involvement

k. Publish new Patient Involvement Strategy by Q2 21/22 and deliver actions thereafter.

l. Review and improve patient representation across all committees, to ensure there is patient representation across all, with training provided. This is linked to the expansion of the Patient Group Consultative Forum.

m. By March 2022, all advisory committees/groups will have patient representation.

Action on Valproate

n. In 2021/22, enhance valproate registry by integrating digital annual acknowledgement of risk form; scoping the extension of the core registry to other regions in the UK and extending the registry to include all AEDs.

o. Through 2021, work will be done to establish the valproate registry governance structure, digitalise the annual acknowledgement of risk form and integrate it directly into the registry, scope the extension of the core valproate registry to other regions in the UK beyond England, and extend the registry to include all AEDs.

Action on teratogens

p. Review of labelling and risk mitigation strategies of other regulators by Q3 21/22.

q. Seek independent patient / stakeholder input and expert advice on development of new risk minimisation measures and communications by Q4 21/22.

r. Update UK guidance on teratogens and amendments to risk mitigation for specific products, as appropriate, by mid-2022.

Managing conflicts of interest

s. Consult on, publish and implement revised code of practice for the Commission on Human Medicines (CHM) and its expert groups by Dec 21.

t. Ensure greater transparency of staff conflicts of interest and processes for managing conflicts of interests via publication of information in an accessible format by Q4 21/22.

Actions to be completed after July 2022:

Medical devices legislation

a. Publish guidance documents for the new devices regulatory regime by end Q3, 22/23 with ongoing engagement with stakeholders over 22/23 to prepare them for the new framework;

b. Implement the medical devices regulatory regime from Q2 23.

c. Agree and implement policy for a significantly enhanced transparency regime for medical devices with key elements being delivered over 22/23.

Medicines legislation

d. Introduction of statutory provisions for the establishment of publicly held medicines registries through the forthcoming Health and Care Bill by Q3 23/24.

e. Use powers in the MMD Act 2021 to put in place new legislation to ensure safe access to innovative products and to protect public health all Sis laid by end Q1 22/23.

Independent expert advice for medical devices

f. Devices Expert Advisory Committee (DEAC) placed on a statutory footing by June 2023.

Greater patient involvement

g. Expand Agency Patient Group Forum by Q3 22/23 to improve diversity and size.

Action on valproate

h. In 2022 onwards, further development of the registry, including the integration of additional datasets on child and maternal health and enabling direct patient reporting into the registry.

Annex 2: Description of the benefit map column definitions:

Key activities (and dates where known)	*This describes the key activities being undertaken by the MHRA to address the key IMMDSR recommendation – this activity should directly create the deliverable*
Key deliverables (and dates where known)	*Describe the key deliverable this should be as a direct result of the work done (activity)*
Indicators	*These are short term indicators which capture the outputs of the deliverable and when you know it has been a success. These should be SMART with a measure and target where possible*
Potential outcomes	*An outcome should describe the impact of the deliverable – this should be able to be directly tracked back to the activity*
Benefit description	*What benefit arises from the outcome? This is usually longer term, sometimes hard to capture and measure. We expect for multiple activities to deliver a similar benefit, this will be reflected on the benefits map – please duplicate in this workbook. Think about the benefits to the Agency and externally. Please refer to the worksheet identifying benefits guide or the Agency's Benefit Management Framework for help on categorising benefits*

IMMDSR recommendation	MHRA action themes	Key activities	Key deliverables	Indicators	Potential outcomes	Benefits (short, medium, long term)
Recommendation 6: 'The Medicines and Healthcare products Regulatory Agency (MHRA) needs substantial revision particularly in relation to adverse event reporting and medical device regulation. It needs to ensure that it engages more with patients and their outcomes. It needs to raise awareness of its public protection roles and to ensure that patients have an integral role in its work.'	**Developing our patient and public engagement and involvement**	Working with divisions to develop pilots for how to get patient input into decision-making: e.g. patient engagement prompts in assessment reports and patient representation on decision-making committees. Patient engagement tool being developed as part of Innovative Licensing & Access Pathway **(from Jan 2021)**.	Patient and public engagement and involvement strategy to ensure staff engage more systematically and consider the patient and public perspective in regulatory decisions.	Number of patients engaged	**Closer engagement with patients leading to more informed decision making by them resulting in improved public health outcomes**	**NM1 Service enhancement** More involvement in decision making
				Number of patient pilot projects completed		
		Develop and introduce clear processes for engagement and involvement, to ensure teams have a systematic means of engaging and involving patients and the public in their work and that we publish how we do that. We intend to deliver and have these processes embedded across the agency by December 2022	Pool of representative patients available to provide input	Impact of patient input on decision making		**NM1 Service enhancement** Improved implementation of regulatory advice
		Establish pilot projects to bring patient input into decision making	Patients have input into decision making through the implementation of the pilot projects	Greater take-up of safety messaging	**HCP and patients react more quickly to risks and select more effective products**	
		Implement Patient and Public Involvement strategy (published Sept 21)	Patient and public involvement strategy delivered	5 key indicators in the strategy	**HCP and patients better understand messages about safe and effective use of products**	**NM1 Service enhancement** Better understanding of messaging and appropriate use and prescribing of products
		Transformation programme to develop a patient focused organisation	Engagement embedded in performance management for delegated grade staff for **2021-22.**	Staff attendance on training programme	**Improved targeting of messaging and outreach leading to an better MHRA profile**	
		Introduce new systems, processes and training to support a change in our culture, so that every member of staff considers the patient and public perspective in their decisions, and that all staff are well supported and involved in delivering that change. We aim to deliver this by December 2022	Patient focused staff objectives in place	Objectives met under staff progress reviews		
			New job descriptions and processes in place		**Patients are appropriately represented and able to input to and influence decisions**	**NM1 Service enhancement** Improved and quicker response to regulatory action and advice
			Change in the Agency culture, so that every member of staff considers the patient and public perspective in their decisions	Outcomes and analysis of survey responses and feedback		
		Annual survey to review effectiveness and impact of patient involvement in committees	Training programme and speaker programme delivered	Establishing wider pool of patient input (drawing in the right patients for the matter under consideration and representative patient views obtained)	**Patients are clear on how they are involved in decision making and how their point of view has been acted upon**	
		Following the public consultation define the Agency's patient and public engagement policy, work with the key operational teams on any necessary legislative changes to the HMRs and MDRs.	MMD Act will enable strengthened obligations on timelines on relevant decision making and patient involvement and transparency. Powers available by early 2021.	How many decisions involved patient input which was considered and actioned	**Better trust and understanding of the Agency's work**	**Patients having confidence and trust in the Regulator and the healthcare system working**
				New balance scorecard indicator for media sentiment		
		Ongoing programme of activities to raise awareness of our public protection roles.	Safer medicines consortium actions to better meet the information needs of women and healthcare professionals, through accessible, clear and consistent advice.	Positivity in response to the awareness campaign	**With raised awareness the public and HCP react more quickly to safety issues**	
			Varied awareness programme delivered including, social media campaign, patient fronted materials, accessibility and format information, partnership communications	Media monitoring including click throughs on website and social media range and reach	**Improved future awareness campaigns from analysis of areas of most impact leading to better designed outputs such as age stratification and better targeting of campaigns**	
				HCP & patient perceptions/awareness (survey) ; reduction in complaints; positive case studies		
				HCP prescribing behaviour (CPRD)		

