Medicines & Healthcare products Regulatory Agency

AGENDA FOR BOARD MEETING HELD IN PUBLIC

10:00 – 12:30 on 16th February 2021

Chair: Stephen Lightfoot

	AGENDA ITEM	PURPOSE	PRESENTER
10:00	INTRODUCTION		
	1. What are the priorities for this meeting and how will the meeting run?	Information	Chair
	2. Are there any Apologies or Declarations of Interest?	Information	All
	3. What were the minutes and actions from the last meeting?	Approval	Chair
10:15	CURRENT CONTEXT		
	4. What are the current key issues from the CEO point of view?	Discussion	June Raine
10:40	HEALTHCARE ACCESS		
	5. How does the Innovative Licensing and Access Pathway fit into the future regulatory offer of the Agency?	Discussion	Sam Atkinson
11:05	PATIENT SAFETY		
	6. What assurance can be provided by the Patient Safety & Engagement Committee?	Assurance	Mercy Jeyasingham
11:20	DYNAMIC ORGANISATION		
	7. What assurance can be provided by the Organisational Development & Remuneration Committee?	Assurance	Anne-Toni Rodgers
11:35	FINANCIAL SUSTAINABILITY		
	8. What is the current financial performance of the MHRA against its 2020/21 Business Plan?	Discussion	Jon Fundrey
11.50	9. What assurance can be provided by the Audit & Risk Assurance Committee?	Assurance	Michael Whitehouse
12.05	EXTERNAL PERSPECTIVE		
	10. What questions do members of the public have for the MHRA Board?	Discussion	Chair
		-	Chair
12.30	CLOSE OF MEETING		

Medicines and Healthcare products Regulatory Agency

Minutes of the Board Meeting Held in Public of 19th January 2021

(10:00 – 12:30)

By Zoom Webinar

Present:

The Board

Stephen Lightfoot	Chair
Professor David Webb CBE	Deputy Chair
Dr June Raine CBE	Chief Executive
Dr Samantha Atkinson	Interim Chief Quality and Access Officer
Dr Barbara Bannister MBE	Non-Executive Director
Amanda Calvert	Non-Executive Director
Professor Bruce Campbell	Non-Executive Director
Jon Fundrey	Chief Operating Officer
Mercy Jeyasingham MBE	Non-Executive Director
John Quinn	Interim Chief Technology Officer
Dr Christian Schneider	Interim Chief Science Officer
Professor Liam Smeeth	Non-Executive Director
Michael Whitehouse OBE	Non-Executive Director

Others in attendance

Rachel Bosworth	Director of Communications
[redacted]	Secretary to the Board and Deputy Head of Directorate
[redacted]	Executive Assistant to the Chair

Government Legal Department

Elizabeth O'Neill	Deputy Director, MHRA, Medicines & Pharmacy, GLD

Department of Health and Social Care (DHSC)

Dr Alastair Hardisty	Head of MHRA Sponsorship and EU Exit, Medicines and Pharmacy Directorate, DHSC
Ronan McDonald	Head of Medicine Regulation, DHSC

Devolved Administrations

Greig Chalmers	Head of Medicines Policy Branch, Scottish Government

Item 1: Introduction

What are the priorities for this meeting and how will the meeting run?

1.1 The Chair set out his expectations and priorities for this public Board meeting which was being live streamed to the registered audience and recorded.

1.2 The Chair welcomed all to the meeting, including the broad range of members of the public attending in the audience.

1.3 The Chair and the Board sincerely thanked Elizabeth O'Neill for all the work she has done for the Agency providing legal advice and preparing the Statutory Instruments for EU Exit, as this was her last meeting before moving to a new role.

1.4 The Chair and the Board also thanked Dr Alastair Hardisty, Head of MHRA Sponsorship at DHSC, for all his work with the MHRA as this was also his last meeting before moving into a new role within DHSC. The Board welcomed his successor, Ronan McDonald.

Item 2: Are there any Apologies or Declarations of Interest

2.1 Apologies were received from Anne-Toni Rodgers.

2.2 Bruce Campbell made a declaration of interest; Professor Campbell will be working with Academic Health Solutions on a consultancy basis working on medical device registration systems. The Chair noted the declaration.

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 on the outstanding actions.

CURRENT CONTEXT

Item 4: What are the current issues from the CEO 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 updates on Covid-19 vaccine, therapeutics and tests, enabling innovation, international work and the Medicines and Medical Devices Bill; (ii) patient safety – including updates on antiepileptic drugs and review of safety of use during pregnancy, the isotretinoin public consultation, and drug alerts and recalls; (iii) dynamic organisation – including an update on mental health and wellbeing; and (iv) financial sustainability – including an update on the Agency Change programme.

4.2 Dr Raine in particular highlighted the efforts and commitment of the Agency's staff; the Board noted a heartfelt thanks to all members of staff for their hard work over the recent months. The Board noted that the Agency has been shortlisted for the Civil Service Science Awards for our innovative synthetic data work to support regulation of Artificial Intelligence software algorithms.

4.3 The Board thanked Dr Raine for her report and provided comments relating to sharing of information with other global regulators including via ICMRA and the Access Consortium; vaccine hesitancy; ensuring outreach of safety messaging to healthcare professionals through various means; the isotretinoin call for evidence; ensuring the MHRA has capacity to manage batch release of Covid-19 vaccines; and proactive vaccines safety vigilance. The Board were assured on each of these points.

4.4 An action was taken to present a proposal for the new Innovative Licensing and Access Pathway to be presented to the Board; the experience and learning from early examples going through the system should be shared.

Action 19: A proposal for the new Innovative Licensing and Access Pathway (ILAP) to be presented to the Board. The experience and learnings from early examples going through this system should be shared.

HEALTHCARE ACCESS

Item 5: How will the new Trade & Cooperation Agreement with the EU impact on the work of the Agency and on the supply of medical products in the UK?

5.1 The Board considered a paper describing how the new Trade & Cooperation Agreement with the EU will impact on the work of the Agency and on the supply of medical products in the UK. The Board noted that the Agency has successfully managed the final stages of Transition from the EU, with no regulatory interruption of supply of pharmaceuticals or devices to patients and ensuring industry are able to continue to conduct regulatory business with the MHRA.

5.2 The Board considered the specific outstanding issues resulting both from the negotiations and from a series of EU Exit related milestones over the coming years. A programme of work has been developed to meet these milestones. The Board noted the imperative to ensure the sustainability of the new Agency operations under the wider Change Strategy.

5.3 The Board provided comments regarding the distinction between UK and GB; the complexity of the Northern Ireland Protocol and the impact on industry; pharmacovigilance databases and data sharing activities; the potential for regulatory fraud and how to mitigate this; how to communicate risks related to patient safety and medicines supply in the new arrangements; new licensing routes to market which are in development including the Innovative Licensing Access Pathway; ensuring the UK can attract innovation; utility of data sources such as CPRD for safety signal validation; strengthening registry data and data linkages; and the value of full population coverage in data sources.

5.4 The Board agreed that a further update on the Trade and Cooperation Agreement with the EU should be presented to the Board meeting in March 2021. The Board commended all involved in ensuring all systems were up and running for 1st January 2021.

Action 20: Present update on the Trade & Cooperation Agreement with the EU to the Board in March 2021.

Item 6: What are the plans to introduce a new registration system to improve the oversight of medical devices in the UK?

6.1 The Board considered a paper on the Agency's plans to develop a register for all medical devices after 1 January 2021 together with broader developments in the medical device data landscape, registries to track long-term outcomes for devices and unique device identification. The Board noted the current capabilities of the devices registration system; the further development needed to create a comprehensive GB devices reference data system (Registration/Unique Device Identification (UDI) system); and the inter-relationship between this proposed system, the NHS Digital Medical Device Information System (MDIS) and work carried out under the NHSX Medical Device Safety Programme.

6.2 The Board noted the important range of benefits this registration system will provide for patient safety. MHRA is engaging with external stakeholders and registries to link data from various sources; it will eventually be possible to link information on implantable devices to a patient's hospital records. The Board noted this will be a complex piece of work and the quality of data will be critical.

6.3 The Board provided comments relating to the important relationships with the devolved administrations in this work; how this work will ensure some of the findings of the Independent Medicines and Medical Devices Safety (IMMDS) Review are addressed; how safety signal detection will work; linkages with national registries; ensuring data from private hospitals is included; and how to monitor how devices are changed and updated through their lifecycle.

6.4 The Board discussed whether the system will register products retroactively – it was noted that the requirement for products to be registered only applies to new products to the market. The Board agreed that ease of access to the medical devices market via this system will be vital for the UK economy and for patient benefit.

6.5 The Board noted that there has been an amendment in the Medicines and Medical Devices Bill for a statutory Devices Expert Committee. The Board agreed that it is important that end-to-end governance of this proposed system should be reviewed. An action was agreed for ARAC to review the governance and risks of the medical devices system proposal.

Action 21: Oversight of medical devices – ARAC to review governance and risks of the medical devices system proposal.

PATIENT SAFETY

Item 7: What are the short, medium and long-term deliverables on the Agency recommendations from the Cumberlege Review?

7.1 The Board considered a paper which provided an overview of the short, medium and long-term deliverables on the Agency recommendations from the Independent Medicines and Medical Devices Safety (IMMDS) Review, led by Baroness Cumberlege. These deliverables and actions are being taken to improve patient safety and how the Agency listens and responds to concerns.

7.2 The Board reviewed the deliverables and provided comments about the linkages with NICE, clinicians and the Safer Medicines in Pregnancy & Breastfeeding Consortium; ensuring consistent advice is given to patients; patients are involved in a systematic manner including maximising the use of patient reported outcome measures in clinical trials. These comments will be reflected in the Agency's Regulatory Science Strategy.

7.3 The Board commented that patient involvement in the licensing process will be vital and noted this is reflected in the ILAP process. It will be important to ensure the Agency is able to demonstrate the outcome of these deliverables in the event of a parliamentary review and for patient safety; the importance for patients to feel that the system is working for them; engaging industry to work together to improve patient safety; and how to work internationally. The Board agreed an action for an update on how these deliverables are measured over time.

Action 22: Present an update to the Board on how the short, medium and long-term deliverables are measured over time.

DYNAMIC ORGANISATION

Item 8: What are the final proposed Terms of Reference for the three new Board Assurance Committees:

- **Audit & Risk Assurance Committee**
- **Patient Safety & Engagement Committee**
- **Organisation Development & Remuneration Committee**

8.1 The Board reviewed and approved the final proposed Terms of Reference for the three new Board Assurance Committees. The Board noted that assurance reports will be presented to the Board by the Chair of each committee on a regular schedule.

