Medicines & Healthcare products Regulatory Agency

AGENDA FOR BOARD MEETING HELD IN PUBLIC

10:30 – 13:00 on 23rd November 2020

Chair: Stephen Lightfoot

	AGENDA ITEM	PURPOSE	PRESENTER
10:30	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
10:40	CURRENT CONTEXT		
	4. What are the current key issues from the CEO point of view?	Discussion	June Raine
11:00	HEALTHCARE ACCESS		
	5. What are the most promising scientific research projects within the Agency that could have the biggest impact on protecting and improving patient health?	Assurance	Christian Schneider
11:20	PATIENT SAFETY		
	6. What is the assurance that the MHRA Enforcement Group can protect patient health by working with global partners?	Assurance	Sam Atkinson
11:40	FINANCIAL SUSTAINABILITY		
	7. What assurance can be provided by the Audit & Risk Assurance Committee on the current risks facing the MHRA and their proposed mitigations?	Assurance	Michael Whitehouse
12:00	DYNAMIC ORGANISATION		
	8. What are the strategic priorities for the new MHRA Corporate Plan (April 2021 – March 2024) and 2021/22 Business Plan?	Discussion	Jon Fundrey

12:20	ANY OTHER BUSINESS 9. What is the proposed membership of the Board Assurance Committees and the special responsibilities of the Non-Executive Directors?	Approval	Chair
	10. What are the 2021 dates for Board Meetings to be held in public?	Approval	Chair
	11. Are there any other urgent items for discussion?	Discussion	All
12:35	EXTERNAL PERSPECTIVE 12. What questions do members of the public have for the MHRA Board?	Discussion	Chair
13:00	CLOSE OF MEETING	-	Chair

Medicines and Healthcare products Regulatory Agency

Minutes of the Board Meeting Held in Public of 26th October 2020

(10:30 – 13:00)

By GoToWebinar conference call

Present:

The Board

Stephen Lightfoot	Chair
Professor David Webb	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
Anne-Toni Rodgers	Non-Executive Director
Dr Christian Schneider	Interim Chief Scientific Officer
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)

Elizabeth Woodeson CBE	Director of Medicines and Pharmacy, DHSC
Dr Alistair Hardisty	Head of MHRA Sponsorship and EU Exit, Medicines and Pharmacy Directorate, DHSC

Devolved Administrations

Kerry Chalmers	Medical Devices and Legislation Head of Unit, Scottish Government
Christopher Garland	Principal Pharmaceutical Officer, Northern Ireland

Item 1: Introduction

What are the priorities for this meeting?

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. Following a governance review in the summer of 2020 a unitary Board has been created, formed of the Chairman, Chief Executive, 7 Chief Officers and 7 independent Non-Executive Directors. This Board does not take regulatory decisions on individual products – it advises on the strategic leadership of the Agency. The agenda is structured around the Agency's four key strategic priorities: patient safety, healthcare access, dynamic organisation, and financial sustainability.

1.2 The Chair thanked Sir Michael Rawlins, the previous Chair of the MHRA, for his significant contribution to the MHRA over the last 6 years and to public health.

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

Item 2: Are there any Apologies or Declarations of Interest

2.1 Apologies were received from Professor Liam Smeeth, Non-Executive Director.

2.2 There were no declarations of interest.

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 agreed these have each been appropriately actioned.

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 diagnostics, and international work; (ii) patient safety – including updates on medicines and medical devices issues and on the Agency's patient and public engagement and involvement strategy; (iii) dynamic organisation – including updates on staff and accommodation, and the Agency's diversity and inclusion strategy; and (iv) financial sustainability – including updates on the Agency change programme and the Spending Review bid.

4.2 The Board thanked Dr Raine for her report and provided comments relating to the Spending Review bid and the Agency's future funding; the key role of NIBSC in the deployment of Covid-19 vaccines; the Agency's role in relation to Covid-19 tests; the strategy to establish real-time safety vigilance; and international collaboration. Communication with patients and the public was raised; it was noted that the Agency aims to test communications with patient representatives and relevant charities prior to publication.

4.3 The Board agreed with the priority issues presented and requested further information on the MHRA's wider work in the health system; an action was taken to provide an update to the Board on the Memorandum of Understanding with NICE.

Action 1: June Raine to provide an update to the Board on the Memorandum of Understanding with NICE by 23 November 2020

4.4 The Board noted that a new Diversity and Wellbeing lead has been appointed at the Agency; an action was taken to hold a Board seminar discussion on diversity and inclusion.

Action 2: Stephen Lightfoot to arrange a Board Seminar discussion on diversity and inclusion by 18 December 2020.

HEALTHCARE ACCESS

Item 5: What is the assurance that the MHRA can regulate multiple Covid-19 vaccine applications in parallel with priority, rigour and independence?

5.1 The Board considered a paper providing assurance that the MHRA can regulate multiple Covid-19 vaccine applications in parallel. The Board considered the MHRA's preparedness to deliver vaccine regulation as a priority, while also ensuring scientific rigour and independence are maintained. The report covered the work the MHRA has undertaken in four priority areas: (i) Early engagement and scientific rigour; (ii) Independence; (iii) Capacity; and (iv) Public and patient safety.

5.2 The Board agreed that the work the Agency is doing in parallel to regulate Covid-19 vaccines does not risk compromising standards: these applications are assessed in depth. The Board provided comments regarding OMCL batch release of the vaccines and was assured that batch release will be scaled up for a mass batch release programme.

5.3 The Board raised concerns regarding misinformation on social media and asked how to ensure the correct information and communication reaches patients; an action was taken to explore what can be communicated to patients on how and why the MHRA made its decisions when new Covid-19 vaccine applications have been determined.

Action 3: Sam Atkinson to explore what can be communicated to patients on how and why the MHRA reaches its decision when Covid-19 vaccine applications have been determined by 23 November 2020.

5.4 The Board provided comments on potential international data sharing and harmonisation of learnings. The Board was assured that the MHRA stands ready to deliver in support of the wider fight against Covid-19.

Item 6: What is the assurance that the MHRA will be ready to operate on Day 1 of EU Transition?

6.1 The Board considered a paper providing assurance that the MHRA will be able to operate on Day 1 following the end of EU Transition. The Board noted that the underlying objective of the Transition programme is to ensure that patients in all parts of the UK will continue to have access to existing and new medicines and devices and to meet healthcare needs from 1st January 2021.

6.2 The Board considered the measures which the MHRA is putting in place in order to be ready to operate on Day 1 of EU transition. The Board expressed its thanks to the GLD Legal team for their extensive work on EU Exit. The Board was reassured by

the pragmatic work the MHRA has been undertaking to maintain continuity of supply to Northern Ireland. The Board agreed on the importance of strong independent assurance on the Agency's work and noted the results of the recent audit by the Infrastructure and Projects Authority of Cabinet Office.

6.3 The Board provided a range of additional comments on the topics of the standstill, the Falsified Medicines Directive, the Statutory Instruments, and quality and integrity of medicines. The Board was assured on the MHRA's preparations to be able to operate on Day 1 after EU Transition.

PATIENT SAFETY

Item 7: What is the MHRA doing to address the recommendations of the Cumberlege Review?