Annex 3: IMMDSR Benefit Map 1 – Patient and Public Involvement

Annex 4: IMMDSR Benefit Map 2 – Responsive Reporting System

IMMDSR recommendation	MHRA action themes	Key activities	Key deliverables	Indicators	Potential outcomes	Benefits (short, medium, long term)
Recommendation 6: 'The Medicines and Healthcare products Regulatory Agency (MHRA) needs substantial revision particularly in relation to adverse event reporting and medical device regulation. It needs to ensure that it engages more with patients and their outcomes. It needs to raise awareness of its public protection roles and to ensure that patients have an integral role in its work.'	**Developing a more responsive, transparent and timely safety and reporting system**	Create common ways of working leading to integrated multiskilled vigilance teams across all medical products.		Improvement in Patient Safety MHRA balance scorecard indicators including adverse drug reactions, Devices – adverse incidents, Adverse blood reactions, Patient safety interventions	Better monitoring of known or potential safety issues, identification of emerging risks and assessment of effectiveness in use	**NC2 Service enhancement** Increased capacity for signal detection and assessment (value add)
		Procure and implement a common improved technology platform for incident management and signal detection, implemented by April 2021.	A new SafetyConnect vigilance service in place and new IT systems in use to report, detect and respond to safety signals more quickly and comprehensively.			
		Design and implement improvements to the engagement platform for vigilance reporting, improving the customer experience and feedback.		Number of reported safety incidents. (Yellow Card data, PSURs, studies etc.) Baseline OBC 2020: Manufacturers - Med = 11,799, Dev = 15,199 Healthcare professionals Med = 23,222, Dev = 5375 Patients Med = 6863, Dev = 1116	Higher levels of reporting	**NC2 Service enhancement** Earlier signal detection and improved safety interventions will result in improved patient safety and wider social economic benefits.
		Subject to approval, plan a long-term campaign **for 2021-22** and undertake engaging with the public directly through user needs sessions.	Increase awareness of the Yellow Card Scheme			
		Development and roll out of a series of Application Programme Interfaces (APIs) which will enable easy connectivity and interaction with third party systems and sites to the Yellow Card System	Enhancement of the Yellow Card APIs will enable data collected to be transferred directly to the patient record to support clinical decision making, and also safety messages from the MHRA to be made available to patients and healthcare professionals from within the NHS App and clinical systems delivering a fully integrated vigilance system.	Improved quality of safety reports leading to quicker signal detection	Reporting system felt to be more user friendly and responsive by stakeholders	**NC2 Service enhancement** Increased user satisfaction of the Yellow Card website and apps
				HCP & patient perceptions/awareness (survey); reduction in complaints; positive case studies		
		National Patient Safety Alert Credentialing (CAS) our accreditation is up for review in Q1 of 2023.	Continued accreditation	Indicators are the evaluation/feedback on alert resolution (measured by CAS)	Timely safety actions by the healthcare system to protect patients	

Safer and more effective use of medical products

↓ Reduce preventable harm to patients

↓ Reduce the number of **disability-adjusted life years (DALY) lost**

↓ Reduce cost to UK healthcare system caused by preventable adverse events

IMMDSR recommendation

Recommendation 6:

'The Medicines and Healthcare products Regulatory Agency (MHRA) needs substantial revision particularly in relation to adverse event reporting and medical device regulation. It needs to ensure that it engages more with patients and their outcomes. It needs to raise awareness of its public protection roles and to ensure that patients have an integral role in its work.'

MHRA action themes

- **Improve evidence for patient safety**
- **Improving medical device regulation**
- **Identifying and managing risk for medicines used in pregnancy**
- **Improving evidence generation for safety surveillance**

Key activities

- Register all devices (by January 2022) and develop a publicly accessible registration system.
- Seek Ministerial agreement for priorities and staged implementation (July 2021). Seek ministerial agreement on new policies (Spring 2022). New legislation to be laid & debated (Summer 2022).
- Link Yellow Card System to NHSD mesh registry to achieve 4th pause condition: when a clinician inputs a revision in the registry they are directed to the YC page to report the revision.
- Use powers to establish a statutory advisory committee for expert advice on devices safety and performance. This will need further policy development and an update to the MMD Act.
- Publish Public consultation (Sept -Nov 2021)
  Analysis and drafting of response (Nov -Jan 2022)
- Enhance data collected about device safety events in MIR form
- Valproate: seek and implement further advice from CHM on new regulatory measures (**Feb 2021**); publish review of AED **in Jan 2021**; establish a registry to monitor use and drive compliance, first phase by **Jan 2021**. Next steps will be to expand the registry to cover the DAs; contraindicate valproate in women not enrolled in the registry; and to use provisions to expand registries to cover all AEDs and other medicines requiring long-term monitoring
- Updated risk minimisation approach for key teratogens: a review of products and current restrictions **Q1 2021**; early patient and stakeholder consultation to define 'major teratogen'- **Q2/3 2021**; develop guidance on risk minimisation and communication with independent patient input and expert advice - **Q4 2021;** develop new risk minimisation materials, if needed - **Q1 2022;** MAHs updating materials - from **Q1 2022;** and product specific comms - **from Q2 2022.**
- CHM EWG on Optimising Data on Medicines used during Pregnancy' report on improving data collection, quality and access via enhanced capture of information and linkage of databases. Published **in Jan 2021;** recommendations on other priority data sources and linkages
- Priority datasets and linkages MHRA will be developed, focusing on:
  - CPRD Aurum Pregnancy Register (PR), CPRD Aurum Mother Baby Link (MBL). Planning for linkage to community dispensing data.
  - National Congenital Anomalies and Rare Disease Registry Service (NCARDRS) linkage to CPRD
  - Linkage of community dispensing data to CPRD data

Key deliverables

- The MMD Act provides powers to establish a publicly accessible Information System for all implants. This registration system will then feed into the MDIS which is owned by NHSD and these are the patient-identifiable registries.
- New medical device statutory framework in place.
  New legislation to be laid after assent**.** Legislative changes for future system to come into effect before **June 2023** (end of standstill period).
- Statutory advisory committee for expert advice on devices safety and performance established.
- Device safety events are linked to manufacturer
- Valporate registry established to monitor use and drive compliance
- Data on total prescription available for use
- Clear communication and tools to manage and mitigate risks for key tertogens in place
- Evidence generation using linked data
- Developed data linkages between CPRD Aurum PR and MBL
- Linked CPRD and NCARDRS and community dispensing data developed

Indicators

- HCP & patient perceptions (survey) / positive case studies
- Number of reported safety incidents. (Yellow Card data, PSURs, studies etc.)
- Number of linked device safety event reports received
- Number of patients engaged
- Number of adverse incidents reported
- Full list of authorised drugs with recognised teratogenic potential. Guidance on risk minimisation measures appropriate to the level of risk developed with relevant stakeholders. New risk minimisation materials where appropriate and number of MAs updated. Evidence of reduced inappropriate prescribing in the longer term.
- Data from registry showing a reduction in number of females of child bearing age prescribed valproate and number of exposed pregnancies
- HCP & patient perceptions/awareness (survey)
- Combined CPRD and NCARDRS and community dispensing data available for analysis