EXTERNAL PERSPECTIVE

Item 9: 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.

SUMMARY OF ACTIONS FROM MHRA BOARD MEETING – 19 January 2021

Action Number	Action	Owner	Date	Status
Carried Forward from previous meetings				
7	Provide an update to the Board on the Memorandum of Understanding with NICE	June Raine	~~23/11/20~~	Chair & CEO Meeting in March
13	Conduct a Board review of CPRD. Further action 19/01/21: Include how to expand data sources for CPRD's role in safety surveillance.	Jon Fundrey	16/03/21	
15	Review Agency Fee structure to ensure closer alignment with costs of delivery	Jon Fundrey	15/06/21	
16	Produce a single 2-year Agency Delivery Plan to replace existing Corporate and Business Plans. Date of 31st March 2023 will be the fixed end date of the plan.	Jon Fundrey	20/04/21	
New actions				
19	Proposal for new Innovative Licensing and Access Pathway (ILAP) to be presented to the Board. The experience and learnings from early examples going through this system should be shared.	Sam Atkinson / Christian Schneider	16/02/21	On agenda
20	Present update on the Trade & Cooperation Agreement with the EU to the Board	Sam Atkinson	16/03/21	
21	Oversight of medical devices – ARAC to review governance and risks of the medical devices system proposal	ARAC	18/05/21	
22	IMMDSR – present an update to the Board on how the short, medium and long-term deliverables are measured over time.	June Raine	20/07/21	

Medicines & Healthcare products Regulatory Agency

Chief Executive's Report to the Board

16th February 2021

This report gives a brief overview of the current issues from the CEO's point of view. The Board is asked to consider and agree the priorities.

HEALTHCARE ACCESS

Covid-19 Vaccines and Therapeutics

1. Taking into account studies looking into the spread of different strains of the virus, work continues as a priority on the impact on vaccine efficacy of these new strains. Although only early data were available, the data were encouraging suggesting that the vaccines are effective against the new UK strain. The Clinical Trials Unit has also approved a trial looking at reactogenicity and immunogenicity of heterologous prime/boost Covid-19 vaccine schedules (using a different Covid-19 vaccine for the second dose).

2. Regarding additional vaccines to the three already approved in UK, discussions are continuing with Novavax and Janssen, and both companies have released vaccine efficacy data in their press releases. Review of the data will commence in the coming weeks. The Clinical Trials Unit has approved an amendment to a vaccine trial to include the paediatric population, children aged 12-17 years.

3. Work continues on possible therapeutic agents for COVID-19 including colchicine, following publication of the ColCorona Trial, and Tocilizumab, following publication of results from the RECOVERY study.

Covid-19 tests

4. In relation to the performance of Covid-19 tests, the Agency continues to work in partnership with DHSC and Public Health England (PHE) on variants. We are working with colleagues at PHE, the COVID-19 Genomics UK (COG-UK) consortium and Great Ormond Street Hospital to develop guidance for manufacturers. We are engaging with Trade Associations and Competent Authorities to facilitate partnership work and encourage manufacturer engagement.

5. We are continuing to work in partnership with Test and Trace to ensure a pipeline of safe and effective Covid-19 tests. The focus is predominately on Lateral Flow Tests, but not exclusively as other technologies for mass testing deployment are being considered. Representatives from the Devolved Administrations are also part of this group. We recently finalised a Target Product Profile (TPP) on breath bio-markers and we are working with partners to develop to develop a matrix TPP framework.

6. We have established an Expert Advisory Group (EAG) on In-Vitro Diagnostics (IVDs) which is providing independent external support and constructive challenge to the development of current and future TPPs and to other Covid-19 related activities. The

EAG will have utility beyond Covid-19 to inform regulatory decisions around In Vitro Diagnostics more generally.

Reagent panel for detecting SARS-CoV-2

7. In mid-December 2020, members of Infectious Disease Diagnostics (IDD) Division of NIBSC were approached by PHE and NHS to make a panel of reagents that could be used by PHE and the NHS to validate and verify Loop-mediated isothermal amplification (LAMP) and other nucleic acid amplification assays for use in the detection of SARS-CoV-2. The product is now in the NIBSC catalogue.

Artificial Intelligence (AI) Round Table with NHS X

8. The MHRA Devices Software Group presented a high-level summary of plans to construct the future regulatory framework for software as a medical device (SaMD) and AI as a medical device (AIaMD) to a Round Table which included representatives from: NHSX, NHS Digital, National Institute for Health and Care Excellence, Health Research Authority, NHS Resolution, Better Regulation Executive, and the National Data Guardian. The response from Round Table participants was overwhelmingly positive and supportive. We plan to undertake informal and formal consultation over the coming months.

Innovative Licensing and Access Pathway

9. The Innovative Licensing and Access Pathway (ILAP) fulfils the ambition for enhanced collaboration between stakeholders (including NICE, the Scottish Medicines Consortium, and patients), alignment of data requirements where possible, and provides a platform for bespoke and timely advice to developers across the whole of the medicines regulatory pathway in support of earlier patient and market access.

10. The ILAP was launched on 1st January 2021 and the Agency has received 10 Innovation Passport applications from a wide range of developers, from large companies to a spin-out from a leading UK University. We have had strong interest from companies who have welcomed our flexible approach to provide a platform for multi-stakeholder input. Product areas include oncology and rare diseases. The ILAP Steering Group has met twice and has agreed the first approval of an Innovation Passport.

Publications

11. A paper describing the design and characterisation of a new Oral Polio Vaccine (OPV) strain, that had recently received the first ever Emergency Use Listing for a vaccine from the World Health Organisation (WHO), was chosen as one of the Editor's favourite papers of 2020 in the Cell, Host and Microbe journal. Authors of the paper included three NIBSC colleagues amongst others from organisations such as University of California, Centre for Vaccine Innovation and Access, PATH, Bill and Melinda Gates Foundation, and University of Antwerp.

12. At the end of January a Senior Scientist in NIBSC Division of Bacteriology contributed to the Microbiome Strategic Roadmap that was published by Knowledge Transfer Partnerships. The report reviews the landscape of microbiome science and innovation within the UK. In line with the "one health" approach, it spans human, animal and plant sectors with key recommendations on how to advance science translation and business creation.

PATIENT SAFETY

COVID-19 vaccine safety

13. On 5 February 2021 the MHRA published its safety surveillance strategy for monitoring the safety of all UK-approved Covid-19 vaccines. To coincide with this, we also published the first of what will be regular Covid-19 vaccine safety reports. These provide details on the suspected side-effects to the vaccines reported through our safety monitoring system, the Yellow Card scheme. The data showed 22,820 reports of suspected side effects, or an overall reporting rate of 3 in 1,000 doses of vaccine administered from 9 December 2020 to 24 January 2021. This reassuring data has shown that the vast majority of reported side effects are mild and in line with most types of vaccine, including the seasonal flu vaccine. These include sore arms and mild 'flu-like' symptoms, which are short-lasting.

14. These data have been thoroughly analysed by the MHRA's scientists and safety experts together with all other sources of evidence and show that the safety of these vaccines remains as high as expected from the clinical trial data that supported the approvals. The safety profile of the vaccines remains positive and the benefits continue to far outweigh any known side-effects. The safety of Covid-19 vaccines will be continually monitored throughout their use in healthcare practice to ensure they remain safe and effective.

15. To support the Agency carrying out statutory Covid-19 vaccine surveillance, the Clinical Practice Research Datalink (CPRD) is receiving near real-time vaccination and hospital data and linking these datasets to daily updated CPRD primary care data. These anonymised data, which are not available through any other route, provide the Agency with up-to-date information to evaluate the safety of the Covid-19 vaccines deployed in the UK population.

Investigating Covid-19 risk factors and outcomes

16. CPRD data have been extensively used to investigate clinical and pharmacological risk factors, health outcomes and health service usage throughout the Covid-19 pandemic. Covid-19 protocols have undergone expedited review by CPRD and a record 33% of these studies have already resulted in publications and submitted manuscripts in the past 10 months. Two new Covid-19 serology and virology datasets linked to CPRD primary care data have been released in February to facilitate further in-depth epidemiological research on the impact of Covid-19 on population health and the health service delivery.

Isotretinoin public consultation

17. To support the ongoing review of psychiatric and sexual disorders suspected to be associated with isotretinoin, on 10th November 2020 we launched a 12-week public call for information. The call has been extended by two weeks to offset any potential impact associated with the December holiday period which may have affected individuals' or organisations' ability to respond to the call for information. The review and call for information webpages have been updated to reflect the new deadline. All registered stakeholders were notified by email on 2nd February and the extension has been actively publicised on various social media platforms. All responses to the call for information will be considered by the Isotretinoin Expert Working Group.

The Medicines and Medical Devices Bill and next steps

18. The Medicines and Medical Devices Act 2021 received Royal Assent on 11 February 2021. The majority of the powers in the Act will come into force two months after Royal Assent. We will then have the necessary powers to make legislative changes to our regulations for medicines, medical devices and clinical trials, enabling us to strengthen our regulatory system in the best interests of patients and the public. We will be working to develop and consult on future legislative proposals, to inform secondary legislation to be made under the powers in the Bill. For example, the Bill enables increased transparency about the data we hold on medical devices and a new devices enforcement framework, and will enable us to implement a new regulatory framework for medicinal products that are manufactured at the site where patients receive care.

International workshop on Medicines in Pregnancy and Breastfeeding

19. In 2020 MHRA hosted a workshop with the US FDA and European Medicines Agency, which examined current regulatory requirements, challenges and opportunities for improving the evidence base to support rational use of medicines during pregnancy and breastfeeding. An article on the key issues from the workshop is due for publication shortly in the journal Clinical Pharmacology and Therapeutics and a copy of the full workshop report will be available on our website to coincide with publication. Future work will focus on building a strategy to enable consistent regulatory approaches for obtaining useful information for these populations.

Sulfasalazine use in severely renally impaired patients

20. The Pharmacovigilance Expert Advisory Group (PEAG) considered a review of sulfasalazine use in severely renally impaired patients and advised that the class warning for 5-aminosalicylic acid compounds should be added. This warning states that these compounds have shown nephrotoxicity and that renal monitoring is advised. It was agreed that the renal monitoring requirements should be tightened and strengthened throughout the product information for sulfasalazine-containing products and harmonised for all aminosalicylates.