7.1 The Board considered a paper providing an overview of the actions which the MHRA is taking in relation to the recommendations from the Independent Medicines and Medical Devices Safety (IMMDS) Review, led by Baroness Cumberlege. The Board noted the activities the MHRA has been undertaking in response to the report; and noted that the Agency is working with DHSC and other healthcare partners in preparation for the government response to the Review and to improve collaborative working across the healthcare system.

7.2 The Board provided comments on patient engagement and involving patients systematically in regulatory decision-making; providing specific feedback to reporters; bringing together and linking data from across the system; how the MHRA works with the NHS and pharmacy services to increase awareness through initiatives such as Medicines Safety week and World Patient Safety day; and engagement across the system with healthcare professionals. The Board was assured on the progress MHRA is making in taking action in relation to the recommendations from the IMMDS Review.

Action 4: Stephen Lightfoot to arrange a discussion on how to involve patients systematically in our regulatory decision-making in a Board Seminar by 23 November 2020.

DYNAMIC ORGANISATION

Item 8: What are the key responsibilities and assurance map of the new MHRA Unitary Board, Board Committees and Management Committees?

8.1 The Board considered the overall shape, key responsibilities and priorities of the revised MHRA Governance framework, which is being rolled out to establish more agile decision-making. The Board agreed that the Patient & Safety Assurance Committee of the Board is an important addition to scrutinise patient safety and engagement and to provide assurance to the Board.

8.2 The Board provided comments on the new Committees and emphasised the importance of linkage in the work of the Committees at the Executive level. The Board recommended scenarios should be drawn up by ARAC to stress-test the MHRA Governance framework to ensure the structure is robust in the event of a significant unexpected event.

Action 5: Michael Whitehouse to arrange for ARAC to draw up scenarios to stress-test the MHRA Governance framework to ensure that the structure is robust by 18 December 2020.

8.3 The headline Terms of Reference for each of the committees was discussed; it was agreed that the detailed Terms of Reference and membership of the Board Assurance Committees need to be finalised and agreed by the Board. The Board agreed the assurance framework should adequately provide clear routes of assurance in all directions across the Agency.

Action 6: Stephen Lightfoot to ensure that the membership and Terms of Reference of the Board Assurance Committees are finalised and agreed by the Board by 18 December 2020.

ANY OTHER BUSINESS

Item 9: What are the key items for discussion at the next MHRA Board Meeting?
9.1 The Board agreed this would be discussed further separately.

Item 10: Are there any other urgent items for discussion?

10.1 The Board noted that there were no other urgent items for discussion at this time.

EXTERNAL PERSPECTIVE

Item 11: What questions do members of the public have for the MHRA Board?

11.1 The Board answered a range of questions from members of the public.

ACTIONS FROM MHRA BOARD MEETING HELD IN PUBLIC ON 26 OCTOBER 2020

Action Number	Action	Owner	Date
Carried Forward From Previous Meeting			
3	Present an overview of how Device Registries, Unique Device Identifiers and Device Databases are being developed in the health system and the MHRA role in their development to strengthen device regulation	John Quinn	23/11/20
5	Arrange a Board Seminar to discuss how the MHRA could engage patients more widely, building on existing engagement activities by other organisations	Stephen Lightfoot	23/11/20
New Actions			
7	Provide an update to the Board on the Memorandum of Understanding with NICE	June Raine	23/11/20
8	Arrange a Board Seminar discussion on diversity and inclusion	Stephen Lightfoot	18/12/20
9	Explore what can be communicated to patients on how and why the MHRA made its decision when new COVID-19 vaccine applications have been determined	Samantha Atkinson	23/11/20
10	Include a discussion on how to involve patients systematically in our regulatory decision making in the Board Seminar agreed in action 5	Stephen Lightfoot	23/11/20
11	Draw up scenarios to stress-test the MHRA governance framework to ensure that the structure is robust when something goes wrong.	ARAC	23/11/20
12	The membership and Terms of Reference of the Board Assurance Committees need to be finalised and agreed by the Board	Stephen Lightfoot	18/12/20

Medicines & Healthcare products Regulatory Agency

Board Meeting held in public

23 November 2020

Chief Executive's Report to the Board

This report gives an overview of the current issues from the CEO's point of view. Separate papers give more detailed information on the Agency's scientific research projects which could have the biggest impact on protecting public health; how the MHRA's Enforcement Group protects patient health by working with global partners; and strategic priorities to enable the Agency to plan for the future. The Board is asked to consider and agree on the priority issues.

HEALTHCARE ACCESS

COVID-19 Vaccines, Therapeutics and Diagnostics

1. A key priority is to enable successful development, licensing and deployment of vaccines, therapeutics and diagnostics for COVID-19. In relation to vaccines, we are undertaking rolling reviews to consistent high scientific standards and with regulatory independence. The announcement of positive results from clinical trials of two mRNA vaccines has been extremely encouraging. The COVID-19 Vaccine Benefit Risk Expert Working Group of the Commission on Human Medicines (CHM) continues to review the emerging data and advise MHRA. Work is ongoing on the IT capability and tools to deliver real-time post-marketing surveillance. NIBSC will be working with the Coalition of Epidemic Preparedness Innovations (CEPI) to monitor and evaluate new COVID-19 viral strains globally and evaluate their impact on vaccine candidates. This follows recent attention to a newer variant strain in mink in Denmark. The CHM COVID-19 Therapeutics Expert Working Group continues to review emerging data on various products, including on monoclonal antibodies for treatment of COVID-19.

2. The Agency continues to work to support the national COVID-19 Testing Strategy. We are currently supporting developments in the 'mass testing' arena. We are also continuing to develop an expanded suite of Target Product Profiles (TPPs). We are also actively participating in a project group to develop alternatives to PCR testing as a means of increasing testing capacity. These projects are in their early stages of development and we are working to tight delivery deadlines. We are concentrating our efforts in post-deployment safety and surveillance. We are working with the NHSEI team to support data capture on any adverse incidents, batch problems and difficulties in using and reading the Tests. We are extending our surveillance activity in this area through engagement with the Medical Devices Safety Officers (MDSOs) in each Trust.

EU Exit – Day 1 Readiness

3. The DHSC and the MHRA have been in discussions with the EU Commission to ensure the continued supply of medicines to Northern Ireland at the end of the Transition Period. The Commission has recently agreed to grant additional flexibilities for a 12-month period, for industry to ensure FMD compliance and that regulatory importation requirements for medicines moving from GB to NI after the end of the transition period are met. The EU will shortly be publishing a Commission Notice containing the technical details of this agreement.

4. Our ongoing focus on communications has delivered 36 pieces of post-transition period guidance for industry relating to GB 'standstill' arrangements, to support the industry in preparing for 1st January 2021. This was followed by a series of nine webinars on key topics. The webinars are oversubscribed in almost all cases with a total of 21,655 registrations of attendance across all the sessions. Additional webinars are being considered for the most popular subjects. In terms of the legislative preparations, Statutory Instruments (SIs) for medicines and medical devices in both Northern Ireland (NI) and Great Britain (GB) will be debated in the House of Commons on the 26th November, and in the Lords on the 1st December. This includes implementing the NI protocol and the Government policy on unfettered access.