Potential outcomes

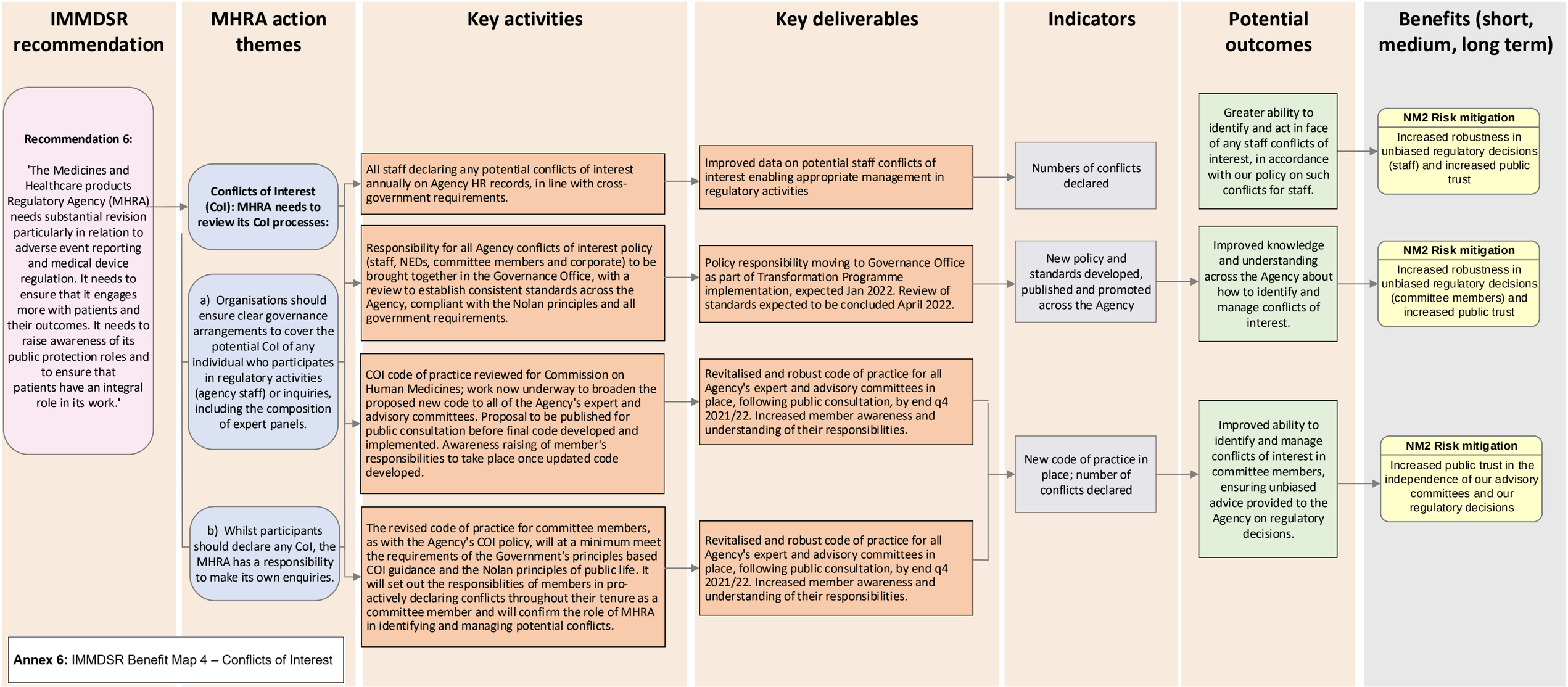
- **Safer innovative products available earlier**
- **Devices on the market are used in the safest and most effective way**
- **Patients have confidence and trust in the regulatory system**
- **Better traceability of devices**
- **New medical devices framework**
- **Medicines used during pregnancy and breastfeeding are safer**
- **Rapid reduction and eventual elimination of valproate (and other teratogens) use**
- **Greater awareness of teratogenic potential of certain medicines and reduction in their prescribing.**
- **More optimised use of data – better monitoring of known or new risks**
- **Prescribing safety indicator reports for GPs to enable case review**
- **Quality improvement programme.**
- **Data available for use by MHRA epidemiology team and wider research community**
- **Evidence based information on these data eg research publications, safety reports**
- **Greater signal generation**

Benefits (short, medium, long term)

- **NM1 Service Enhancement** — Increase in public trust
- **NM3 Public Health** — Better informed final medical devices
- **NM3 Public Health** — Improved accountability for medical device manufacturers
- **NM3 Public Health** — Reduce and minimise preventable harm for sodium valproate
- **NM3 Public Health** — Reduction in number of children exposed to valproate in utero
- **NM3 Public Health** — Improved information on medicines used in pregnancy
- **NM3 Public Health** — Improved decision-making with regards to medicines used in secondary care
- **NM3 Public Health** — Quality Improvement programme
- **NM3 Public Health** — Improving the ability to impact on individual patient care – connect decisions to an individual patient care for impact where a risk has been identified
- **NM1 Service Enhancement** — Having access to data for more robust evidence generation
- **NM1 Service Enhancement** — Early signal detection leading to early regulatory interventions

- **Early intervention for safety concerns**
- **Safer and more effective use of medical products**
- **↓ Reduce preventable harm to patients**

Annex 5: IMMDSR Benefit Map 3 – Improving Evidence


IMMDSR recommendation
MHRA action themes
Key activities
Key deliverables
Indicators
Potential outcomes
Benefits (short, medium, long term)
Recommendation 6:
'The Medicines and Healthcare products Regulatory Agency (MHRA) needs substantial revision particularly in relation to adverse event reporting and medical device regulation. It needs to ensure that it engages more with patients and their outcomes. It needs to raise awareness of its public protection roles and to ensure that patients have an integral role in its work.'
Conflicts of Interest (CoI): MHRA needs to review its CoI processes:
a) Organisations should ensure clear governance arrangements to cover the potential CoI of any individual who participates in regulatory activities (agency staff) or inquiries, including the composition of expert panels.
b) Whilst participants should declare any CoI, the MHRA has a responsibility to make its own enquiries.
All staff declaring any potential conflicts of interest annually on Agency HR records, in line with cross-government requirements.
Responsibility for all Agency conflicts of interest policy (staff, NEDs, committee members and corporate) to be brought together in the Governance Office, with a review to establish consistent standards across the Agency, compliant with the Nolan principles and all government requirements.
COI code of practice reviewed for Commission on Human Medicines; work now underway to broaden the proposed new code to all of the Agency's expert and advisory committees. Proposal to be published for public consultation before final code developed and implemented. Awareness raising of member's responsibilities to take place once updated code developed.
The revised code of practice for committee members, as with the Agency's COI policy, will at a minimum meet the requirements of the Government's principles based COI guidance and the Nolan principles of public life. It will set out the responsiblities of members in pro-actively declaring conflicts throughout their tenure as a committee member and will confirm the role of MHRA in identifying and managing potential conflicts.
Improved data on potential staff conflicts of interest enabling appropriate management in regulatory activities
Policy responsibility moving to Governance Office as part of Transformation Programme implementation, expected Jan 2022. Review of standards expected to be concluded April 2022.
Revitalised and robust code of practice for all Agency's expert and advisory committees in place, following public consultation, by end q4 2021/22. Increased member awareness and understanding of their responsibilities.
Revitalised and robust code of practice for all Agency's expert and advisory committees in place, following public consultation, by end q4 2021/22. Increased member awareness and understanding of their responsibilities.
Numbers of conflicts declared
New policy and standards developed, published and promoted across the Agency
New code of practice in place; number of conflicts declared
Greater ability to identify and act in face of any staff conflicts of interest, in accordance with our policy on such conflicts for staff.
Improved knowledge and understanding across the Agency about how to identify and manage conflicts of interest.
Improved ability to identify and manage conflicts of interest in committee members, ensuring unbiased advice provided to the Agency on regulatory decisions.
NM2 Risk mitigation
Increased robustness in unbiased regulatory decisions (staff) and increased public trust
NM2 Risk mitigation
Increased robustness in unbiased regulatory decisions (committee members) and increased public trust
NM2 Risk mitigation
Increased public trust in the independence of our advisory committees and our regulatory decisions
Annex 6: IMMDSR Benefit Map 4 – Conflicts of Interest

Medicines & Healthcare products Regulatory Agency

BOARD MEETING HELD IN PUBLIC

18th January 2022

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 The sixth meeting of the Patient Safety and Engagement Committee (PSEC) was held mid-December. The two main issues on the agenda were the public consultation on the medical devices' legislation and how the outcomes and progress from the Independent Medicines and Medical Devices Safety Review (Cumberlege Review) will be measured. The board can be assured both areas are progressing.