Levothyroxine and assessment of evidence for adverse events on product-switching

21. The Commission on Human Medicines (CHM) considered evidence from the Yellow Card Scheme and scientific literature relating to the reporting of adverse events in patients switched between different levothyroxine tablet products and whether this had any impact on current advice for generic prescribing which was endorsed in 2019. The CHM noted that the majority of patients remain well on a generic prescribing regime but up to 10% of patients taking levothyroxine do not feel well on the treatment, and some are very sensitive to changes between different brands of levothyroxine tablets.

22. The CHM recommended that generic prescribing should still be supported but that it would be helpful for prescribers and pharmacists to be made more aware of the potential for adverse events on brand switching. The CHM endorsed updates to product information to alert prescribers and patients to the fact that a minority of patients may experience adverse events on product switching, and noted the importance of communicating the proposed product information updates to patients and prescribers.

DYNAMIC ORGANISATION

International

23. The MHRA's International Office continues to coordinate our international effort working with regulators around the world on matters relating to Covid-19 vaccines and therapeutics. We participated in the International Coalition of Medicines Regulatory Authorities (ICMRA) workshop on Covid-19 variants and the ICMRA workshop on pregnancy and lactation. We continue to lead the ICMRA Covid-19 Working Group work on vaccine vigilance and on the digital transformation on inspections.

24. We took part in the first Access Consortium Heads of Agency call this year, where Health Canada has now taken the Chair. The Access Consortium is a medium-sized coalition of regulatory authorities that work together to promote greater regulatory collaboration and alignment of regulatory requirements. It comprises the national regulatory authorities of Australia, Canada, Singapore, Switzerland and the UK.

25. The All-Party Parliamentary Group on Access to Medicines and Medical Devices which met on 20th January was an opportunity to set out the Agency's current opportunities to develop international collaboration and a report will be produced in due course. The FDA was also present on the panel and presented the background and successes of Project Orbis.

Agency Change programme

26. The new MHRA Director of Transformation, Davinder Virdi, is now in post and will support the Executive Team to lead the Agency through the detailed design of the future organisation and implementation of the transformation programme. A series of engagement sessions has been held with MHRA staff including a meeting with all Directors, the Senior Leadership Group, a Managers meeting, and two All Staff Meetings to set out the high level design of the Future Operating Model and to engage and consult staff as we enter the next phase of detailed work. At the beginning of this new phase we are working to define how we will best utilise staff's expertise to inform the detailed decisions we need to take, as well as to identify a limited numbers of areas for early implementation on a 'no regrets' basis, building the momentum for and evidence of real change.

FINANCIAL SUSTAINABILITY

Business Plan 2021/22

27. Progress is being made on developing the Agency's 21/22 Business Plan/ Delivery Plan. During January, the business was commissioned to develop the objectives underpinning the draft business priorities, as well as identifying delivery challenges and any trade-offs arising from static budgets. The current focus is ensuring that the Delivery Plan is fully aligned with and delivers the transformation strategy. There will be further discussions during February to ensure this alignment and that in-flight projects are rationalised. A proposal for stakeholder engagement is also being worked up for the Executive Committee and Agency Board to consider.

June Raine
Interim Chief Executive
February 2021

Medicines & Healthcare products Regulatory Agency

Board Meeting Held in Public

16 February 2021

How does the Innovative Licensing & Access Pathway (ILAP) fit into the future regulatory offer of the Agency?

Issue:

To provide the Board with an update on the Innovative Licensing & Access Pathway (ILAP)

Action required by the Board and by when (timings):

The Board is invited to:

1. Note the progress of the development of the Innovative Licensing and Access pathway.
2. Consider and comment on the future priorities and direction for developing the ILAP proposition.

Implications for patients and the public:

This paper addresses the general status of the ILAP project and includes details on the approach to providing faster patient access to innovative products and support for enhanced patient engagement.

Which aspect(s) of the Business Plan does this paper address?

All

Author(s):

Director, Licensing

Expert Medical Assessor, Licensing

Head of Strategic Communications and Marketing,

Portfolio Management, TD[3]

Board Sponsor:

Sam Atkinson

How does the Innovative Licensing & Access Pathway (ILAP) fit into the future regulatory offer of the Agency?

The Innovative Licensing & Access Pathway (ILAP[1]) fulfils the ambition for enhanced collaboration between stakeholders such as the National Institute for Health and Care Excellence (NICE[2]), the Scottish Medicines Consortium (SMC[3]), and patients. ILAP also provides for alignment of data requirements where possible, and provides a platform for bespoke and timely advice to developers across the whole of the medicines regulatory pathway in support of earlier patient and market access.

A. Overview

3. Our ambitious new pathway for accelerating time to market for innovative medicines was launched in the UK in December 2020 and has been open for business since 01 January 2021.

4. This integrated framework for innovative medicines is known as the Innovative Licensing and Access Pathway – or ILAP, with the MHRA working closely with NICE and SMC as partners.

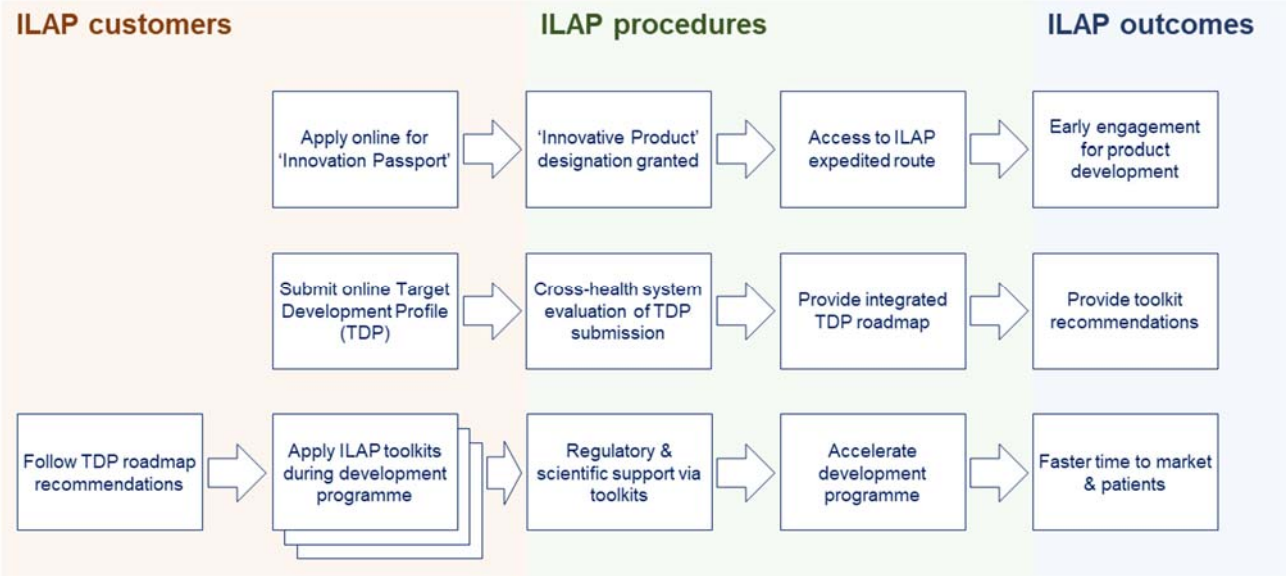
5. Ambitious goals have been set for this pathway to (i) significantly reduce the time to market for new innovative products using flexibilities in our regulatory toolkit, (ii) develop and attract new revenue streams for regulatory business, and (iii) respond to recommendations from the Independent Medicines and Medical Devices Safety Review (IMMDSR[4]) report relating to better patient engagement and UK health system integration.

6. These goals will be realised through the novel ILAP framework. It has established a new 'Innovative Medicine' designation, provides a flexible toolkit of regulatory and scientific support mechanisms, and supports applicants with an integrated development roadmap.

7. The framework provides opportunities for enhanced engagement and responsiveness at early stages of innovative products' development programmes – in terms of additional regulatory, scientific, and stakeholder input. This includes interactions externally with patients, NHS England and NHS Improvement (NHSE&I), NICE, the SMC, and internally across the MHRA – include the Clinical Practice Research Datalink (CPRD[5]), and the National Institute for Biological Standards and Control (NIBSC[6]). The framework supports expedited, efficient, and innovative approaches to the product development programme – including iterative assessments, iterative risk management, proactive pharmacovigilance, and a whole-lifecycle approach to evidence generation.

1 https://www.gov.uk/government/publications/innovative-licensing-and-access-pathway-ilap-for-medicines
2 https://www.nice.org.uk/
3 https://www.scottishmedicines.org.uk/
4 https://www.immdsreview.org.uk/
5 https://www.cprd.com/
6 https://www.nibsc.org/

8. The key aspects of the scheme are the designation (Innovation Passport), the road map (Target Development Profile), and the tool kit, all brought together in the overarching Innovative Licensing and Access Pathway:



9. Expected outcomes of ILAP are:

- Earlier engagement between the Agency, healthcare system partners (including NICE and SMC, NHSE&I and other stakeholders), patients, and the developers of innovative products.
- In collaboration with NICE and SMC, a method to grant Innovation Passport () designations – a first for joint decision making between the regulatory and the HTA bodies. This enables full access to ILAP, and which also provides innovative oncology medicines a route through to Project Orbis[7].
- A product-specific roadmap tailored to the needs of each innovative product, which signposts the expedited path through development and towards faster patient access – the Target Development Profile (TDP).
- Innovative methods and flexible toolkits that accelerate availability of robust data – e.g. integration of novel trial designs and early authorisation, and which therefore support faster patient access.

10. The development approach for ILAP included approaching four companies and inviting them to submit candidate products to a pilot TDP procedure. Responding to company feedback has helped shape the development and launch of the ILAP proposition. The pilot activities have also been key to establishing collaborative ways of working between MHRA, NICE, SMC, and NHSE&I.

11. Early indications are very positive. At least two of the four companies in the pilot have stated their intentions to proceed with the full ILAP roadmap recommendations for development of their innovative products.

[7] https://www.fda.gov/about-fda/oncology-center-excellence/project-orbis

B. ILAP Launch

12. General awareness of ILAP began building around September 2020 through industry engagement and press coverage. The launch of ILAP in December 2020 was supported by a detailed communications campaign from the Agency's Communications team. Prior to its official launch, ILAP was also the subject of a front page article in the Financial Times.

13. Public support for the launch of ILAP was provided with joint statements from MHRA, the Department of Health and Social Care (DHSC[8]), NICE, Health Research Authority (HRA[9]), Health Improvement Scotland (HIS), BioIndustry Association (BIA[10]), and the Association of the British Pharmaceutical Industry (ABPI[11]). Supporting social media was also delivered by partners.