5. To ensure we are operational for 1st January 2021, IT systems for both GB and NI are being prepared. These IT systems have been developed so that they can operate irrespective of access to EU databases, which is contingent on the outcomes of the negotiations. Plans have been developed for each division of the MHRA to ensure people, processes and operations are in place for 1st January 2021. Additional staff to support the customer service centre through transition have been recruited and additional staff in other teams are being onboarded through October and November.

International work

6. The International Office continues to coordinate our international effort working with regulators around the world on matters relating to Covid-19 vaccines and therapeutics. MHRA is playing an active role in the International Coalition of Medicines Regulatory Authorities (ICMRA) where we co-chair the Covid-19 Working Group and lead two projects; one on vaccine vigilance readiness and another on the digital transformation of inspections. We are working together with the Access Consortium (Australia, Canada, Switzerland, Singapore and the UK) on information sharing with regards to ongoing vaccine assessments. This is accomplished by Access partners working together, aligned by high standards of scientific rigour and integrity, with reduced regulatory duplication. Work continues to prepare the wider Agency for active participation of the Access Consortium from January 2021 onwards.

7. The press release that announced the Access consortium also announced Project Orbis: A project to facilitate the simultaneous submission and assessment of innovative cancer treatments to leading international drug regulators. The programme is coordinated by the US Food and Drug Administration and involves Canada, Australia, Switzerland, Singapore and Brazil to review and approve promising cancer treatments. Several projects are underway and the MHRA is participating as an observer for the remainder of this year and then as a full participant for products from 2021.

8. Regarding bilateral relationships, the International Office recently organised a bilateral call with Israel for Licensing colleagues to discuss the regulations in the UK for cannabis-based products for medicinal use. This an area where we expect continued engagement. We are holding a further preparatory call with the Japanese regulator ahead of a Heads of Agencies bilateral call scheduled for 15 December, which will focus on enhancing cooperation between regulators. We continue to work on securing our membership of key international regulatory organisations such as the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) and the International Medical Devices Regulators Forum).

CPRD support for two new clinical effectiveness pragmatic clinical trials

9. Following on from the jointly hosted conference by CPRD, NIHR and HDRUK in 2018 showcasing the potential for using real world data to support clinical trials, NIHR launched a funding call for ambitious data-enabled trials. CPRD successfully collaborated with the University of Birmingham and with Alder Hey Children's NHS Foundation Trust to gain funding from the NIHR Call to support two large Phase IV pragmatic clinical effectiveness trials. CPRD will support delivery of these trials utilising the Interventional Research Service Platform trial management services. CPRD has worked closely with the MHRA Conflict of Interest subgroup to ensure all appropriate mitigations are applied where required.

PATIENT SAFETY

10. **Isotretinoin –** A public call for information was published on 10th November. This review is being undertaken by MHRA with advice from the Commission on Human Medicines and the Isotretinoin Expert Working Group due to concerns about the possible association between isotretinoin and suspected psychiatric and sexual disorders. The consultation will run until 2nd February 2021.

11. **Hand sanitisers** - As a result of the Borderline Section's online review of hand sanitiser products marketed in the UK with Coronavirus/ COVID-19 claims, the team has registered over 190 cases and have so far issued over 48 Urgent Notices requesting the removal of COVID-19 related claims or removal of the products from the UK market. The Urgent Notices issued cover a large number of products and the Borderline Section continues to investigate a large number of complaints related to hand sanitiser products advertised with COVID-19 related claims.

12. **Recalls and alerts** – there was one drug alert in October concerning Optiray ioversol injection due to reports received from healthcare professionals on the difficulties in attaching the Luer lock adapter; one class 3 medicines recall for metoprolol tablets as the manufacturer informed us that when decommissioning at the pharmacy and scanning the serialised 2D code, the status of certain packs may report as 'EXPORT'; and one class 2 medicines recall of Boots Dermacare hydrocortisone ointment as a precautionary measure due to retained samples showing presence of Pseudomonas aeruginosa.

13. **MedSafetyWeek** MHRA was on the planning team working closely with colleagues from UMC, Kenya, Singapore, Ghana and Slovakia for the launch of MedSafetyWeek at the beginning of November. There were over 70 countries involved from across 4 continents. In conjunction with MedSafetyWeek, two new countries launched the Med

Safety App in their country; Pakistan and Nigeria. This launch also coincided with enhancements to the apps to improve the use of branding across email notifications, improve user experience and to add security enhancements. Nigeria has expressed their gratitude to the MHRA team and wider WHO and UMC for their support with the app and had a successful launch which the MHRA attended virtually.

14. The second pilot edition of the Medical Devices Safety Bulletin has been published. This pilot project is an attempt to resolve how we communicate devices safety messages that do not meet National Patient Safety Committee criteria. The main item for this edition was on the T34 ambulatory infusion pump, which has been the subject of numerous Field Safety Notices for a range of technical problems for some time. The introduction of a new battery has enabled the continued use of this pump, as an interim measure. This pump is used widely in healthcare settings, but the palliative care in hospices is one area that is particularly dependent on the continued availability of this device.

DYNAMIC ORGANISATION

Inspections

15. The laboratories team conducted their first remote bioequivalence inspection of a facility in India. Due to travel restrictions, no overseas inspections have been possible since March. Having identified the risk of having limited oversight of these clinical trials' and subsequently generics during this pandemic period, a project was started to develop methods to enable data and study conduct to be reviewed remotely. Several new approaches have been adopted with both the clinic and the laboratory toured using video, which allowed the operation of equipment to be checked and also the inspectors to witness study activities. The next inspection is already planned, and the project will be developed further to source more software and to implement across other inspection types that the team perform.

Mental health and wellbeing

16. Mental health and wellbeing has always been at the centre of our work supporting staff, and we enhanced this further in recognition of the challenges brought about by COVID-19. We put in place a range of additional support mechanisms and communications to staff and managers, and more recently, as we face winter and shorter, darker days and a further lockdown coming at the same time as a peak of Agency business priorities, we have a renewed focus. Sam Atkinson has been appointed as our Mental Health at Work Champion, and we are launching a calendar of focussed activities and communications to support staff.

Staff Meetings

17. Staff received an update on progress with the Agency Change Programme at all-Staff meetings on 5th and 6th November. The meeting agenda included a case study on outcomes, presented by the University College London team with whom Devices collaborated to deliver an innovative device, the Ventura CPAP which helps keep COVID-19 patients from needing artificial ventilation and is now used round the world as well as in UK hospitals.

Civil Service Awards

18. It has been announced that the MHRA Clinical Trials Unit has been nominated in the Resilience and Rapid Response Award of the Civil Service Awards. This is recognition

of the roleplayed by the Clinical Trial Unit in supporting robust but speedy review of clinical trial applications.

FINANCIAL SUSTAINABILITY

Agency Change programme

19. Our work on the future operating model continues at pace, exposing the significant decisions that the Agency must take in order to be financially viable going forward while at the same time moving to deliver its vision of being a truly world-leading and innovative regulator. ExCo have been doing considerable work to understand the key interventions required to deliver on that vision. We are in the process of recruiting a Transformation Director with appropriate and specific change experience to support MHRA through the upcoming phases of detailed design and implementation and will seek to engage with DHSC on our developing plans following our discussion with non-executive colleagues at the Board seminar.