1.2 The Committee was given an update on the Isotretinoin review and had feedback from one of the Committee's patient representatives on recent meetings with NICE and Health Technology Wales. The Committee also reviewed and revised the PSEC Terms of Reference and the 2022 work programme. The revised Terms of Reference are presented to the board in a separate paper.

2. Introduction

2.1 The sixth full meeting of PSEC was held on the 10th December 2021.

3. PSEC discussed each of the following items at the meeting on the 10th December 2021;

Detail on the medical device regulation consultation, can PSEC be assured that the public are being engaged with properly?

3.1 Before the public consultation on the new legislation affecting medical devices, a meeting was held with the MHRA's Patient Group Consultative Forum (PGCF) to determine how patients could be engaged in the process to review medical devices regulations. This led to a survey issued to the PGCF, British Heart Foundation Heart Voices Group, and the wider public via MHRA social media. 200 responses were received, and the Committee received an early summary of themes arising from these responses. A range of channels were used to reach people including advertising through Facebook. Supportive guidance documents were provided to explain technical information. Formats included pictures. A webinar was held, and the consultation was also promoted through cross Agency networks.

3.2 The Committee discussed several areas raised including underrepresented groups such as the digitally excluded. Also, how to work with other organisations in reaching patients and the public through joint work. With the need to continually consult on a variety of developing areas this might encourage a more sustainable way of working. It noted that there is a plan for consultation to be on-going with patients and the public through focus groups on devices legislation. The Committee suggested that focus groups targeting specific classes of devices might elicit useful input.

3.3 Some key themes emerging from consultation responses triggered debate, for instance whether patient and public involvement should be part of the legislation or instead supported in guidance. The discussion centred on the flexibility of legislation that might have to be in place for many years. Some of the reasons therefore not to have it in legislation included engagement processes might change, or even make it hard for the MHRA to implement if companies are unable to comply.

How are the outcomes and progress of the short, medium and long-term deliverables from the Cumberlege Review being measured?

3.4 PSEC has regular updates on the short-, medium- and long-term deliverables of the Cumberlege Review before it is presented to the Board. This allows the Committee to spend more time interrogating information arising from the implementation of the Cumberlege recommendations. The Committee is particularly interested in the outcomes of strategies to implement the recommendations. There are many areas that have had to change due to the recommendations of the Cumberlege Review and it is important that there are actions leading to effective ways of working that protect the public. A benefit map was presented that detailed activities, key deliverables, indicators, potential outcomes, and benefits.

3.5 The committee reviewed how the map would work, the need for qualitative as well as quantitative data, what targets were missing and what would be the success factors. Other issues included ensuring an iterative process, and the need to work with partners or independent organisations to evaluate what was working. The Committee discussed the impact of patient input on decision-making through the whole life cycle of medicines and devices and welcomed the work on the benefits map. It was still in development in terms of measures and metrics, early indicators, the outcomes that should be expected and other areas. However, it tried to capture the Cumberlege deliverables in a comprehensive and detailed manner against timelines.

Reviewing the Terms of Reference and proposed work programme for 2022

3.6 The Terms of Reference for the Patient Engagement and Safety Committee were last reviewed in January 2021. An annual review is part of these terms of reference. Although it was not proposed that the purpose and responsibilities of the Committee change the way its responsibilities were set out were re-worded to make the section clearer. It is still the intention that the Committee provide scrutiny, challenge, assurance, and guidance. The Committee will now meet quarterly instead of bimonthly. However, it will have the powers to comment on issues via email exchange, or schedule extra meetings. The Committee agreed that a patient representative will form part of the quorum.

3.7 The work programme scheduled topics on patient safety and patient and public engagement for the next year. Some areas already considered at earlier meetings would be returning to the Committee so that progress could be monitored, other topics would be new. The Committee were reminded that the work programme needed to be flexible enough so that areas of interest could be added if needed during the year.

Isotretinoin Review

3.8 The Committee were given an oral update on the plans for the publication of the Isotretinoin review.

Feedback from meeting other health organisations on patient and public involvement

3.9 Feedback was given by one of the patient representatives from meetings with NICE and Health Technology Wales on their approach to patient and public involvement. The Committee discussed the progress on patient and public involvement in the MHRA, the increase in resources that will happen to enable this, and comparison with other healthcare organisations. It was acknowledged that there was some way to go given the ambition of the organisation. The Committee will continue to scrutinise and seek assurance for the board that timely progress is being made.

Public consultations

3.10 The committee will be informed via email of public consultations before they are issued. This action will be implemented from the end of January 2022.

4. Conclusion

4.1 The meeting considered two substantial papers: the public consultation on the medical devices' legislation, and the benefits map for the Cumberlege Deliverables. The Committee were assured that these areas were progressing. The Committee approved, with one amendment, the proposed changes to the Terms of Reference and Work Programme. An update was given on the logistics for the Isotretinoin review publication. The Committee has not seen the report.

Mercy Jeyasingham
Chair Patient Safety and Engagement Committee
Non-Executive Director MHRA
January 2022

Medicines & Healthcare products Regulatory Agency

BOARD MEETING HELD IN PUBLIC

18 January 2022

Title	What are the updated Terms of Reference for the Patient Safety & Engagement Committee?
Board Sponsor	Mercy Jeyasingham
Purpose of Paper	Approval

What are the updated Terms of Reference for the Patient Safety & Engagement Committee?

1. Executive Summary

1.1 The Terms of Reference for the Patient Safety and Engagement Committee (PSEC) were reviewed and updated at the PSEC meeting held in December 2021. The updates to the Terms of Reference include amendments mainly to the wording, and the provision of flexibility to the frequency of meetings in extraordinary circumstances.

The Board is asked to comment and approve the updated Terms of Reference.

2. Introduction

2.1 The Terms of Reference for the PSEC were last reviewed in January 2021 when the Committee was established. An annual review is part of these terms and therefore the Terms of Reference were reviewed at the meeting of the PSEC held on the 10th December 2021.

3. Reviewing the Terms of Reference

3.1 The Terms of Reference have substantially stayed the same. The purpose has not been changed, but subsection 2.5 of the Responsibilities section, has been re-ordered and re-worded. This is to ensure that the remit of the Committee is to scrutinise, review risk, assure, guide and challenge. The two bullet points that that been re-worded are:

i) “Scrutinise the processes, systems and structures within the Agency to ensure patient safety is paramount in regulation” which has been changed to “Provide guidance and input into the development of strategies, including maximising the methods used by the Agency to engage with patients and the public”; and

ii) “Consider ways in which engagement with patients and the public can be maximised and their concepts of risk and benefit can be incorporated into regulatory decision making” which has been changed to “Seek assurance that the public/patient perception and concepts of risk and benefit can be incorporated into regulatory decision-making”.

These changes with the other bullet points under Section 2.5 provide greater clarity on responsibilities and builds on the experience of operating the Committee for almost a year.