14. Information about ILAP is published on the MHRA website[12] – including guidance for applicants, Innovation Passport qualifying criteria, descriptions of the toolkits, and fee information. This content was developed collaboratively and with input from ILAP partners (NICE and SMC). See Annex 4 for a summary of the Innovation Passport qualifying criteria.

15. Since 01 January 2021, the Agency has received ten Innovation Passport (IP) applications from different-sized companies (including large companies and a spin out of a leading UK university). Revenue due from ten IP applications is worth £36k, with potential additional fees of £45k for follow-on TDP applications, plus further possible revenues per product as a result of fees charged for scientific advice and fees per ILAP tool adopted as a result of TDP roadmap recommendations.

16. These applications including products for the following conditions:

- Graft versus Host Disease
- von Hippel Lindau disease
- Alzheimer's like dementia
- Prevention of SARS CoV-2
- Non-small cell lung cancer
- Unhealing complex and chronic wounds
- Unresectable locally advanced or metastatic triple-negative breast cancer

17. We have had strong interest from companies who have welcomed our flexible approach to provide a platform for multi-stakeholder input. We have held numerous *ad hoc* meetings with companies to discuss the range of options available. There is also interest from NHSE&I with regards to their future drug repurposing programme.

C. Licensing & Access Routes

18. ILAP is designed to provide a flexible framework within which all types of innovative devices and medicinal products can follow different routes to reach market access, authorisation, and approval. In this respect, ILAP provides a platform that brings additional benefits (such as earlier engagement with NICE and SMC, and broader product designation) when compared to existing regulatory and market access pathways. Depending on the maturity of the development of the innovative product, ILAP also allows entry of the product at different stages of the pathway (from non-clinical data, pre-first in Human studies), benefiting from tools available within the toolkit, and leading to eventual earlier authorisation and access.

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8 https://www.gov.uk/government/organisations/department-of-health-and-social-care

9 https://www.hra.nhs.uk/

10 https://www.bioindustry.org/

11 https://www.abpi.org.uk/

12 See https://www.gov.uk/government/news/the-mhra-innovative-licensing-and-access-pathway-is-open-for-business and https://www.gov.uk/government/publications/innovative-licensing-and-access-pathway-ilap-for-medicines

19. A well-advanced innovative product could still take advantage of the ILAP toolkit, including for entry into Project Orbis, and the use of tools for collection of real world data or patient engagement activities. However, it is unlikely that products in the ILAP would use the GB-specific reliance route to licensing. The ambition of ILAP pathway is to expedite approval and not wait for the European Medicines Agency (EMA) Committee for Medicinal Products for Human Use (CHMP[13]) decision. The potential remains for the toolkit to be beneficial – even at later stages in the product development pathway – but companies are encouraged to apply early.

20. Products eligible for inclusion in the ILAP are based on a broad and inclusive definition of innovation that means a large proportion of CHMP products are eligible. This is alongside other products, such as repurposed medicines, which is a key area for the NHS. Of note, the EMA priority medicines (PRIME[14]) scheme has often been criticised that their criteria are too strict: the denial rate stands currently at over 70%. This is in contrast to the open approach proposed for ILAP.

21. The table below compares ILAP with the existing Early Access to Medicines Scheme (EAMS[15]) and the NHS Accelerated Access Collaborative (AAC[16]).

	MHRA Innovative Licensing & Access Pathway (ILAP)	**MHRA Early Access to Medicines Scheme (EAMS)**	**NHS Accelerated Access Collaborative (AAC)**
Product designation	Innovation Passport (IP)	Promising Innovative Medicine (PIM[17])	Early or late stage product – not a designation
Qualifying criteria	Specific criteria – broad and inclusive definition of innovation, decision made by the ILAP Steering Group	Specific criteria – unmet medical need and requirement to demonstrate major advantage	AAC Board recommendation based on proposals from the AAC secretariat
Applicable to medicines	Yes	Yes	Yes
Applicable to devices	New tools underway to co-develop medicines with in vitro diagnostic (IVD[18]) and device combinations	No	Yes
Early-phase supported	Yes	No	Yes
Late-stage supported	Less likely	Yes	Yes
Access to Orbis	Yes	No	No
Access to ACCESS	Yes	No	No

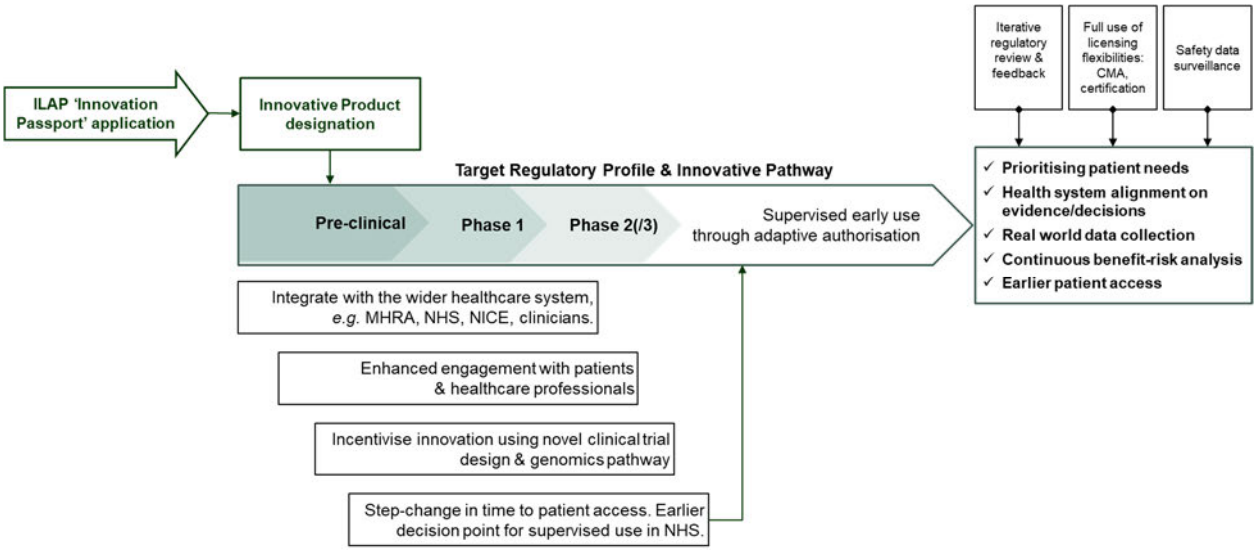
13 https://www.ema.europa.eu/en/committees/committee-medicinal-products-human-use-chmp
14 https://www.ema.europa.eu/en/human-regulatory/research-development/prime-priority-medicines
15 https://www.gov.uk/guidance/apply-for-the-early-access-to-medicines-scheme-eams
16 https://www.england.nhs.uk/aac/
17 https://www.gov.uk/guidance/apply-for-the-early-access-to-medicines-scheme-eams#promising-innovative-medicine-pim-designation
18 https://www.gov.uk/government/publications/in-vitro-diagnostic-medical-devices-guidance-on-legislation

22. Decisions around the direction of ILAP are made by the ILAP Steering Group. Membership is drawn from across the MHRA, plus representatives from NICE and SMC. The Steering Group determines the status of Innovation Passport applications, and provides a strategic input to the development of ILAP. The Agency provides secretariat support for the ILAP Steering Group. Meetings are held every fortnight. This group demonstrates the firm commitment from the Agency to work collaboratively and meaningfully with our partners and other stakeholders in the patient access pathway.

23. Careful attention has been paid to possible conflicts of interest during the ILAP pilots and also in establishing the ILAP Steering Group. Steps are being taken during the current phase of the ILAP project to align information sharing policies and formalise governance arrangements across all the partner organisations participating in ILAP.

24. No appeals process is available to challenge Steering Group decisions on Innovative Passport applications. This was agreed amongst partners and is reflected in the standard operating procedure that has been developed to support ILAP.

25. ILAP offers a complimentary framework within which products may also carry additional designations, such as the PIM designation of EAMS. The explicit mission of ILAP is to reduce significantly the time to patients for innovative products. A designation such as PIM is just one of a number of methods and approaches that ILAP can support to accelerate the product development programme and leverage expertise from across the UK health system.



D. Future Regulatory Offerings from the Agency

26. The Agency has articulated that its strategic direction of travel includes moving towards developing as an innovative regulatory body for innovative new products.

27. The context of the current environment in which the Agency must develop includes responding to the challenges set by the Cumberlege IMMDSR report, establishing a post-EU regulatory framework, turning towards global opportunities for collaboration, learning from the experience of COVID-19, leveraging the capabilities of the wider UK health system, and evolving new regulatory approaches for ever-advancing therapies and increasingly innovative products.

28. ILAP has been designed to meet the needs of this dynamic environment. The focus of the proposition and its toolkits includes key themes such as patient centricity, therapeutic strategies, industry demand, health system partner collaboration, financial sustainability, priority support for innovation, and ensuring a global outlook.

29. At launch, nine different tools were provided under the ILAP umbrella. These support a "pick and mix" approach to tailoring an access pathway that meets the needs of different innovative products. For information, these tools are summarised in Annex 1.

30. Regular reviews of the available tools are planned into the ILAP release schedule for 2021 (at least two more releases are planned). This provides opportunities to respond to emerging customer requirements and address directly any feedback on outcomes. Continuous improvement will also allow the ILAP proposition to mature in a direction that best meets the needs of patient and which supports market access for innovative products. This direction could develop (for example) into a more cohesive and structured catalogue, or perhaps pursue the flexibility offered by the highly responsive 'pick and mix' approach.

31. The ILAP Steering Group remains responsive to requests from its members, patient groups, industry representatives, and health system partners in terms of the direction and priority for developing future regulatory offerings within the ILAP framework.

32. The initial launch of ILAP is being followed by further releases that will broaden the scope of tools available, improve operation of the pathway, and improve the overall customer experience. For information, a list of tools next in line to be developed are summarised in Annex 2 below[19].

33. Since its origins with the Tiger Team in 2019, cross-Agency engagement has featured active collaboration and extensive input the development of ILAP from colleagues representing different divisions from across the whole MHRA.

34. ILAP is expected to keep developing. Future additional tools are expected to be defined in response to strategic priorities, for example increased support for devices, and to also meet evolving customer needs, for example to support global collaboration.