Finance Transformation

20. The recruitment phase of Finance Transformation is now largely complete with one or two roles yet to join the Agency. However, the adoption of the Government Finance model of Strategic Finance, Financial Control and Finance Business Partnering supported by Transaction processing is now complete. This means that the Agency now has a full team of dedicated finance business partners to support Divisions on the finance implications of the changes and investments they need to make. The next phase of Finance Transformation will focus on the tools and processes needed to support the organisation as it evolves e.g. business planning and budgeting.

June Raine
CEO
November 2020

Medicines & Healthcare products Regulatory Agency

Board Meeting held in public

23 November 2020

IMPACTFUL SCIENTIFIC RESEARCH AT THE MHRA

Issue: What are the most promising scientific research projects within the Agency that could have the biggest impact on protecting and improving patient health?
Action required by the Board and by when (timings): • **Identify** areas of interest which should be considered for the Agency's portfolio which then can be further developed for the Agency's Regulatory Science Strategy; noting that the areas identified in this paper are not the only areas of interest, given the Agency's wide scientific portfolio. • **Comment** on the proposal to combine and prioritise oversight in a more defined organisational structure with a Centre for Regulatory Science.
Implications for patients and the public: Scientific research performed by the Agency, strategically aligned to a patient-centric Science Strategy, will create important outcomes enabling medical products developing, licensing and surveillance, and evolve current regulatory frameworks.
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?** Deliver world-leading Research and Innovation
Author (s): Christian K Schneider with input from colleagues from key Divisions
Chief Officer sponsor: Christian K Schneider

Introduction

1. Science and research underpin virtually all activities of the MHRA. The Agency has a unique setup with combining areas of strong data research at the Clinical Practice Research Datalink (CPRD), laboratory research at the National Institute for Biological Standards and Control (NIBSC), and regulatory science at the MHRA Regulatory Centre which underpin the Agency's statutory functions and its mission.

2. The Board requested a view on the Agency's science and research including areas of high impact on protecting and improving patient health – including but also beyond pure laboratory research as undertaken at NIBSC.

Areas of science and research at the MHRA

3. The science landscape of the Agency is diverse, which can be seen as an asset in itself. Many research areas are highly impactful and internationally respected, such as for example NIBSC's work on eradication of the poliovirus, detection of SARS-CoV-2 material in sewage water, or research around the human microbiome. It is therefore challenging to lay out which research projects have the *biggest* impact on protecting and improving patient health. For example, NIBSC's work on viral standards, emerging diseases and vaccines has existed for several years but is now highly visible due to the pandemic.

4. However, for the purpose of this paper, key areas are highlighted which will have major impact especially with a view to patients and the healthcare system as described in the NHS Long Term Plan, the Office of Life Sciences Industrial Science Strategy, and which underpin the Agency's Regulatory Science Strategy going forward.

Strategic alignment

5. The diversity of the Agency's scientific portfolio will be combined and prioritised by the Agency's Regulatory Science Strategy which will give strategic goals and principles for individual projects' alignment, including (but likely not limited to):

    - Their ability to directly protect and improve patient health;
    - Their ability to support the Innovative Licensing and Access Pathway;
    - Their ability to streamline, safely accelerate or improve current regulatory principles.

    Above topic areas are considered prime candidates for the Agency's impactful and outcome-focused science and research portfolio.

Recommendation

6. The Board should note that the areas described as particularly impactful in this paper are not the only impactful areas the Agency is engaged in, and nor are these other areas necessarily less strategically aligned. For example, NIBSC's Regulatory Science Research Unit programme work covers essential themes beyond those discussed in this paper. NIBSC will be actively working on: Assuring access to monoclonal antibodies as biological medicines; the threat of global infectious disease; regenerative and cell-based therapies – accelerating access to treatment for neurodegenerative disease; using biologics to overcome antimicrobial resistance; stratified and personalised medicine and genomics; and specialised models for evaluating biologics.

7. Most areas of research in science have organically grown. The NIBSC Science Strategy 2019 to 2029 governs the laboratory-based science and research of the Agency and will be integral part of the Agency's Regulatory Science Strategy. It is emerging that these areas can indeed be organised into topical clusters as laid out in this paper. Depending on available resource, it may be desirable to have scientific and strategic oversight of cross-Agency Regulatory Science by a small, yet powerful Centre for Regulatory Science at the Agency.

8. An important aspect is academic collaboration, which is already well established across the Agency, and involvement of patients in order to confirm and enhance impact and relevance. The Centre for Regulatory Science could help fostering and cross-linking these academic contacts, and integrate Horizon Scanning more closely with the Agency's future scientific direction. An Agency-wide Innovation and Science Steering Committee may be a good addition to the Agency's portfolio, governing the innovation, science and research portfolio.

9. An Agency Regulatory Science Strategy has consciously not been written yet due to the ongoing work on prioritisation of the Agency's priorities and shape; but also the external setting of the Agency and budgetary considerations and priorities are important factors to consider, directly impacting on what is possible and realistic and what is not. Such a strategy will have to be consulted on with internal stakeholders, and also be informed by the contributions of patients and external stakeholders.

Request to the Board

10. The Unitary Board is requested to
    - **Identify** areas of interest which should be considered for the Agency's portfolio which then can be further developed for the Agency's Regulatory Science Strategy; noting that the areas identified in this paper are not the only areas of interest, given the Agency's wide scientific portfolio.
    - **Comment** on the proposal to combine and prioritise oversight in a more defined organisational structure with a Centre for Regulatory Science.

Topic area 1: Genomics and Diagnostics

The current situation

11. As already evident also by increasing cross-Divisional research projects at NIBSC resulting in novel cutting-edge standards, patients are benefitting, and will benefit, from two major areas of diagnostics: Genomics/precision medicine, and infectious diseases diagnostics.

12. Diagnostics are a key area in realising the potential of a preventive healthcare system. The MHRA is developing and implementing a robust regulatory system for diagnostics that is both responsive to the in vitro diagnostics (IVD) industry and will ensure that UK patients have access to effective and safer diagnostics. The NIBSC genomic reference materials programme has been developing standards for the measurement of DNA variants and is one of the few producers of primary standards for genomic diagnostics. The Agency has a strong network of national and international collaborators that is constantly strengthened, which will be used to further build on the UK's already world-leading genomics science base and embrace the potentially transformative nature of genomics.

13. At present, the Agency's activities have been focused and limited to precision oncology, particularly for the delivery of WHO international standards for cancer diagnostics, and for diagnosis of inherited rare diseases like Fragile X syndrome or Prader Willi and Angelman syndromes. Such International Standards make diagnosis more reliable, which is especially impactful in areas where they support novel diagnostic procedures like liquid biopsies, or where mutations can reliably be detected that are druggable.

14. The major impact of the Agency's research on standards for infectious diseases diagnostics has been demonstrated by the ability to quickly respond to the Covid-19 pandemic by preparing CE-marked research reference material for establishing SARS-CoV-2 assays within a few weeks. Existing platforms could be used, and NIBSC's strong network has enabled key donations of material required to create an antibody standard as well. The Agency's work is not focussing only on Covid-19; numerous other infectious disease diagnostics are in the Agency's current and future portfolio, enabling not only more reliable diagnostics (including panels for respiratory pathogens, for example) but also development of vaccines. Vaccines are an important cornerstone to patients' and people's health and can be applied to fighting antimicrobial resistance.