3.2 Other changes include mandating a lay representative as part of the quorum, as well as changing the meeting frequency to quarterly. Meeting quarterly will bring the Committee in line with the changes agreed at the September 2021 Board meeting concerning governance. Due to less frequent meetings some flexibility is needed on how business can be conducted outside scheduled meetings. Therefore, the ability to ratify decisions via correspondence and conduct business through correspondence or extraordinary meetings have been added to subsection 5.3 under Quorum, and 6.1 under Frequency of Meetings respectively.

3.3 *Please see Annex 1 for the updated Terms of Reference.*

4. Conclusion

4.1 The updated Terms of Reference clarify the responsibilities of the Committee, add a lay representative to the quorum and ensure flexibility of conducting meetings outside quarterly meetings.

Mercy Jeyasingham
Chair Patient Safety and Engagement Committee
Non-Executive Director MHRA
January 2022

Annex 1.

Medicines and Healthcare products Regulatory Agency

Patient Safety and Engagement Committee

Terms of Reference

1. Purpose

1.1. The purpose of the Patient Safety and Engagement Committee is to provide independent consideration of patient safety and patient engagement, such that these are paramount in decision-making at the Medicines and Healthcare products Regulatory Agency (MHRA), and to advise the Board accordingly.

2. Responsibility

2.1. The Committee is responsible for monitoring and advising the Board on aspects of patient safety in the Agency's procedures for its initial assessments of medicines, medical devices and blood products, the continued surveillance of their use, and its processes for dealing with information derived from surveillance such that:

i. Patient safety is the primary priority.

ii. There is a culture of continuous, iterative improvement.

2.2. The Committee has the responsibility to consider, and advise the Board on aspects of the ways in which the Agency engages with patients and with the public, such that:

i. Patient views are consistently considered in regulatory decision-making

ii. The Agency is responsive to the needs of patients and their concepts of risks and benefits, in its consideration of patient safety.

iii. Processes are in place to encourage the acquisition and analysis of, and decision-making based on information from patients/the public at all stages of the Agency's regulation of medicines, medical devices and blood products. As well as informing patients and the public of the associated outcomes.

2.3. Make recommendations to the Audit and Risk Assurance Committee concerning the internal audit programme, to the extent that it applies to matters within this ToR.

2.4. Periodically review its own effectiveness and report the results to the Board.

2.5. To meet these responsibilities the Committee will:

- Scrutinise the processes, systems and structures within the Agency to ensure that patient and public engagement is utilised throughout regulation – including the initial assessment of medicines, medical devices and blood products, surveillance of their use, and decisions made as a result of possible safety signals.
- Review the Risk Register regarding patient safety, patient and public engagement, and report concerns to ARAC.
- Provide assurance to the Board that the Agency has appropriate procedures in place for preventing, detecting and addressing any safety or quality issues with medicines, medical devices or blood products, in the interests of patient safety.
- Seek assurance that the public/patient perception and concepts of risk and benefit can be incorporated into regulatory decision-making.
- Provide guidance and input into the development of strategies, including maximising the methods used by the Agency to engage with patients and the public.
- Provide challenge to the Executive on aspects of the regulatory systems that could be modified to improve patient safety and patient engagement.

2.6. In order to meet its duties and responsibilities the Committee is authorised by the Board to:

- Seek any information it requires from any MHRA employee.
- Obtain outside legal or other professional advice if required.

3. Transparency

3.1. Following each Committee meeting, and at the next appropriate meeting of the Board, the Committee will formally report to the Board on the assurance it can provide on the effectiveness of patient safety as well as patient and public engagement.

4. Membership

4.1. The Committee will comprise a minimum of three Non-Executive Directors of the MHRA, one of whom will be appointed as Chair of the Committee. Three Executive Directors will also be members of this committee and are expected to attend all committee meetings:

- Chief Scientific Officer
- Chief Safety Officer
- Chief Quality and Access Officer

4.2. Regular invited attendees include non-voting members and two lay members.

4.3. The Committee will appoint independent representatives (lay members) who will hold non-voting positions on the Committee, to supplement its range of skills and experience. Two lay members will be appointed in line with the recruitment principles of the Agency's Expert Committees.

4.4. The Committee will operate in accordance with the unitary status of the Agency Board by taking a collaborative approach, utilising constructive challenge, to fulfil the purpose and responsibilities set out above.

4.5. The independence of the Committee will be further maintained by the Non- Executive Chair having a casting vote where consensus cannot be reached, and a vote is required. Before a decision to move to a vote is made, the Chair will in all cases consider whether continuing the discussion at a subsequent meeting is likely to lead to a consensus.

4.6. Committee members shall comply with the Committee's Terms of Reference, which set out the scope of the Committee's work and its authority.

4.7. Other directors and staff shall be invited at the discretion of the Committee when matters relating to their areas of responsibility are being discussed.

5. Quorum

5.1. The quorum of the committee will be five members, including at least two Non-Executive members, at least two Executive members and at least one lay member

5.2. Deputies will only be permitted in exceptional circumstances, with prior, written agreement from the Chair. When appointed, deputies will have the same Committee rights and responsibilities as non-deputies.

5.3. If a meeting is not quorate it may still proceed, with agreement from a majority of Committee members (including those not in attendance). In such circumstances, any decisions made will be non-binding and will require subsequent ratification, however decisions may be ratified by correspondence. If any members are not content to ratify through correspondence or on the basis of the minutes, this may trigger a further discussion in the next following meeting or in extraordinary circumstances, a short extraordinary meeting may be held.

5.4. A decision put to a vote at a quorate Committee meeting will be determined by a simple majority of voting members and deputies present. In the case of an equal vote, the Chair of the Committee at that meeting will cast a second, deciding vote.

6. Frequency of Meetings

6.1. The Committee will meet quarterly and otherwise, with the flexibility to discuss matters arising via correspondence or extraordinary meetings as the Chair of the Committee deems necessary.

7. Secretariat

7.1. The Committee Secretariat will be responsible for:

- Preparing the agenda in consultation with the Chair;
- Commissioning Committee papers;

- Circulating Committee papers to members and invitees, normally five working days before each meeting;
- Documenting the outcome of all votes taken in the Committee meeting minutes;
- Producing and circulating draft minutes of the Committee meetings to members, normally ten working days after each meeting; And
- Maintaining an action log.

8. Minutes

8.1. Minutes of the meeting will be taken by the Committee secretariat and circulated after to the meeting attendees for consideration and comment, to be officially ratified at the following meeting.

9. Review of Terms of Reference

9.1. The Committee will review its ToR at least annually. Amendments to the Terms of Reference will be subject to review and approval by the Board.

Updated: 20 December 2021

Medicines & Healthcare products Regulatory Agency

BOARD MEETING HELD IN PUBLIC

18 January 2022

Title	"What are the strategic priorities for the regulation of AI as a Medical Device and how can this be developed effectively?"
Board Sponsor	Laura Squire
Purpose of Paper	Strategic Direction

What are the strategic priorities for the regulation of AI as a Medical Device and how can this be developed effectively?

1. Executive Summary

1.1. Following the departure from the European Union, the Medicines and Healthcare products Regulatory Agency (MHRA) has become a sovereign regulator. One of the freedoms that come with this is the ability to reform medical device regulation to ensure it better fits software and artificial intelligence (AI). MHRA have embarked upon an ambitious Software and AI as a Medical Device Change Programme to achieve just that, reforming medical device regulation as it applies to software and AI before July 2023.

1.2. Our vision is that we will have streamlined regulation of software and AI, a system that encourages responsible innovation, provides swift market access to the products patients need and means patients and healthcare professionals can trust that the digital health technology they use.