35. For information, a summary of comparison of expedited Global regulatory pathways is provided in Annex 3.

E. UK Health System Integration

36. Partnership arrangements are already in place with NICE. A joint ILAP Steering Group (including NICE and SMC) was established in January 2021. It will meet every fortnight to consider Innovation Passport applications and review ILAP priorities for resourcing and toolkit development. Other potential future partners include NHSE&I, the National Institute for Health Research (NIHR[20]), and the HRA.

37. As the ILAP proposition matures, and the toolkit increases the scope of services offered, there will be a corresponding increase in engagement across the UK health system. For example, the first use of the ILAP tool "Novel Methodology & Innovative Clinical Trial Design" will bring forward formal engagement with NIHR and HRA.

38. The path to future releases and updates to the ILAP proposition involves broad consultation and collaboration across the whole UK health system. This is highly desirable. It will allow the depth of scientific, technical, clinical, ethical, commercial, and regulatory knowledge available from the health system to be leveraged for the benefit of faster patient access to more innovative products.

[19] See also https://www.gov.uk/government/publications/innovative-licensing-and-access-pathway-ilap-for-medicines/application-tools#future-tools-of-the-toolkit

[20] https://www.nihr.ac.uk/

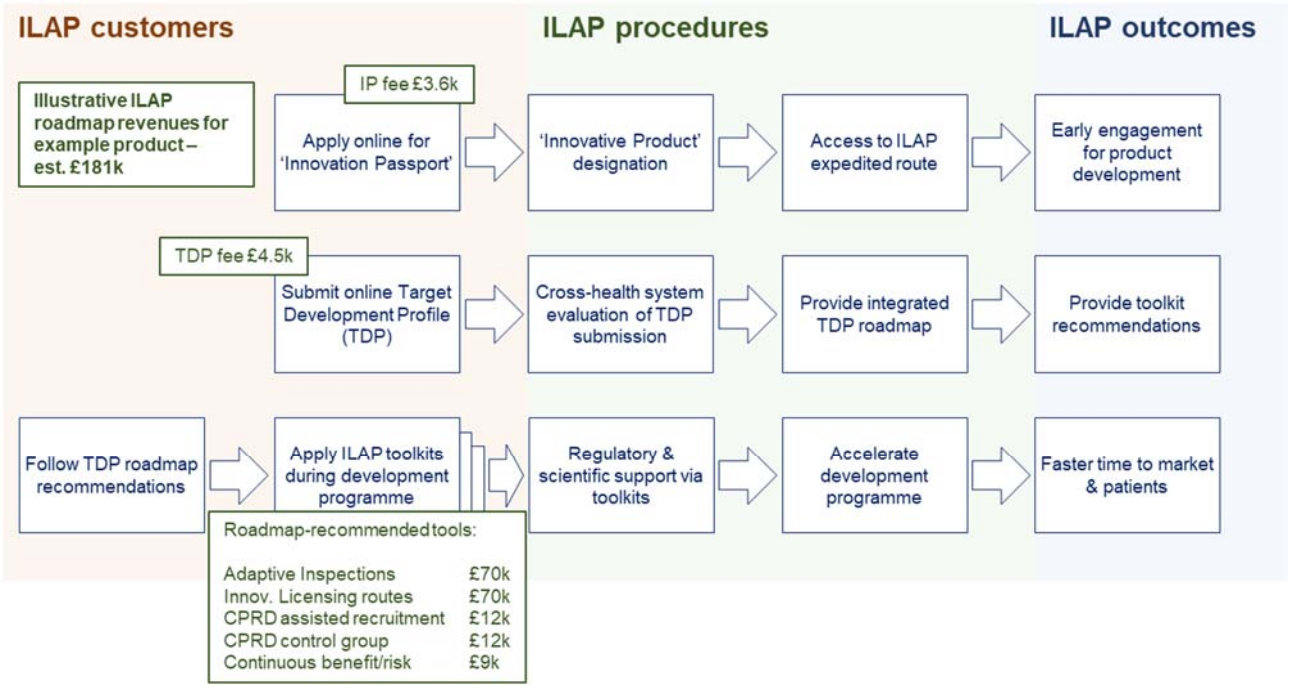
F. ILAP Revenues & Marketing

39. A market analysis on potential demand has not been carried out. However, based on analysis of EMA approvals for new active substances and extensions of new indications over two years (2018 and 2019), approximately 10 molecules with significant benefits come through each year. ILAP could see higher volumes (42 and 30 respectively in the same two years) since ILAP eligibility criteria are broader and would include all new active substances. From the future applications submitted to the EMA, 21 products of significant benefits are likely to be eligible for this pathway.

40. The importance of an integrated marketing and communications strategy is recognised by the project. Proactive and reactive media handling is already in place. Development of a marketing campaign for ILAP is dependent on:

- Market analysis to establish the likely demand for ILAP in key target markets and sectors.
- Customer insights to establish better understanding about users' requirements of the service.
- Internal capacity to satisfy demand in target product areas (for example ATMPs, biologicals).
- Price modelling to establish payback timings and rates of return on investment.

41. Extrapolating fees chargeable for one of the pilot products, and following all TDP roadmap recommendations, could generate approx. £181k revenue. This could be derived from application and toolkit fees accruing along the path to an eventual marketing authorisation:



G. Measures of Success

42. The ILAP Steering Group have proposed an initial list of measures for monitoring progress with ILAP. This is subject to agreement with partners, including NICE.

- Numbers of IP applications requests over time.
- Positive/negative IP outcomes.
- IP fees earned cumulative.
- Numbers of TDP request over time.
- TDP fees earned over time.
- Number of times the TDP individual tools are requested over time – list all tools available from the tool kit.
- Fees earned per tool.
- Number of patient engagement activities over time.
- Comparison of final GB marketing approval date with other regions – EMA, the US Food and Drug Administration (FDA[21]), and globally.
- Comparison of final GB approval date with first health technology assessment (HTA) decisions of NICE and SMC.

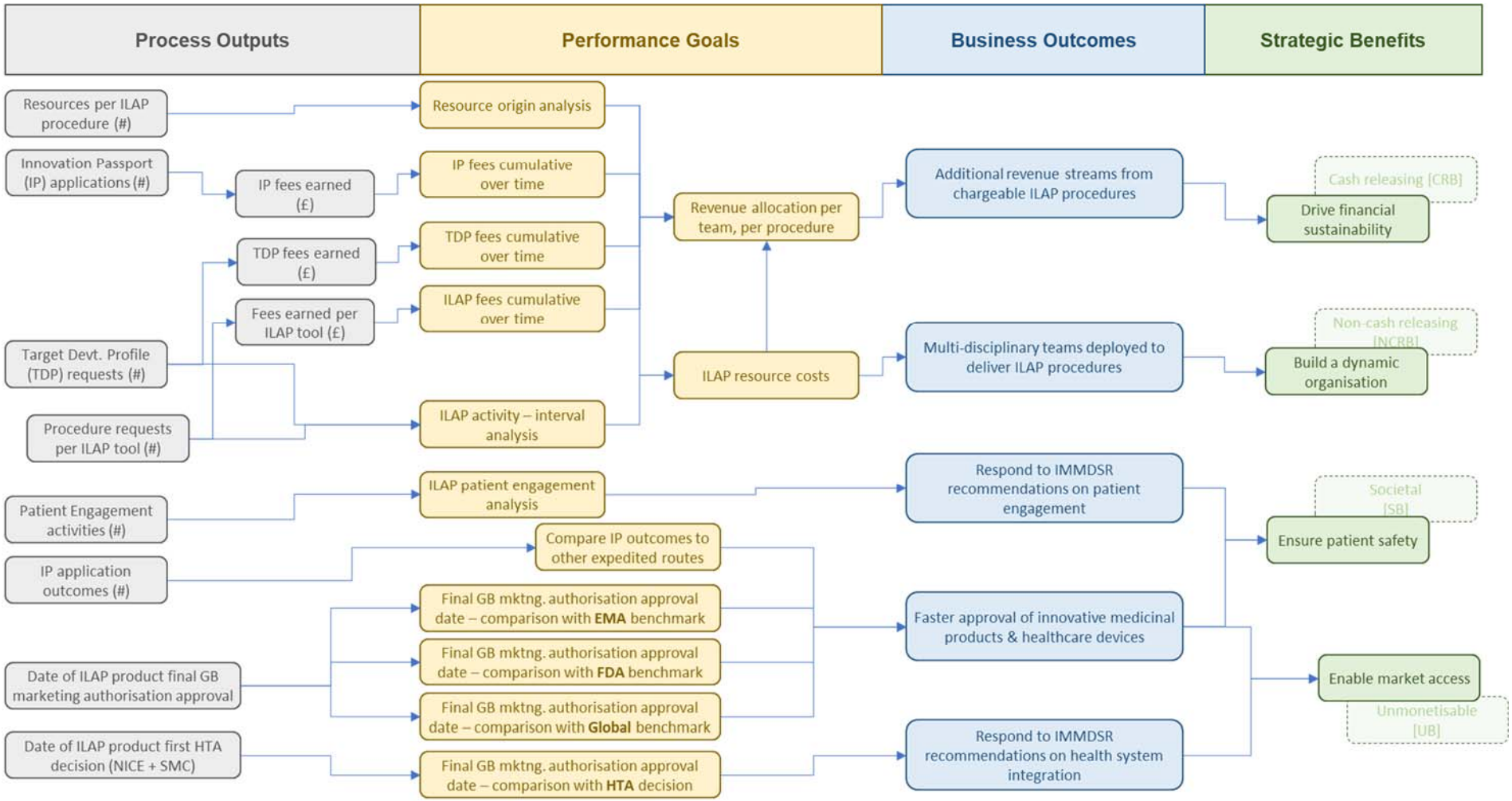
43. Meetings with partners are being sought to validate this proposed list of measures and also to develop an agreed set of success criteria. NICE representatives have been engaged already to confirm their availability during early February 2021 to work on this list.

44. Further management information will be gathered that compares the frequency and volume of procedures following ILAP, EAMS, and AAC routes, monitoring of designations (such as IP and PIM), and also to compare throughput and outcomes with equivalent global expedited pathways, *e.g.* PRIME from the EMA.

45. Additional measures are needed for patient-focussed outcomes and faster market access. The source of data to support these measures, and the way in which outputs are linked to outcomes, is in scope for the next release of ILAP.

[21] https://www.fda.gov/home

46. Process outputs and performance goals for ILAP are being discussed and agreed with the Agency's partners. The economic framework below is under development with support from Policy division. It serves to illustrates how metrics for process outputs, performance goals, and business outcomes can be linked to strategic benefits. Further work on this framework is expected in coming weeks.