Future outlook

15. The principal challenge lies in the timely delivery of genomic standards, with a current rate of delivery of one panel of standards every one to two years for single variant materials, due to the genomic complexity of each standard requiring significant effort to resolve. The requirement for clinically relevant

regulation and genomic standards is increasing at a rate much faster than can currently be met. Indeed, the pipeline for genomic standards is potentially unlimited, with a significantly expanding profile of markers being used in diagnosis (including companion diagnostic testing), therapy-response, and prognosis. The ability to deliver on international primary standards, as well as working standards designed in response to NHS needs, is essential to define the sensitivity and specificity of existing and future genomic technologies, thereby ensuring patients precise diagnosis and access to safe treatments both nationally and internationally. As we continue to produce further standards, we must therefore aim to support current practices while also starting to address emerging areas, such as circulating tumour DNA and other non-invasive biomarker standards (RNA, circulating tumour cells, DNA-methylation patterns, extracellular vesicles, microsatellite instability and tumour mutational burden).

16. This topic area may be further enhanced with an important future project, the Yellow Card Biobank, which is currently being explored. This entails a biobank using a spontaneous reporting system (UK Yellow Card Scheme) as a data source for genetic information. This would be the first of its kind in the world bringing together stakeholders across health and government sectors, academia and the pharmaceutical industry. Research findings from the Yellow Card Biobank would form a key part of the regulatory evidence used in the Agency's role in protecting public health by ensuring medicines including vaccines are as safe as possible and by making medicine optimisation part of routine clinical practice. An interesting aspect in this is that synergies of knowledge and equipment (next generation sequencing expertise at NIBSC and identifying future genomic standards, for example) can be exploited.

Topic area 2: Data science

<u>The current situation</u>

Synthetic Data Generation

17. The potential applications of Artificial Intelligence (AI)/Machine Learning (ML) algorithms for clinical decision making and supporting patient care are vast. However, many algorithms are not validated, leading to concerns about performance and patient safety. Moreover, the data used to train and test these algorithms could be biased in a way that may disadvantage population sub-groups. Synthetic data could provide the solution to testing and validating algorithms; however, this requires the synthetic data to faithfully replicate real patient data, without inadvertently duplicating an actual patient record. Currently there are few truly synthetic data solutions available, and furthermore the methods used to generate the data are not transparent and they are only suitable in certain contexts.

18. Based on CPRD anonymised primary care data, CPRD has developed a novel method to generate synthetic data as a cost-effective solution for

algorithm training and validation. These high-fidelity datasets are completely artificial, but capture the complex clinical relationships found in the original data. This highly innovative methodology which enables completely bespoke synthetic datasets to be created from a range of data sources, provides regulators and MedTech innovators a robust route for algorithm validation and regulation. To date two proof-of-concept synthetic datasets, one focused on cardiovascular disease risk factors and a second COVID-19 synthetic dataset focused on sociodemographic and clinical risk factors have been made available for research (www.cprd.com/content/synthetic-data). The methodology used and experimental results have been published in the prestigious journal Nature Digital Medicine *Generating high-fidelity synthetic patient data for assessing machine learning healthcare software* on November 09, 2020 (https://www.nature.com/articles/s41746-020-00353-9).

Data-enabled clincial trials

19. The cost of delivering clinical trials is spiralling, which in part is due to failure of 50% of trials to recruit patients to time and target. There is enormous scope for routinely collected data in electronic health records (EHR) to be used in innovative ways to faciliate patient recruitment and support most cost effective trial delivery.

20. For the few past years, CPRD has been rapidly growing its popuation coverage and GP practice network across the UK, in tandem with developing its interventional research services platform (IRSP) with the aim of delivering a UK data-enable clinical trials service. CPRD's service offering is based on centralised and standardised searches of the CPRD database which covers 25% of the UK population, against the clinical trial protocol inclusion and exclusion criteria. Patients are located who may be suitable to participate in a trial and these potential eligible patients are then clinically reviewed by their GP to determine whether they are suitable for a trial. The GP will then invite suitable patients to take part in the trial, which may be based in any setting. This highly selective method results in fewer screen failures and lost time at screening. This will be a key component of the Agency's Innovative Licensing and Access Pathway.

21. Building on this method of data-enabled patient recruitment, CPRD can also support pragmatic randomised clinical effectiveness post marketing trials managed centrally through the IRSP, capturing patient data directly from the clinical record. CPRD has recently successfully collaborated with the University of Birmingham and with Alder Hey Children's NHS Foundation Trust to gain funding from to support two Phase IV pragmatic clinical effectiveness trials; evaluating direct oral anticoagulant therapy in 3000 patients with atrial fibrillation; and inhaled corticosteroids in 1,854 children with mild asthma, respectively.

Real-world evidence in clinical trials

22. There are vast amounts of real-world data routinely being collected on patients, for example, in electronic patient health records, and disease and patient registries. Real-world data (RWD) is analysed to make inferences about the effects of different treatments, producing real-world evidence (RWE). Extensively used for monitoring drugs and devices after approval, RWE is utilised much less frequently for demonstrating the efficacy or effectiveness of an intervention to gain an initial approval or an extension of an indication for an existing product. Use of such pre-existing data sources has the potential for accelerating access for patients of affordable products by increasing the speed and reducing the cost of development programmes. It can even enable developments which were previously thought to be unfeasible becoming feasible, with the consequent benefits to public health, e.g. for medicines repurposing projects.

23. The MHRA is in a unique position to enable the use of RWE in clinical trials through experience with the Clinical Practice Research Datalink (CPRD) services including RWD-led patient recruitment, creation of virtual control groups, and real-world pragmatic clinical effectiveness trials. The MHRA has set up a cross centre Real World Data group and recently produced its first guidance document which included input from the Commission on Human Medicines RWD ad hoc group. The MHRA's draft guidance on randomised controlled trials generating real-world evidence to support regulatory decisions is currently out for public consultation.

Enhanced reporting and surveillance systems

24. Novel technology, including AI/ML is equally important in delivery of enhanced reporting and surveillance systems. The Agency has commenced an innovative research project to understand how such techniques can used to enhance signal detection for both medicines and devices. This will explore use of novel analysis techniques, and data-fusion approaches to ensure optimal use of all data resources available to the Agency. Alongside this research, enhanced reporting systems will aid improved data collection and long term follow up of incidents (including those related to technology), with implementation of smart forms to ensure stakeholders are prompted to provide the most important information in the easiest way.

Near real time pharmacovigilance and RWE generation

25. The growing availability of RWD has also provided both an opportunity to strengthen pharmacovigilance and benefit risk monitoring. The Agency has developed an enhanced proactive near real time approach to vaccine vigilance using data from the CPRD to rapidly build the evidence base on the use and real world safety of vaccines in line with the growing size of the vaccinated population following deployment which has now supported the continuation of several vaccination campaigns, most recently the childhood Meningitis B vaccine. The Agency are also using CPRD to proactively monitor

patient outcomes and are working to develop a patient registry for girls and women taking sodium valproate which will generate valuable evidence on the adherence to risk minimisation measures put in place by the Agency and the experiences of those prescribed the drug and their children.