1.3. This paper outlines: the key benefits as well as challenges that AI as a medical device (AIaMD) can pose over and above other software, the principles and pillars that underpin MHRA's AIaMD reform programme, a summary indication of what gaps were identified that the programme intends to fill; broad details of the three work packages for AIaMD, and finally an indication of how these work packages will be delivered.

1.4. The MHRA has an opportunity to become a global leader in the regulation of AIaMD and to demonstrate the Agency's capacity to support responsible innovation whilst minimising risk to patients and public. The MHRA's strategic priorities for the regulation of AIaMD and how this regulation can be developed effectively are described in detail in this paper, but can be distilled into the following priorities:

1.4.1. Signal and strengthen best practice development and deployment methods for AIaMD to protect patients and ensure manufacturers have robust products.

1.4.2. Grasp the challenges that AIaMD can provide over and above Software as a Medical Device (SaMD) and respond to these challenges in a proportionate way, crafting processes that work for AIaMD.

1.4.3. Find and amplify the patient voice and provide meaningful opportunities for industry to provide feedback into the development of this new regulatory framework.

1.4.4. Work across government to provide a 'joined-up offer' to market, aligning where possible and where distinct requirements must remain, demystify the process.

1.4.5. Drive international harmonisation, working with key international partners to align requirements and drive state of the art for AIaMD.

1.5. The Board are asked to consider these plans, the progress to date, and recommend any other areas for development.

2. Introduction[1]

2.1. The regulation of AIaMD fits squarely within and across the MHRA's Delivery Plan 2021-2023. The strategy outlined meets the core goals of this plan for AIaMD in particular:

2.1.1. **Enabling innovation** by making the route for developing these devices clear; and
2.1.2. Reforming the path from **innovation** to **access** to make it smooth; and
2.1.3. Ensuring that AIaMD and the wider **safety** system is appropriately evidenced, minimising risk to patients.

2.2. The commitment is to approach this by putting patients at the centre of the regulation of AIaMD and to work collaboratively with key stakeholders to deliver on these goals. Whilst these are common goals for regulation of all medical products, the approach for AIaMD needs to be adapted to address some challenges unique to this area (e.g. interpretability, evidence, and adaptivity) which are cut across innovation, access and safety. If we grasp these challenges, we sharpen wider reforms underway for medical devices / IVDs and SaMD, making them fit for purpose for AI, thereby delivering upon the Agency's ambitions for AIaMD specifically.

2.3. With some simplification, AIaMD (and AI in a medical device) is just AI that has a 'medical purpose.' Mostly commonly, this medical purpose will be in the realm of diagnosis, prognosis, treatment, or monitoring of disease or injury.[2] Tentative market surveys indicate that approximately 80 percent of the UK market in AI for health and social care is directed toward diagnostics or triaging. For the near-term, much of the AIaMD market is assistive, augmenting rather than wholly replacing the judgment of patients or healthcare professionals.

2.4. The proper definition of 'AI' is highly contested. Nevertheless, the International Medical Device Regulators' Forum (IMDRF) recently proposed the following description: "Artificial Intelligence (AI) is a branch of computer science, statistics, and engineering that uses algorithms or models to perform tasks and exhibit behaviours such as learning, making decisions and making predictions. The subset of AI known as Machine Learning (ML) allows computer algorithms to learn through data, without being explicitly programmed, to perform a task."

2.5. AI promises to deliver tangible benefits across health and social care for patients and public. The breadth of applications of AI is already staggering, with many different examples across screening, early diagnosis, prognosis, through to treatment and management of chronic conditions. If you take any major disease, you will likely find a host of AI tools across that spectrum of applications that work toward predicting, diagnosing, treating, and managing conditions better than the current standard of care. For instance, consider just ophthalmology.

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[1] N.B. I have used examples to illustrate particular points, concepts, or issues throughout – these are illustrative but draw from MHRA's experience.
[2] N.B. This is highly simplified a more detailed explanation on what will qualify as a medical device or IVD software can be found in MHRA guidance.

There are many use cases across the patient pathway from screening, to early diagnosis, through to prognosis, and management of chronic conditions across many major conditions such as glaucoma, age-related macular degeneration, and diabetic retinopathy.[3] Broadly, these use cases all work toward the goal of preventing conditions from ever arising, diagnosing them earlier if they do arise, and effectively treating or managing to meaningfully impact patient care. The challenge now is translational, to ensure promising models fit the real world, function well in clinical settings, making the leap from 'promising to proven.'

2.6. AIaMD can (but does not always) pose challenges for medical device regulation over and above classically programmed software and other medical devices, namely:

2.6.1. **Interpretability of AIaMD** – because AI learns relationships from data, the model produced may be too complex to be interpretable to humans or the relationships the model has learned may be hidden. There are methods to render models at least somewhat interpretable (but these come with their own difficulties) and there are some machine learning methods that are out-of-the-box interpretable to humans. To contextualise and provide an example: depending on the model used, some AI triaging models will be unable to describe precisely why a particular patient was triaged in the way they were. This can impact how users - whether they be healthcare professionals or patients – interact with the device, how it may influence clinical judgment, and our ability to understand whether outcomes were correct or not.

2.6.2. **Evidencing AIaMD** – connected to the last issue, evidencing AIaMD can be more challenging versus classically programmed software. This can be for a variety of reasons; some reasons include:

2.6.2.1. It is difficult to link to scientific or clinical evidence if you do not know what the model finds significant.[4] Generating sufficient evidence for these devices often relies more heavily on validation or testing of the model. This means that we may often not properly understand the performance of a model until it is deployed into populations and generates real world evidence.

2.6.2.2. AI models are trained on data, if the training or validation datasets do not reflect the real world to begin with or if that data becomes stale, the performance of that model will likely dip. Behind this performance drop is the very real risk of patient harm, for example, this can translate to:

a Models to predict sepsis failing to generalise from one hospital to another because the model fit one hospital like a glove but not the other.
b Models to detect skin lesions of concern performing less well in populations of patients with darker skin due to a skew in the training set.
c Image segmentation models failing to perform well across different imaging equipment or different populations where the quality of images differs.

[3] Wang et al, Artificial Intelligence and Deep Learning in Ophthalmology
[4] To state more precisely: know in enough granular detail.

2.6.2.3. It can difficult to claim equivalence between two AI models when bringing these devices to market, as they are typically trained on different datasets with different parameters. This means the most common route to bring a medical device to market provides significant safety issues and may be unavailable for a lot of AIaMD.

2.6.3. **Adaptivity of AIaMD** – because AI learns relationships from data, it can also relearn those relationships. This retraining adjusts the parameters of the model itself, changing the performance of the model.[5] It is important to note that not all AI is adaptive, that there are risks to having a static model, and there are methods to update models in a gated, controlled fashion. Additionally, some kinds of AI can be fragile, meaning a small change in training data can cause a large change in performance. This means a retrained model may have completely different performance characteristics to the previous iteration. This could be good news, as perhaps the iteration has improved performance, or, it could be bad news, meaning the model no longer performs appropriately, a patient safety risk then emerging.

2.7. Working across MHRA and wider government, Software Group are reshaping medical device regulation to meet these challenges but also ensure that the UK has a regulatory system that is proportionate, streamlined, and is one that encourages responsible innovation. This work underpins many different government and wider public sector strategies. For instance, the Life Sciences Vision charges MHRA with delivering "the world's leading regulatory model for digital health products." This work on AIaMD will be a key part of answering that call, also meeting the challenge of many other challenges such as the ask to have "clear and understandable AI regulation" in the Data Saves Lives Strategy.