Annex 1 – Summary of ILAP toolkits

Ref.	Tool Name	Description
1.	Adaptive Inspections	Designed to support the over-arching innovative licensing pathway to enable transformed regulation. An adapted pathway of 'enabling' and 'assurance' supported by regulatory inspections will be established on a product-specific basis, which may include manufacturing, live phase, and pre- or post-authorisation inspections (including real world data aspects) dependent on risk and licensing conditions. This will provide additional assurance to patients that UK medicines brought to them faster will have no compromises on safety standards.
2.	Certifications	Building on the Agency's scientific advice approach, the Certification tool provides developers with an enhanced official regulatory review of packages of Common Technical Document (CTD) data (including module 1). The process will provide applicants with specific and actionable feedback on the expectations for marketing authorisation and the regulatory requirements, highlighting potential deficiencies and where there are key issues to address.
3.	Continuous Benefit Risk Assessment + RWE	Provide applicants with guidance and support to ensure that the agreed approach delivers the right data to fill potential gaps in evidence within the right timeframe, to further define and characterise a product's benefit:risk profile but also to support cost:benefit decisions. Realise the benefits of Real World Data to support rapid generation of evidence on real-world benefits and risks of products to best support patient safety alongside facilitating access.
4.	CPRD Assisted Patient Recruitment	Innovative locate-and-recruit service driven by real world data (RWD) to provide a fast, targeted, and efficient approach to recruitment into clinical trials in any setting. Includes phase II and phase III clinical trials, and phase IV clinical effectiveness pragmatic trials within primary care. CPRD will model inclusion and exclusion criteria for prospective clinical trial populations to select potentially eligible trial subjects. They then organise further clinical review within General Practice to subsequently invite highly selected potential trial subjects to participate in the clinical trial involved.
5.	CPRD Control Groups	Provide access to primary care real-world data, plus linked secondary care data, to enable the use of real-world data virtual control arms. This can replace "historical controls" with more sound and RWD as a comparator, either as natural disease course ("virtual placebo") or against the therapeutic standard of care. CPRD expertise can provide balanced options for generation of external control arms, e.g. to manage the difficulty of distinguishing treatment effects from other factors in the context of a single arm trials, or in more conventional trials to determine generalisability of clinical trial outcomes.

Ref.	Tool Name	Description
6.	Enhanced patient engagement	Patient engagement is the effective and active collaboration of patients, patient advocates, patient representatives and/or carers in the processes and decisions within the medicine lifecycle, along with all other relevant stakeholders when appropriate. This tool provides opportunities throughout the Pathway for companies to consider the 'patient's experience and voice' in a meaningful way in how they develop their innovative products.
7.	Innovative and Flexible Licensing Routes	The innovative and flexible licensing routes tool includes the following potential routes to market for medicines: ▪ Accelerated assessment ▪ Rolling review ▪ Approval with conditions ▪ Conditional marketing authorisation ▪ Approval under exceptional circumstances ▪ Project Orbis ▪ Australia, Canada, Singapore, and Switzerland (ACSS[22]) Consortium The routes include expedited timelines for review, pragmatic approaches to evidence requirements and international options (where available).
8.	Novel Methodology & Innovative Clinical Trial Design	Designed to establish a system and culture that is receptive and supportive of novel methodologies in both the clinical and pre-clinical space to develop new medicines or new indications. This includes innovative clinical trial designs, manufacturing, and endpoint development. We will also demonstrate that innovative methodologies are acceptable to all stakeholders, for example by issuing an opinion on the proposed methodology or technology.
9.	Rapid Clinical Trial Dossier Pre-Assessment	Provides sponsors of clinical trials with feedback from MHRA Clinical Trial Unit assessors on their trial documentation, prior to formal submission.

[22] https://www.gov.uk/government/news/uk-medicines-regulator-joins-up-with-australia-canada-singapore-and-switzerland-regulators

Annex 2 – Summary of future ILAP tools

Ref.	Tool Name	Description
1.	Advanced Therapy Medicinal Product (ATMP) Centre Accreditation	A potential MHRA accreditation of centres with specific expertise in ATMP development to provide assurance that trials and/or manufacture conducted by these centres are as safe as possible and meet an MHRA accredited standard, providing patient confidence in their regulation. Organisations in the scheme would exceed the basic GxP regulatory standards by having additional standardised procedures and a proven track record in this field, ensuring high-quality data, to facilitate regulatory decision making and ensure the highest standards for protection of patients
2.	Coordinated approval of research involving investigation of both a medicine and medical device	This tool offers a combined assessment of clinical trials that involve both an investigational medicine and an investigational medical device. Looking to optimise the regulatory pathway for research for combined medicines and medical devices.
3.	Combined in vitro diagnostic (IVD) and investigational medicinal product development	This tool looks to offer a combined assessment of clinical trials where there is an investigational medicine and IVD such as. a companion diagnostic. This is to optimise and where necessary adapt the clinical trial regulatory pathway for research that requires combinations of medicines and in vitro diagnostics
4.	CPRD Control Groups	The CPRD Control Group tool provides access to CPRD primary care real world data to enable the use of real-world data virtual control arms drawn from relevant and high-quality real-world data as comparators. Uses and applications of virtual control groups are currently being assessed but may be of potential use as natural disease course or standard of care comparators. They may have a specific role in distinguishing treatment effects from other factors in the context of a single arm trials
5.	Development of quality standards	Quality standards can be written or physical materials that help provide assurance of the quality of a material or product, or the performance of the analytics used in the control strategies for the material or product. This tool would look to use the MHRA's existing quality standards setting functions of the British Pharmacopoeia and NIBSC to identify and develop standards through the TDP process that would support the assurance of product quality and facilitating the assessment of the medicine.

Annex 3 – Global Regulatory Network Comparisons

The ILAP project conducted an assessment of global expedited regulatory pathways with the following review objectives:

- Identify and describe the expedited regulatory pathways of major medicines regulators – EMA, FDA, Therapeutic Goods Administration (TGA[23]), and Health Canada[24].
- Establish the demand and uptake trends for expedited pathways.
- Compare the MHRA proposition to those of the identified global regulators.
- Interest from Swissmedic[25] around our ILAP criteria which are used to filter products for Project Orbis.

i. **EMA**
The PRIME scheme offers enhanced support for development of medicines that might offer major therapeutic advantages over existing treatments, or which benefit patients without treatment options and therefore target unmet medical needs. Commencing 2016, and up until November 2020, approx. 240 applications and eligibility requests[26] have been made to the PRIME scheme. Key features include accelerated approvals leading to marketing authorisation applications, early engagement on regulatory strategies and development plans, and scientific advice fee waivers for SMEs.

ii. **FDA**
Four main expedited review and development pathways are offered: Accelerated Approval, Fast Track, Priority Review, Breakthrough Therapy. Approx. 60% of novel drugs approved in 2019 by FDA's Centre for Drug Evaluation and Research (CDER[27]) used one of these expedited pathways. Key features include approvals based on surrogate endpoints, enhanced regulatory engagement, guidance on development programmes, and rolling reviews for applications for biologics and new drugs.

iii. **TGA**
Offers two expedited approval pathways – Priority Review and Provisional Approval. Goal is to fast-track prescription medicines to market and therefore make available to patients sooner (than compared to standard pathway). Between January 2018 and July 2019, a total of 28 applications[28] had followed expedited pathways (16 via priority review, 18 via provisional approval). Features include early and ongoing benefit:risk assessments, flexible review process, and early availability of products still completing clinical trials.

[23] https://www.tga.gov.au/
[24] https://www.canada.ca/en/health-canada.html
[25] https://www.swissmedic.ch/swissmedic/en/home.html
[26] https://www.ema.europa.eu/en/human-regulatory/research-development/prime-priority-medicines
[27] https://www.fda.gov/about-fda/fda-organization/center-drug-evaluation-and-research-cder
[28] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6698240/

iv. **Health Canada**
Also offers two expedited approval pathways – Priority Review and Notice of Compliance with Conditions (NoCwC). Approx. 30% of all products have followed an expedited pathway. Applications may be subject to both pathways during their lifecycle. Features include shortened review targets, and new drug/new indication NoCwC in return for additional post-market studies.

As well as recognition of best practice across the global regulatory community, the review also identified several key points of difference for the ILAP proposition:

Innovation Passport
Access to the pathway is controlled through a new innovative product designation that provides a signal to stakeholders across the health system, and which links the development of a product roadmap to patient access.

Target Development Profile (TDP)
Provides a roadmap of future interactions with scientific, regulatory, and clinical experts from across the Agency and the wider UK health system. This illustrates the support that Companies can expect, thereby providing more regulatory certainty for innovative products and novel approaches.

Integrated Partnership Procedure (IPP)
Multi-stakeholder engagement that enables the execution, coordination, monitoring, and control of activities required to fulfil the TDP roadmap.

Patient Engagement
The focus on patient-centricity provides reassurance for partners, customers, and stakeholders that innovative product development programmes and regulatory decision-making always considers the patient voice in a meaningful way. This means that designated innovative products will address patients' needs.

Pathway Toolkit
Provides innovative, flexible regulatory activities and approaches which are designed to bring clinically-important and promising products to patients faster and efficiently.

Annex 4 – Innovation Passport Criteria

The Innovation Passport (IP) designation acts as the gateway to ILAP and its future related activities. The qualifying criteria for IP designation have been developed jointly by MHRA, SMC, NICE, and NHSE&I. It is worth noting that IP eligibility criteria are more open than those used for AAC.

All three criteria should be met for a positive opinion. Entry can be as early as non-clinical data:

Criteria 1: details of the condition, patient or public health area

a) **The condition is life-threatening or seriously debilitating.**
Applicants are expected to provide summaries of the condition and the life-threatening or seriously debilitating nature including symptoms, life span and quality of life aspects, and current treatment landscape.

or

b) **There is a significant patient or public health need.**
Significant patient or public health needs require clearly-defined evidence of a specific need (e.g. need for paediatric formulation, anti-microbial resistance), putting the need into the context of the current patient or public health setting. This evidence is likely to be generated from information in the public domain and/or patient engagement activities. For a justification of 'significant', the magnitude of the issue(s) should be discussed in a problem statement along with the identified gaps that remain in the current treatment landscape.