Future outlook

26. Although the methods develop by CPRD have demonstrated that it is possible to generate bespoke clinically plausible synthetic datasets that can be used to validate and train algorithms, many research questions remain. Some of these will be addressed in work funded by NHSX. The next step is to scale up learnings and launch a synthetic data generation service. Based on feedback from stakeholders, the synthetic data generated from this services can be used for a variety of applications including training and validation of clinical algorithms, boosting sample size to scale up datasets, conditional generation of data fields to address imbalances in real world data, for in silico trials and for external control groups in single arm trials.

27. CPRD's data-enabled clinical trials capabilities are pioneering but unlike the observational research servicies, they are in their infancy. The next stage will be to raise awareness of these services amongst industry and build up a portfolio of clinical trials, supported by metrics and case studies demonstrating efficiencies.

28. The use of RWE in clinical trials is relatively new but with interest from industry mounting, there will be a growing demand for expert regulatory advice and decisions in this area. To retain a global lead in RWE, it is essential that the MHRA builds on its knowledge, to offer tailored scientific advice to applicants to ensure use of RWE will satisfy regulatory requirements. It is also vital that there is sufficient capability in the interpretation of RWE within the MHRA assessment teams to inform regulatory decisions and reduce the time of product development, and capacity to use the CPRD and appropriate epidemiological approaches to generate RWE important for informing regulatory decisions and monitoring patient safety and outcomes.

Topic area 3: Advanced Therapies and regenerative medicine

The current situation

29. Advanced therapies (i.e., gene therapy medicinal products, cell-based medicinal products and tissue engineering products) are increasingly establishing themselves as promising, sometimes breakthrough, treatment modalities. The Agency has considerable experience in regulating these medicines and has established a research and science programme that can considerably support the UK Life Sciences landscape in this area.

30. NIBSC's Division for Advanced Therapies is engaged in the research for biological standards for gene and cell therapies, in collaboration with other Divisions of the Institute, for the creation of physical and process standards to facilitate the translation of new discoveries within the regenerative medicine field. It also hosts the UK Stem Cell Bank (UKSCB), established in 2003 as the UK's national repository for human embryonic stem cell lines derived within the UK. The UKSCB store, characterize and supply ethically approved stem cell lines for both basic research and the development of cellular therapies as medicinal products. The UKSCB is also engaged in numerous UK and international research projects, playing an important role in the UK's regenerative medicine infrastructure.

Future outlook

31. In such a novel and continuously evolving field, it will be important for the Agency to actively research and monitor across the different scientific activities so that synergies can be found. For example, the research aspect of how to characterise cell-based medicinal product ("what's in the tube?") could inform regulatory guidance ("what should be in the tube?"). Given the strong UK landscape in this area, the Innovative Licensing and Access Pathway (ILAP), (which is currently piloted and should be operation ready after the end of the Transition Period), should be enhanced by innovative regulatory approaches and practice. For example, Adaptive Inspections for advanced therapy medicinal products would enable inspections at key data and decision points to verify data and certifications, providing additional assurance for patients that medicines brought to them faster are also of high quality with manageable risks. MHRA intends to develop a new Advanced Therapy Centre Accreditation, which would support the ambition to make the UK the destination of choice to develop innovative manufacturing, for example Point of Care products. Regulatory science will help finding out how such accreditation schemes will enhance data quality and be able to streamline the regulatory process as a whole. Ongoing and future work on a new framework for the manufacturing of Point of Care products, applicable to all types of medicinal products, will complete the Agency's ambitious offer.

Topic area 4: Regulatory Science and research

The current situation

32. Regulatory Science can be defined as, "the application of the biological, medical and sociological sciences to enhance the development and regulation of medicines and devices in order to meet the appropriate standards of quality, safety and efficacy". The Agency has been a strong player in assessment, inspection and control of medicines and devices, and has accumulated considerable knowledge. The Agency's Science Strategy will foster and enhance an approach where assessors, inspectors and scientists use their gained knowledge and insights, in a non-product-specific

manner (thus not breaching confidentiality), to create scientific analyses and outcomes which will help evolve and improve the regulatory framework.

33. Scientists and assessors across the agency have been publishing key opinions leadership papers in internationally recognised journals already, which are paradigms for Regulatory Science. For example, in a recent publication on “Streamlined approval of biosimilars: Moving away from the confirmatory efficacy trial”, senior experts from the Regulatory Centre have laid out, from years of experience, a more streamlined science-based regulatory paradigm for development of biologicals that highly similar versions of medicines already authorised where patents have expired. The principles have gone into the UK Guidelines on Biosimilars which have been publicly consulted, and if followed will allow for faster development timelines and reduced cost for medicines which are then more affordable and be made available for many more patients.

Future outlook

34. While “regulatory affairs” is the discipline of applying current principles and regulations to the assessment, inspection and control of medicines, “regulatory science” is the discipline that seeks to adapt these principles and regulations to an ever evolving complexity and changing science of novel products where the current principles cannot be readily applied anymore. It will be important to create awareness, but also time, for staff to explore where their work results in knowledge that can be used to evolve the current regulatory thinking and rules. A key area which the Agency must and will engage with is regulatory research in the area of patient-reported outcomes as meaningful clinical endpoints, and how these can be implemented into the Innovative Licensing and Access Pathway from early on in order to add more evidence on patient-relevant benefit read-outs of clinical trials, supporting patient centric drug development. This will enhance regulatory science on innovative clinical trial design which is vital for evolving the regulatory framework via the Innovative Licensing and Access Pathway and also allow innovations in the processes of ensuring product release and post-market surveillance.

Topic 5: Focus areas for NIBSC (NIBSC Science Strategy 2019-2029)

35. The Agency Board, NIBSC’s Scientific Advisory Committee and NIBSC Senior Management Team (SMT) adopted the NIBSC Science Strategy 2019-2029 in December 2019. This was written with a view for NIBSC to continue to be a global leader in safeguarding the quality, safety and efficacy of biological medicines; the safety of the patient was explicitly put at the centre of its work.

36. It was based on the guiding principles: Scientific excellence for global public health - Our workforce is our key enabler - Sustainability and efficiency - An

attractive national and global collaborative partner - Nurturing organisational excellence.

37. The NIBSC Science Strategy will be part of the overall Agency's Science Strategy. It was decided that the following topic areas should take the focus for further development for the years 2019-2024 – conscious that areas not listed are not considered unimportant. In fact, many other areas like international influenza standards are important for global public health, NIBSC's reputation and income.

38. **Advanced Therapies (Advanced Therapy Medicinal Products, ATMPs), cell therapies, gene therapies and tissue engineering:** Please refer to Topic Area 3.