2.8. Fundamentally, if we are to have a jurisdiction that supports development to deployment and provides a high degree of assurance that any given AIaMD is robust and appropriately evidenced, we must address the unique challenges that AI can pose, namely: interpretability, evidencing AI, and adaptivity. For instance, clarity on how the human uninterpretability of some AIaMD fits with medical device requirements is core not only to the development and evidence generation of these devices but also to how these devices access the market, and finally indispensable to understanding the risks the device might pose. It is also important to recognise that work on AIaMD in particular is necessary but not sufficient to meet the ambitions of the MHRA's Delivery plan 2021-2023. That is, this plan is built upon wider reforms in medical devices / IVDs and SaMD more broadly. For example, work on innovative routes to market for medical devices / IVDs is underway and on SaMD in particular. The task for AIaMD is not necessarily to craft a wholly separate method for market entry but ensure the path for SaMD effectively addresses the core challenges that AIaMD can pose.

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[5] To illustrate the difference between classically programmed models and AI models, consider two weather prediction models. First, a model that has variables such as barometric pressure, temperature, and humidity and a weighting between those variables that then calculates some output prediction for the weather. Data on each of those variables is updated on an hourly basis but the weighting between those variables does not change unless the meteorologist manually adjusts the model itself. Second, an AI model that incorporates the same variables but uses last week's variable data and then the actual state of the weather recorded to retrain the model, thereby changing the weighting between the variables of the models and its performance. These examples illustrate the difference between merely updating input data versus retraining models but also underline the importance of ensuring training data is of quality; garbage in garbage out.

2.9. This paper sets these plans into the context of wider reforms to medical device regulation and reform to SaMD more generally, providing detail on the specific work packages directed at AIaMD.

3. Principles and pillars that underpin this reform

3.1. Software Group developed a number of principles to guide this reform process, these principles inform the work packages and potential change to the regulatory framework. These principles include:

3.1.1. **Software as a medical device (SaMD) is foundational** – if the regulation of AIaMD is to be placed on firm foundations, we must get the regulation of SaMD right first. AIaMD can pose novel challenges over and above SaMD but many current issues are not unique to AIaMD but common to SaMD generally.

3.1.2. **AI exceptionalism** – we must address the challenges that AI can present but not paint all AIaMD with the same brush. Proportionate regulation of AIaMD requires us to realise that AI can be uninterpretable to humans but it may not be, that AI can be adaptive but it can also be static, and so on.

3.1.3. **Lead but not depart –** we seek to advance the state of the art in regulating AIaMD and demonstrate the UK's unique selling point for AI in health and social care but also ensure that our jurisdiction is harmonised and accelerating international consensus in this area. It is anticipated that the UK's unique selling point for AIaMD will be as a proving ground, with joined up access to data, a clear path to market, and the support to encourage responsible innovation.

3.2. These principles underpin the five central pillars of our approach and how we will work across the Agency to achieve our aims:

3.2.1. **Patient Voice –** The regulation of AIaMD should not be a technocratic exercise, patients and public must be at the heart of the conversation. MHRA must not only produce documents that are technically detailed for manufacturers adept at navigating medical device regulation but also produce accessible digests for developers new to the sector and outputs that speak to patient concerns and priorities.

3.2.2. **Unlocking Innovation** – We will work across the Agency and with external partners to ensure innovation in AIaMD is supported, the path from development to deployment being clear and work to ensure that the safety of devices is considered at the outset and by design.

3.2.3. **Turning Innovation into Access** – The route to market for AIaMD will be transparent, joined up with other parts of the system, and supported by robust guidance to facilitate access to AIaMD. To support an innovative market, MHRA itself must innovate, for example by crafting streamlined regulatory processes that work for SaMD and AIaMD,

making expectations clear via the judicious use of Target Product Profiles, and exploration of how techniques such as synthetic data might be mobilised to provide further confidence that AIaMD is safe and effective.

3.2.4. **Effective and responsive safety mechanisms** – Access to innovation requires MHRA to have a surveillance and risk management system that identifies and minimises the risk that AIaMD can pose; a system that is responsive when concerns have been identified.

3.2.5. **Collaboration through Partnerships** – Software Group cannot reform AIaMD working in isolation, we must continue to work with key academic, industry, and wider government partners, but also seek to coordinate some of this work as it applies to AIaMD. This includes international cooperation and joint-working wherever possible.

3.3. These principles and pillars represent the core commitments of the MHRA as outlined in the Delivery Plan 2021-2023 and are embedded in the below work packages and supporting wider reforms.

3.4. With respect to collaborations, Software Group have identified over 35 substantive collaborations on SaMD and AIaMD across: MHRA itself, international bodies as well fellow regulators, across government, and a number of non-governmental national initiatives. To highlight just a small number of these partnerships:

3.4.1. Working as One Agency to get the regulation of software and AI right and share key learnings across MHRA.
3.4.2. Working with key international bodies such as the International Medical Device Regulators' Forum, key international partners such as the FDA, and core standards setting organisations to advance the state of the art for AIaMD.
3.4.3. Working across government to ensure the UK provides a 'joined up offer' to the global market of AIaMD. Given this, we will continue to be a core part of the Multi Agency Advisory Service and work closely with key partners, for instance, NHSX, the National Institute for Health and Care Excellence, the Health Research Authority, the Care Quality Commission, and NHS Digital, as well as wider government such as the Office for AI.
3.4.4. Working with core academic, industry, and third sector bodies to support projects that advance the start of the art for SaMD and AIaMD, drawing these conclusions into how we should best regulate these devices.

4. What's needed?

4.1. At the end of 2020, MHRA's Software Group conducted a regulatory appraisal of medical device regulation as it applies to software and AI across the product lifecycle. This process identified current issues and pain points with the current regulation as well as common challenges in the SaMD/AIaMD market. The Group triaged these issues, considered solutions from other jurisdictions, bodies, and sectors against the impact these solutions would have on the market.

4.2. We sought to answer the question: what's missing to provide further confidence that AIaMD is safe, effective, and that the UK public have access to innovative technology that meets a clinical need? Broadly, we found:

4.2.1. That decent legislative footholds already exist for most of the issues that were identified; and
4.2.2. That the majority of medical device methods, principles, and requirements remain sound for AIaMD.

4.3. However, we also found that there were gaps, even if much of the legislative framework and principles remained fit for purpose. We found what is required is:

4.3.1. Clarity often via guidance for how to meet broad medical device requirements in the context of AIaMD; and
4.3.2. Streamlined and adapted processes that work for SaMD and AIaMD; and
4.3.3. The frameworks, tools, and standards to demonstrate conformity to requirements; and
4.3.4. A joined-up contiguous offer with partners such as NICE, CQC, HRA, etc

4.4. The MHRA Devices Software Group set out 11 work packages across SaMD and AIaMD. Three specific work packages deal with AIaMD and the key objectives are set out below. The MHRA will take forward these work packages to develop policy positions and implement solutions in light of responses to the Consultation on the future regulation of medical devices in the United Kingdom and through further consultation and work with key partners across government, industry, health services, academia, patients and the public. As noted, the bulk this change will be in the form of guidance, implementation of new processes, and other non-legislative work.

5. AIaMD work packages

5.1. The three work packages seek to address the novel challenges that AI can pose for medical device regulation in a proportionate way. Many of the deliverables build on other work packages for SaMD and medical devices / IVDs in general. The precise deliverables will be partially contingent upon the finding of the public consultation and will be published in line with the official government response in early 2022.