Criteria 2: the medicinal product fulfils one or more of the following areas:

a) **Innovative medicine such as an advanced therapy medicinal product (ATMP), or new chemical or biological entity, or novel drug-device combination.**
A full regulatory description of the product would be expected so that the product status can be determined (e.g. name of drug substance, pharmaceutical form, route of administration, mechanism of action).

b) **The medicine is being developed in a clinically significant new indication.**
A description of the new indication should be provided in the context of the patient group, including the novelty of the proposal.

c) **Medicine for rare disease and/or other special populations such as neonates and children, elderly and pregnant women.**
A description should be provided of the use of the medicine in a particular special population.

d) **Development aligns with the objectives for UK public health priorities such as the Chief Medical Officer, Department of Health and Social Care (DHSC) or Life Sciences Sector Deal (including those in Devolved Administrations, where appropriate).**
A description should be provided how and where the product will fulfil public health priorities.

Criteria 3 the medicinal product has the potential to offer benefits to patients

For this criterion the applicant is expected to provide a summary of how patients are likely to benefit from the product or indication coming to market, including proposed improved efficacy or safety, contribution to patient care or quality of life, as compared to alternative therapeutic options. This should be based on evidence from the applicant with the product.

The claims can be supported either by data from valid non-clinical models of the condition or if justified extrapolated from another relevant model.

Depending on the stage of development of the product, if available, clinical data in a relevant population of patients can be provided. Applicants are strongly encouraged to include the views from patients or patient organisations around the benefits of a product in their evidence, if available.

Medicines & Healthcare products Regulatory Agency

Board Meeting Held in Public

16 February 2021

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

Issue:

Summary of the first meeting of the Patient Safety and Engagement Committee.

Action required by the Board and by when (timings):

To note the issues under discussion and request any further actions.

Implications for patients and the public:

The Patient Safety and Engagement Committee is an assurance committee of the Board that provides independent consideration of patient safety and patient engagement, such that these are paramount in regulatory decision-making.

Which of the theme (s) in the Corporate Plan 2019/2023 does the paper support?

If relevant, which Business Plan strategic activity does it support?

Contributing to system wide response to the Independent Medicines and Medical Devices Safety review, including a fundamental review of our engagement with UK patients and the public to impact public health and patient safety

Author (s):

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

Chair's Summary of the Patient Safety and Engagement Committee (PSEC) held on 3rd February 2021.

Background

The first meeting of the Patient Safety and Engagement committee was held on the 3rd of February 2021.

There were two main items of business. The first was the Patient and Public Engagement and Involvement Strategy. This item took up most of the meeting, but discussions led to recommendations for the second item, the work schedule for the Committee. There was an item of any other business about the Clinical Practice Research Datalink (CPRD).

Patient and Public Engagement and Involvement Strategy

This strategy was developed in response to a major public consultation on how the Agency could further engage and involve patients and the public in its work. The strategy had been shared with the Patient Group Consultative Forum of the Agency and after amendments had also been discussed by the Executive Committee. Following consideration by the Committee it would be further developed and shared with the Board before a further short public consultation in advance of finalising and publishing the strategy.

The Committee sought clarification and raised issues for further development. Clarification was needed on working with individual patients as well as patient groups. More thought is needed about capturing patient experience and knowledge, as opposed to their "views". It was also suggested that the Agency needs to engage health professionals, and especially doctors, as an important conduit to reach patients – the Committee was assured that work is under way to develop a healthcare professionals' strategy and this would come to a future meeting of the Committee. There was support for using the implementation of the Innovative Licensing and Access Pathway for medicines to look at people's understanding of risks and benefits, and consent.

The outcomes listed in the Strategy were welcomed but some needed to be more specific, some were hard to measure and should be more focused on outcomes. For example, there were some areas where it needed more stringent outcomes such as Clinical Trials protocols. These needed to do more than recommend patient reported outcome measures. The work under way to develop the Agency's culture was welcomed. Staff will need to believe that the patient perspective adds value. If not, there is a risk that getting patient input may become a tick box activity.

There was some discussion on how to measure cultural shifts in the organisation. Exploring the idea of an engagement index used by some organisations might be a way to start to do this.

Prospectively collecting evidence on what had been effective and being able to publish in peer reviewed journals would be an important measure of the evaluation of the strategy, as well as publicising the MHRA's achievements on this area. Cross agency co-ordination and responsibility for the strategy was important and the Committee noted that the number of staff for this work within the Agency, is relatively small compared to other organisations.

Work Schedule

The discussion on the Patient and Public Engagement and Involvement Strategy led to some key priorities for the Committee. The main one was the Independent Medicines and Medical Devices Safety Review and the need to look at patient harms, patient experience, and the involvement of patients in decision making. The Committee requested more information on surveillance and the Yellow Card scheme, especially how this is changing under the roll out of vaccines for COVID. It was agreed that a draft work schedule be brought back to the next Committee meeting by the Chief Executive Officer.

Any Other Business

A review of the Clinical Practice Research Datalink had been carried out and the Executive felt that the correct governance route for agreeing the implementation framework would be through PSEC. Unfortunately, due to short notice, the papers were not ready for the Committee. The Chief Executive Officer suggested that this item be brought to the next Committee meeting.

Conclusion

Discussion of the Patient and Public Engagement and Involvement Strategy raised a number of issues that need to be clarified and explored. The Patient Safety and Engagement Committee is scheduling meetings every two months in advance of meetings of the Board, until the end of the calendar year. It has started to prioritise its work programme.

Mercy Jeyasingham
Chair Patient Safety and Engagement Committee
Non-Executive Director MHRA
February 2021

Medicines & Healthcare products Regulatory Agency

Board Meeting Held in Public

16 February 2021

What assurance can be provided by the Organisational Development and Remuneration Committee?

Issue: The Organisational Development and Remuneration Committee (ODRC) met on 4th February 2021 with the aim of providing assurance to the Board.
Action required by the Board and by when (timings): The Board is asked to consider the ODRC's consideration of the following topics and provide feedback: a. People Survey. b. Talent. c. Organisational Development. d. People Strategy. e. Continuing/Future Topics of Consideration.
Implications for patients and the public: The Organisational Development and Remuneration Committee provides independent and objective advice to the Agency Board and the Chief Executive on their responsibilities relating to workforce planning, development and rewards at the Medicines and Healthcare Products Regulatory Agency (MHRA); with the aim of developing a regulatory organisation which effectively delivers for patients, the public and other stakeholders.
Which of the theme (s) in the Corporate Plan 2019/2023 does the paper support? All and particularly Organisational Excellence **If relevant, which Business Plan strategic activity does it support?**
Author (s): Anne-Toni Rodgers (Chair)
Board Sponsor: Anne-Toni Rodgers (Chair)

Organisational Development and Remuneration Committee 04 February 2021

Chair's summary of key outcomes

1. What assurance on the People Survey can be provided by the Organisational Development & Remuneration Committee?

The Committee received a presentation on the MHRA results following the October 2020 Civil Service People Survey from Jon Fundrey & the Human Resources (HR) Director. In addition to the traditional areas of focus (Leadership, Management, Organisational Effectiveness, Learning & Development etc) additional questions were added to understand the impact of Coronavirus and remote working and specifically for the MHRA questions regarding change management, wellbeing and customer service.

There was a high level of participation from the Agency staff and we are assured that the Agency has a clear understanding of the views of staff and their wellbeing, locally and cross Agency.

The Committee was reassured that in this era of remote working the majority of the workforce has a positive impression of their managers & team members efforts to keep in touch and their pride in working for the MHRA; however, we echo the Agency's concerns regarding the negative impact on COVId-19 of staff mental health, and are assured by their focus on responding to this issue.

The Committee is assured that the Agency has a clear plan to manage cross agency communication of the People survey results and develop local/team response strategies; and that these will be reviewed and monitored for progress by the People and Culture Committee over the coming months. The Committee recognised that whilst staff report their managers are supportive of their wellbeing there should be immediate cross agency consideration of leadership during change and that it would be helpful to develop a deeper understanding feedback vs customer needs, (a high proportion of staff report that they understand customer's needs, and it would be helpful to understand who are considered customers i.e. patients vs stakeholders)

The Agency's staff have showed that whilst facing the challenges of 2020 they have a high level of self-awareness, they have remained focussed, have taken a pride in their work and delivered for patients. We are assured that the Agency recognises the current challenges to staff health and well-being and that with this year of further change they will maintain a focus for support in this area.

2. What assurance on Talent can be provided by the Organisational Development & Remuneration Committee?

The Committee received a presentation on the Agency's Talent Board and its process for identifying, supporting and developing Talent, along with the Agency's approach to succession planning, from the Director of HR. The Committee is assured that the Agency follows and effectively delivers a process that meets cross-industry standards. The Committee asked that given the coming year of organisational change that the Talent Board review the Agency's Talent and Succession plans and in addition to identifying internal talent, look externally to identify talent that might benefit the Agency and the patients it serves.

3. What assurance on Organisational Development can be provided by the Organisational Development & Remuneration Committee?

The Committee discussed the Agency's Organisational Change Planned Timeline, Principles for Change, high level risks and plans for communicating the future operating model to staff. The discussion reinforced the need for messages to be straightforward, since the key question 'what does this mean for me' will be at the forefront of everyone's mind. There was a focus on having a clear timeline for next steps, and the proposal for the design phase of February to May was considered to be too long if the target of change by year end is to be met. The Committee considered that the new structure should be 80% in place by April.

The Committee recognised that when organisations face change up to 20% of talent may 'jump ship'. The Agency should quickly work to combine its understanding of its people with the leadership capabilities and expertise required to develop a world leading innovative regulatory organisation to focus on retaining this talent within the new structure.

The Committee also recognised as with all organisations there will for some resistance to change; the view was expressed that 'blockers' should be identified and managed by mid-March. A particular risk to be managed is the propensity for people to agree with a decision, and then not support its implementation, a recent example being the Customer Service Centre which had been agreed by the Corporate Executive Team but subsequently the transfer of staff to the Centre was blocked, unnecessarily extending delivery of a change that delivers benefit for the Agency and the people it serves.

The Committee considered that additional risks to delivering the organisational change would become apparent during and after the staff meetings (w/c 8 February), and that future assurance which could be provided to the Board would be informed by these meetings.

The committee was pleased to note the recent appointment of the Transformation Director

4. What assurance on The People Strategy can be provided by the Organisational Development & Remuneration Committee?

The Committee received a presentation on the People Strategy from the Director of HR. Both the Agency People Strategy and the Civil Service People plan have expired. Given the unique nature of the Agency it was agreed that a new People Strategy should be developed and a clear plan for its preparation and delivery was presented. The Committee approved this plan and are assured that it will build upon the One Agency Design Principles, the priorities outlined in the Agency's Corporate Plan and with a consideration of people related risks within the Agency Risk Register. The committee will review the first draft of the People Strategy in March 2021.