39. **(Cancer) immunotherapies:** The advent of next generation ('next-gen') sequencing coupled with advances in genetic diagnosis have opened the door to personalised cancer vaccines. They reveal the need for bioinformatics standards, a novel concept that will be applied across increasing numbers of therapeutic areas. They challenge our conventional approach to clinical trials: how should a trial in which every patient receives a different personalised therapeutic be assessed? Many more individualised products are currently in preclinical development and clinical trials, including vaccine-based approaches, cellular therapies such as chimeric antigen receptor (CAR)-T cells and monoclonal antibodies (mAbs) with immunoinhibitory or immunostimulatory properties. The development and licencing of immunotherapies is hampered by a lack of validated functional in vitro and in vivo potency assays that can model the complex dynamic and spatial interactions of cells and other factors. Regulatory oversight faces a significant challenge in the development of predictive bioassays for the potency and the immunotoxicology of immunotherapeutics because therapies targeting different mechanistic pathways, and/or different cell types, will require bespoke in-vitro and in-vivo models. This growing field requires development of relevant standards.

40. **Clinical diagnostics, including companion diagnostics for personalised medicines:** Please refer to Topic Area 1. NIBSC will be able to support diagnostics for infectious diseases (including some not currently supported by NIBSC products), non-infectious diseases (e.g. genetic markers for cancer, or neurodegenerative disorders such as dementia), and support certain kinds of biologics, such as mAb-based cancer therapies that are targeted to groups of patients identified on the basis of genetic or phenotypic characterisation of the diseased tissues. This characterisation requires the use of 'companion diagnostics' alongside the medicines; both parts of the therapy will require their own standards.

41. **Monoclonal antibody-based products:** The therapeutic and commercial success of mAbs owes much to advances in antibody engineering technology which has led to the generation of highly effective products to treat a wide range of key diseases. The WHO has recognised a global need for the

standardisation of biotechnology products such as mAbs, over concerns in their quality, efficacy and safety. Through our WHO programme of mAb standardisation, we are facilitating the development, calibration and qualification of potency bioassays for these important products and need to continue to develop this area of work. The emergence of second-generation mAbs like bi-specifics, antibody–drug conjugates, antibody fragments, single domain antibodies, or conventional mAb formats optimised for effector function, pharmacokinetics or stability, means this class of product is becoming ever more sophisticated. NIBSC will engage on projects enabling functional and structural characterisation of antibodies, generation of reagents for immune-profiling of clinically important adverse immune responses (unwanted immunogenicity), or novel assay platforms enabled by novel formats like nanobodies.

42. **Biosimilar medicines:** The biosimilar route to market authorisation requires a candidate product to be shown to be “highly” similar to a reference product. Their complexity means that the testing and licensing of biosimilars must be carried out with great care. This has a significant impact on NIBSC’s work programme and role in the regulatory environment, with a particular focus on the production of supporting reference materials and research into safety aspects such as product immunogenicity.

43. **Re/emerging diseases:** The current Covid-19 pandemic, and earlier outbreaks of Ebola virus in West Africa and Zika virus in Central and South Americas are reminders of the enormous health impact of the unexpected (re-)emergence of infectious diseases and their capacity to alter their epidemiology and pathogenesis in new settings. The close working relationship with international organisations such as the WHO means that NIBSC is well placed to contribute to the international response to re/emerging diseases. It is essential that NIBSC addresses the global spread of re/emerging pathogens, by recognising the need for rapid, accurate diagnosis coupled with pre-clinical and para-clinical research to develop vaccines. The standardisation programme, addressing public health needs identified by key stakeholders such as the WHO and will support the development and evaluation of appropriate reference materials.

44. **New vaccines and vaccine combinations:** The challenge ahead for immunisation programmes will be to devise vaccination strategies that protect the very young, whose immune system has yet to mature, and the elderly, whose immune system is in decline. We should therefore be prepared for new combinations of existing vaccine antigens, an increasing use of new adjuvants, and alternative timing of delivery. Looking ahead, improved investment in developing country vaccine manufacturers, to solve vaccine supply issues and reduce economic pressure on public health, has the potential to drive the implementation of new and less expensive versions of existing vaccines. NIBSC will review its current work portfolio in this area and react to the developments of the global market (including vaccines that might reach the UK market from other regions in the world) as necessary and feasible.

45. **Antimicrobial Resistance and the eradication of disease**: NIBSC will continue to support the global polio eradication programme through the development of new vaccine strains for poliovirus that will help prevent the re-emergence of this disease. Moreover, the emergence of microbes that are highly resistant to multiple antimicrobial agents (anti-microbial resistance, AMR) poses a significant and rapidly increasing threat to global public health. Vaccines have an important role in the overall strategy to address this global problem by preventing diseases that would otherwise be treated, whether appropriately or inappropriately, with antibiotics. Vaccines targeting multidrug resistant bacteria are at various stages of development and will likely progress towards approval during the next 5-10 years. NIBSC will continue to provide novel measurement standards that are required to support such vaccine development, and its diagnostics standardisation programme will ensure the accurate characterisation of infections thereby avoiding the misuse of antibiotics.

46. **The human microbiome:** Advances in high throughput nucleotide sequencing technologies have facilitated studies of the bacteria (microbiota) that colonise humans in unprecedented detail, so much so that many health problems are now attributed to their imbalances (dysbiosis), and microbiome therapies are the subject of numerous clinical studies. The lack of microbiome standards presents a challenge for the translation of microbiome research into innovative therapeutics. NIBSC has made important progress in this area developing DNA standards for gut and respiratory tract microbiomes. The complex requirement to develop standards based on populations of microorganisms rather than the historic approach of developing a reference material to support the measurement of a single microorganism will require NIBSC to contribute to the development of appropriate bioinformatics standards. NIBSC will continue to support developments in microbiome therapy, an area that is anticipated to continue to expand over the next decade.

47. **Analytical technologies:** There has been significant progress in developing new, or improving existing, physicochemical techniques for the analysis of biological molecules and to support the development of genomics, proteomics and metabolomics, with particular progress in areas such as nucleic acid sequencing, mass spectrometry and imaging. This progress has been accompanied by significant increase in capability in computing power and data analysis techniques based on pattern recognition and statistical theory, and large public scientific databases. The progress is greatest where this capability has been combined in emerging areas such as single-cell analysis, next generation sequencing, high throughput imaging, and flow cytometry on unlabelled cells. NIBSC must be aware of and involved in the efforts to calibrate and standardise these methods as their use expands from research into diagnostics and manufacturing.

48. **New standards production technologies and their impact on "classical" standardisation approaches:** Biological medicines are increasingly being

used in more complicated product delivery systems, starting with examples such as pre-aliquoted vaccines in single use syringes, extending to therapeutic cells embedded in 3D scaffolds for implantation and to other emerging ideas. These complex products increasingly stray into the area of medical device regulation and will present new challenges for standardisation. Reference materials for such products will need to consider both the biological and physical components of the product and will present new challenges for physicochemical analysis as well as for biological activity. In addition, companies are increasingly validating the biological activity of their products during rather than post-manufacture. This affects the timeframe and format of how biological activity is measured and offers opportunities for the development of innovative reference materials to support manufacturing processes and emerging technologies.

49. The Covid-19 pandemic has led to inevitable re-prioritisation, and the NIBSC SMT will at an appropriate time recalibrate the NIBSC Science portfolio and focus areas of the NIBSC Science Strategy.