5.2. **AI Rigour (AI RIG)** – This work package shapes medical device regulation, crafts supporting frameworks, and encourages standards development to ensure that AIaMD has a robust evidence base that provides further confidence with respect to safety and effectiveness across all populations in which it is intended to be deployed. This work package is the foundation for the work packages on human interpretability and adaptivity. Key priorities likely include:

5.2.1. Expanding upon the Good Machine Learning Practice Principles for Medical Device Development which the MHRA jointly published with FDA and Health Canada in October 2021. This expansion might provide further details on each of the principles and link these to medical device regulatory requirements as well as supporting standards.

5.2.2. A suite of deliverables to ensure AIaMD meets the needs of different ethnicities, genders, ages, and other notable sub-populations. We anticipate that these deliverables will emphasise that AIaMD needs to perform across all populations in which the device is intended to be used, while emphasising wider design considerations to ensure AIaMD meets the need of different communities.

5.2.3. Releasing AIaMD best practice development and deployment guidance that describe the phases of development and deployment that manufacturers might progress through from design, to premarket and to post market duties.

5.3. **Project Glass Box** – For the near-term, much AIaMD is assistive, meaning that humans will be in the loop for some part of the process, often inputting data or making some kind of medical decision on the basis of AIaMD outputs. There is a large literature demonstrating that humans interact with computers differently than they do with other systems or humans. For instance, the risk of automation bias is heightened in the context of SaMD and further complicated for AIaMD that is uninterpretable to humans. This means that a large pillar in establishing the safety of AIaMD is how the patients of healthcare professionals use and interpret that device. Key priorities for this work package are likely to include:

5.3.1. Making plain the critical contribution that evidence relating to human factors, usability, or ergonomics makes to the safety of AIaMD. We shall seek to emphasise that the ultimate criterion of performance is the performance of the human-AI team rather than the AI model in isolation.

5.3.2. Providing guidance outlining the key information users of the AIaMD should generally be provided with to enable the safe and proper use of the device, linking this to wider duties of transparency.

5.3.3. Exploration of human uninterpretability of AIaMD and post hoc explanation methods, drawing links to how uninterpretability might change the kind of evidence collected for AIaMD and how this might influence how patients and clinicians interact with the device.

5.4. **Project Ship of Theseus –** AIaMD learns relationships from data being, also being capable of relearning these relationships. Medical device regulation must shift to meet this challenge, providing streamlined processes that enable retraining but also assurance that the model continues to function as intended. Key priorities likely include:

5.4.1. Providing a framework to break down the challenge of adaptivity into its components, namely, static models that degrade over time, ‘batch trained’ models that retrain ‘every now and then’ that require streamlined processes to manage, ‘individual models’ that are highly personalised to individuals which look more like custom made devices, and finally ‘continuous learning on streaming data’ where data is constantly fed into the model, this data being used as training data.

5.4.2. Building on new SaMD change management processes to ensure these processes fit AIaMD and capture additional risks that retraining can bring.

5.4.3. Supported by a Regulators' Pioneer Fund grant, exploration of metrics that could signal significant or substantial changes in adaptive learning AI algorithms. This work should inform any change management guidance for AIaMD but also potentially provide tools for manufacturers to assess changes to their model.

6. How we're delivering

6.1. Software Group recognise that this programme of work must be supported and led by strong patient and industry engagement. Accordingly, we are crafting both a Patient Engagement Strategy and an Industry Engagement Strategy to support this programme of work going forward. This is not the start of such engagement nor will it be the end, but these strategies are needed to deepen engagement, reflect and amplify patient voice, also ensuring these regulations are practical for industry.

6.2. The Group will work to ensure the patient engagement strategy fits within existing MHRA efforts but also builds on existing groups that have strong expertise in engaging the public on the use of digital health technology. Moreover, Software Group also recognise that we need to not only consider patient and public views on software and AI as a medical device but the regulatory process itself.

6.3. Working with the Partnerships Directorate, the Group will also ensure that there are ample opportunities for industry to feedback and work with us in developing specific deliverables once the roadmap is published. MHRA have already worked with Trade Associations to ensure an early view from industry has informed and guided this strategy, we plan to deepen this consultation but also broaden engagement. We recognise the need for agile regulation in this area, and that this is only possible if it is supported by swift feedback processes for industry.

6.4. The above work programme builds upon wider reforms for both medical devices and SaMD. However, if much of the above work programme is to be pragmatic and not impose undue burden on the market, it must be enabled by robust standards. Software Group is working closely with BSI to identify and contribute to standards development to support the programme of work. Additionally, Software Group are also contributing to reporting guidelines, assurance frameworks, and other tools with the view to providing manufacturers with the tools to demonstrate that their AIaMD is both safe and effective.

6.5. Software Group are not working on this regulatory framework alone. These plans have been developed in concert with wider government and key stakeholders. In addition to usual processes, we have also established the AI RIG Tiger Team, a small group of data science, clinical, and regulatory expertise to guide the development of these work packages and provide detailed feedback on proposed deliverables. Further, we also envision that major deliverables will also see wider scrutiny from system partners before a draft is published, for instance, NICE and NHS England and NHS Improvement.

6.6. Success of these reforms is predicated on these regulations fitting like a puzzle piece with other regulated parts of health and social care, minimising overlap and aligning where possible to avoid unnecessary burden on the market. In pursuit of this, MHRA are a core partner in the Multi Agency Advisory Service (MAAS), this body will provide both a key forum to align requirements but also a service to signpost and assist manufacturers. In addition, we also recognise the need for concerted efforts to align and de-duplicate across key touchpoints and so have bilateral projects such as aligning SaMD classification with NICE Evidence Standards Framework classification. The result of this should be a clear path to market, de-duplicated requirements, and a service to act as a guide for any remaining ambiguity.

6.7. We must fit the regulation of AIaMD within its national context but also place it within its international context. It is of critical importance that this new regulatory framework represents and drives international consensus. In this regard, Software Group has developed strong relationships with key international peers. Explicitly, the first joint publication between FDA and Health Canada highlighted above should be the first not the last. Further, as a Group, we are also driving international consensus by being a member of the International Medical Device Regulators Forum Working Group on AI Medical Devices; being a core part of the G7 AI Governance Working Group; engaging in multilateral groups for harmonisation of digital health technology regulation and inputting into multiple key standards and reporting guidelines.

7. Conclusion

7.1. The MHRA has established a comprehensive programme of work to bring regulatory reform and modernisation to SaMD and AIaMD in particular. Our aim is to address the key challenges that AI can pose for medical device regulation in a proportionate way, ensuring patient safety is maintained but also that the UK public has access to innovative technology that meets a need. The Change Programme will work across and utilise the diverse expertise of the Agency as well that of core partners, ensuring innovation is given a clear, contiguous path to market, that we have a robust and responsive way to identify and respond to safety signals, and that patients and public will be at the core of this system. We also believe that this work on AIaMD sharpens wider reforms for SaMD and medical devices / IVDs in general, ensuring that the key ambitions outlined in the MHRA's Delivery Plan 2021-2023 are met for AIaMD.

7.2. What does this mean for patients, healthcare professionals, and industry? For patients, it means that they will be able to have increased confidence that AIaMD encountered in a direct to consumer context and those tools that assist clinicians are safe and effective. For healthcare professionals, better regulation will allow them to intelligently place their trust in these devices, meaning these tools will be better integrated into clinical pathways. For industry, the UK market for AIaMD will have a clear, smooth route to market that supports responsible innovation.

7.3. The Board is asked to consider these plans, the progress to date, recommend any other areas for development and specifically consider the following questions:

7.3.1. Does the Board agree with the strategic priorities identified in point 1.4; and

7.3.2. Does the Board consider that the paper has identified and addressed the core issues and challenges that will support effective regulation of AIaMD?

Laura Squire
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