5. Areas of Focus

The Committee has identified the following as a future/continued focus for its work:

- Organisational Change (including: Principles for Change, Processes, Talent, Accountability, Diversity, Timelines, managing risk).
- People Strategy.
- Talent & Succession Planning.
- Executive Renumeration Decisions.
- Culture.
- Delivering One Agency.
- Executive /Management mentorship.
- Sounding Board for specific challenges as they may occur.

Medicines & Healthcare products Regulatory Agency

Board Meeting Held in Public

16th February 2020

What is the current financial performance of the MHRA against its 2020/21 Business Plan?

Issue: A summary of the current financial performance of the agency based on the first nine months of the year.
Action required by the Board and by when (timings): The Board is requested to note the agency's financial position at the end of December 2020 (nine months of the financial year) and propose opportunities for improvement.
Implications for patients and the public: The agency is currently making a financial loss which must be addressed to make the best use of public money.
Which of the theme (s) in the Corporate Plan 2019/2023 does the paper support? **If relevant, which Business Plan strategic activity does it support?** All
Author (s): Deputy Director of Finance
Board Sponsor: Jon Fundrey

What is the current financial performance of the MHRA against its 2020/21 Business Plan?

1. This paper provides a summary of the agency's financial performance against the 2020/21 budget. The year-to-date results for the 9 months of the current financial year are subject to audit and as such are preliminary. The full year forecast estimate has been updated to reflect the actual financial performance as at end-December 2020. Forward-looking estimates and statements are based on management's current views and assumptions and, as a result, are subject to risks and uncertainties that could cause actual results to differ materially from those projected.

2. The Agency achieved a better financial performance vs budget for the 9 months to 31 December 2020 incurring an operating deficit of £3.4 million compared to £6.6 million planned. This is explained by additional income from an influx of national procedure applications and the completion of outstanding work on decentralized authorizations and variation procedures. Year to date operating costs were less than budget albeit the 2020/21 cost base has increased from last year mainly due to an increase in salary costs. The overall agency cost base is estimated to remain largely in line with the Financial Year budget and last year, as an increase in pay costs is offset by lower non-pay costs. The agency is currently forecasting a Financial Year operating deficit of £7.5 million versus a planned deficit of £9 million. The total planned deficit is £2.2 million after DHSC funding and a forecast change expenditure of approximately £20 million.

Finance Report — December 2020

December 2020	Last YTD Actual £M	This YTD Actual £M	This YTD Budget £M	*Variance vs Budget %*	Last Year Actual £M	This Year Forecast £M	This Year Budget £M	*Variance vs Budget %*
Trading Income	88.2	84.7	86.4	(2%)	117.5	110.1	115.3	(4%)
Income from DHSC	19.5	21.4	20.9	2%	27.0	28.5	27.9	2%
Other Income	0.0	0.0	0.0	0%	0.0	0.0	0.0	0%
TOTAL INCOME	**107.7**	**106.1**	**107.4**	**(1%)**	**144.5**	**138.6**	**143.2**	**(3%)**
Staff Costs	64.4	67.3	67.7	1%	86.9	90.9	90.4	(1%)
Operating Costs	42.4	42.2	46.2	9%	61.4	55.2	61.6	10%
TOTAL EXPENDITURE	**106.7**	**109.5**	**113.9**	**4%**	**148.3**	**146.1**	**152.0**	**4%**
OPERATING SURPLUS	**0.9**	**(3.4)**	**(6.6)**		**(3.8)**	**(7.5)**	**(8.9)**	
DH Brexit Funding	0.0	0.0	12.8	(100%)	11.0	12.8	12.8	0%
ESC Funding	0.0	0.0	0.0	0%	1.6	0.0	0.0	0%
HMT Pension Funding	0.0	2.2	2.2	0%	2.2	2.2	2.2	0%
DH Funding Non-Cash	4.9	3.0	3.0	0%	6.6	4.0	4.0	0%
DH Capital Funding	4.5	4.5	4.5	0%	6.0	6.0	6.0	0%
TOTAL EXTRA FUNDING	**9.4**	**9.7**	**22.4**	**(57%)**	**27.4**	**25.0**	**24.9**	**0%**
Change Staff Costs	0.9	0.5	0.7	22%	1.5	0.7	0.9	23%
Change Costs	6.1	10.6	13.8	23%	5.9	19.0	21.4	12%
TOTAL CHANGE COSTS	**7.0**	**11.1**	**14.4**	**23%**	**7.4**	**19.7**	**22.3**	**12%**
TOTAL SURPLUS	**3.4**	**(4.9)**	**1.4**		**16.2**	**(2.2)**	**(6.3)**	

Staffing

FTE (rounded, as at 31 December 2020) - Actuals and Vacancies From Oracle Fusion

	Perm FTEs	Contract FTEs	Actual FTEs	Funded FTEs	Variance (FTEs)	Actual YTD (£k)	Budget YTD (£k)	Variance (£k)
Total FTE	**1,217**	**112**	**1,329**	**1,302**	**(27)**	**67,206**	**67,720**	**514**

Medicines & Healthcare products Regulatory Agency

Board Meeting Held in Public

16 February 2020

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

Issue: The Audit and Risk Assurance Committee met on 1 February 2021 with the aim of providing assurance to the Board.
Action required by the Board and by when (timings): The Board is asked to endorse the need for greater focus on benefit realisation risks and how this is reported to the Board.
Implications for patients and the public: The Audit and Risk Assurance Committee will provide assurance to the Board that the Agency has the necessary systems, controls and governance to manage risks and discharge its financial responsibilities in line with public sector requirements.
Which of the theme (s) in the Corporate Plan 2019/2023 does the paper support? **If relevant, which Business Plan strategic activity does it support?** All and particularly Organisational Culture/Efficiency
Author (s): Michael Whitehouse
Board Sponsor: Michael Whitehouse

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

1. This report sets out the Audit and Risk Assurance Committee's (ARAC) response to an action assigned to it at the 26 October 2020 Board meeting and summarises key outcomes from ARAC 's meeting on 1 February 2021.

   Action: ARAC to review the financial scenarios and risks around the Future Operating Model.

2. ARAC reviewed the corporate risk register, the outline for the new operating model as endorsed by the Board at its January 2021 meeting in committee, and discussed the timetable for its implementation together with progress to date.

3. Adapting to the reduction in fee income, the change in trading fund status, and the significant investment required to replace legacy systems with enhanced digital capability are significant challenges. The time frame to resolve them is very short and a two year delivery plan is being developed for approval by the Board for the start of the new financial year in April 2021.

4. ARAC was assured that the corporate risk register comprehensively addressed the key issues and scenarios which need careful management if the Agency is to be both financially resilient and remain an effective Regulator.

5. ARAC consider that the management of these and other uncertainties could be strengthened by making a distinction between implementation and benefit realisation risks. The scale and necessary speed of the change to move to the new operating model and matrix way of working inevitably increases risk. This is because of the interdependency and time criticality of many of the changes being introduced. In spite of best intentions there will always be some optimism bias and unforeseen circumstances. Where these arise, they can be better managed if the implications for intended benefits are understood in terms of public health and/ or financial resilience, and potential reputational impact. The implementation plan to be considered by the Board in March would be strengthened by an analysis of the underlying risks and how these are being managed.

Other issues covered by ARAC:

Financial performance

6. ARAC emphasised the importance of maintaining transparency on the impact of COVID-19 on the 2020/21 financials. The impact on costs thus far has been positive because the Agency spent a lot less on travel and subsistence, and other staff-related costs were also well below pre-lockdown levels. Inspections lost revenue due to lockdown because their current operating model is predominantly physical with inspectors visiting manufacturing sites.

External Audit

7. ARAC received and approved the NAO /KPMG plan for the external audit of the Agency's financial statements for 2020/21 together with the accounts and annual report preparation timetable. The interim audit was under way and no issues of concern were brought to ARAC's attention. The Agency is on target to present its Annual Report and Accounts (following ARAC's scrutiny) to the Board for approval at its meeting on 15 June 2021.

Internal Audit

8. Internal Audit has completed five of its reviews as part of its annual programme. ARAC was given assurance that Internal Audit would complete its full programme on time to inform the governance statement which Dr Raine has to sign as Accounting Officer with the Annual Report and Accounts.

9. ARAC approved a number of changes to Internal Audit's remaining 2020/21 programme including a review of the Agency's cyber security (as requested by John Quin) reflecting heightened external risks.

10. ARAC considered two Internal Audit Reports - Patient Engagement (moderate assurance) and Medical Devices (limited assurance). ARAC was very pleased that Mercy Jeyasingham, Chair of the Patient Safety and Engagement Committee, was able to join the discussion of these reports.

11. **Patient Engagement.** This concluded that the basic building blocks to strengthen patient engagement were defined including a patient engagement strategy. The imperative now was to develop them and embed them consistently in the MHRA's way of working. In doing so it would be important that the Agency drew on the experience of other organisations including NICE. While better patient engagement was relevant across the Agency, it was important that the Agency had a senior responsible officer to ensure that all relevant actions were effectively coordinated and benefit realisation monitored.

12. **Medical Devices.** This report assessed the framework which the Agency had put in place to ensure the successful implementation of the recommendations of the Independent Medicines and Medical Devices Safety Review by Baroness Cumberlege. ARAC was concerned by the limited assurance which arose largely from the need for greater clarity over specific responsibility for ownership of the implementation of each recommendation, their coordination, and how their impact in strengthening patient engagement and trust would be assessed.

13. ARAC concluded that both reports highlighted three wider actions which could help strengthen governance.
    - While the Agency is generally assiduous in responding to new demands placed upon it with a range of activities, it needs to be consistently confident that these are coordinated effectively, with senior responsibility assigned to ensure this happens.
    - Significant changes in approach should be underpinned by a robust benefit realisation framework.
    - There should be clarity over the level of resources allocated to a major new initiative or activity. For example ARAC sought assurance that resources allocated to implementing improvements in the regulation of medical devices were sufficient and would be used cost effectively.

14. An underlying theme in ARAC's discussions was the importance of cultural change as a key enabler .The Agency's impressive response to COVID-19 and the regulatory approval of the new vaccines was achieved by the careful balancing of the effective management of risk to public safety while securing the benefits of innovation. Mainstreaming this approach is important to the Agency's new ways of working.

15. The Board is asked to endorse the need for greater focus on benefit realisation risks and how this is reported to the Board.