Medicines & Healthcare products Regulatory Agency

Board Meeting

23 November 2020

The MHRA Enforcement Group

Issue: What is the assurance that the MHRA Enforcement Group can protect patient health by working with global partners?
Action required by the Board and by when (timings): This paper is designed to provide the Board with assurance.
Implications for patients and the public: The work of the Enforcement Group directly impacts the security of the supply chain and the availability of unlicensed medicines and is therefore essential for public and patient safety.
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?** Public safety
Author (s): MHRA Enforcement Group
Chief Officer sponsor: Sam Atkinson

Introduction

1. Law enforcement capabilities exist for no other reason than to reduce criminal threats to vital interests. The focus of the MHRA Enforcement Group ('the Group') and of this paper is on reducing the threat posed to public health by the illegal trade in medicines ('medicines crime'). The illegal sale of benzodiazepines, opioids and nonbenzodiazepines through the black market presents risks of acute harm and long-term dependence. Benzodiazepines alone are implicated in more than 1000 deaths in Great Britain each year.

2. Without robust enforcement, such offending can also undermine regulatory regimes - weakening public confidence, reduce legitimate supply, distort domestic markets, damage the reputation and competitiveness of the UK industry overseas, and bring about financial loss to individuals and fiscal loss to the economy. Crime is also an affront to society in general. Many of these broader harms associated with medicines crime can in turn bring about indirect detriment to public health. Although prioritising direct threats to public health, the Group's mission is therefore very much about protecting the overall public interest.

3. This paper describes in broad terms the nature of the prevailing criminal threat and the Group's response to it. As illegal medicine supply networks are often as unabashedly global as the legitimate trade they mimic, this paper focuses specifically on threat reduction activity undertaken by the Group at an international level. With the UK entering a new trading relationship with both the European Union and the rest of the world in January 2021, the paper seeks to provide assurance to the Board that the Group's understanding of the threat, its existing response, and additional measures planned for 2021, will continue to protect the UK public from criminal threats.

A picture of the threat

4. The World Health Organisation (WHO) has identified the illegal trade in substandard and falsified medicines, a subset of medicines crime, as one of the most urgent health challenges for the next decade. It estimates that more than one in ten medicines in low and middle-income countries is substandard or falsified. Both generic and innovator medicines can be falsified, ranging from very expensive products used in the treatment of cancer to very inexpensive products for the treatment of pain.

5. In common with most forms of economic crime, the threat from medicines crime conforms to a pyramidal structure. At its broad base, high volume, low harm offending, often involving error and opportunist conduct is common. The capstone of the pyramid represents a much smaller volume of the more serious, complex and organised forms of offending. These are not rigid partitions, and both detrimental upward progression and beneficial downward influence are the reality. To address the most egregious criminal threats, therefore, the Group treats the pyramid as a dynamic and interdependent whole – a system composed of multiple moving parts with multiple opportunities for impactful intervention.

6. Although initially manifesting itself in a variety of ways, from a criminological perspective, the aim of medicines crime is to meet informal online demand. Whether met by licensed products unlawfully removed from the regulated UK supply chain, or unlicensed generic stock imported into the UK, unregulated online marketplaces are

almost always the shared destination.

7. In 2020, analysis conducted by the National Crime Agency identified in the region of 150,000 illegal listings for medicines on the dark web alone over a twelve-month period. Many of the medicines on offer were potentially harmful to public health. Criminal profits from medicines crime can also be substantial, with organised crime groups estimated to have achieved sales of £15.4m from three illegal websites over just three years.

8. Intelligence suggests that the Group's success in tackling the diversion of licensed medicines from licensed wholesalers has reduced supply to the black market. However, the informal demand for UK specification medicines online remains high. There is evidence that the resulting supply chain imbalance has recently led to instances of product theft, and dealers misrepresenting imported generic stock as of UK origin. Penetration of the regulated UK supply chain by falsified and substandard medicines remains vanishingly rare.

9. The pursuit of offenders and their profits through criminal justice interventions remains the primary focus of the Group's current response to medicines crime. Recognising that the threat is multi-dimensional, dynamic, multi-sectoral and global, it follows that the Group's response must be similar. Subject to securing funding, in 2021, the Group aims to lead, support and coordinate a broader menu of threat reduction activity aimed at preventing offending and designing-out systemic vulnerabilities. This will complement its successful prosecutorial and asset denial work, strengthening overall protections for the public.

EU transition period

10. The end of the EU transition period in January 2021 is likely to herald significant changes to the UK's relationship with the EU and potentially to that between Great Britain and Northern Ireland. Experience has shown that criminal actors won't hesitate to exploit any new vulnerabilities or opportunities revealed as the water level recedes. In the longer-term, it is quite feasible that offenders will seek to profit dishonestly from any regulatory and procedural asymmetries between the UK, EU and the rest of the world. The Group's current assessment, however, is that with or without a negotiated settlement, in the short-term at least, the end of the transition period is likely to have a neutral impact on the criminal threat and the Group's ability to respond to it.

11. As the primary function of criminal intelligence analysis is to reduce uncertainty, the Group invests heavily in maintaining a single, comprehensive picture of the current and likely future medicines crime threat. This will help ensure its response keeps pace with, if not ahead of, any changes in the nature or scale of the international threat following the end of the transition period.

A global response to a global problem

12. The illegal trade in medicines is substantially a cross-border one. It follows that meaningful, regular and timely international collaboration is essential, both to protect UK interests here at home, and for the UK to play its part in defeating the global criminal threat. Formalising international collaboration at both strategic and tactical levels has brought significant rewards for the Group leading to positive outcomes for public health. To some extent, the corollary of this success is the growing recognition of the Group within its global peer community as a thought leader in the field.

13. The Group enjoys strong bilateral relationships with international regulatory and law

enforcement partners. The focus at a tactical level is on interoperability and the sharing of actionable intelligence and related good practice. Operational relationships with the United States, the Republic of Ireland and India have proved especially strong and productive. In the year to March 2020, through these relationships, the Group received seventy-five actionable intelligence reports from European Union Member States and seventy-nine reports from partners in third countries. This intelligence sharpened the Group's understanding of the nature and dimensions of the cross-border threat. In turn, in the last twelve months, investigative collaboration with eight international partners has also taken place, in respect of five specific criminal investigations.

14. As the original conceptual architects, the Group plays an active part in the annual Operation Pangea initiative. Coordinated by Interpol, Operation Pangea is now a well-established multinational period of operational focus on disrupting the online sale of counterfeit and illicit health products. It also aims to reduce demand by raising awareness of the risks associated with buying medicines from unregulated websites. Preparation is already underway for the Group's participation in Operation Pangea in the spring of 2021.

15. As the threat from unlicensed and falsified medicines is fundamentally internet enabled, and the internet itself is borderless, the Group works to prevent UK access to such products by identifying and removing illegally trading websites. These sites are invariably hosted overseas, often in hard to reach jurisdictions, so successful take-down action requires challenging cross border engagement with individual domain registrars and those responsible for their regulation. In the last three years Group action has led to the identification and removal of sixty-six illegally trading websites hosted overseas. Whilst this work undoubtedly disrupts the illegal online supply of medicines, the Group aims to adopt a more holistic approach to countering both the supply and demand limbs of the online threat during 2021.

16. In addition to day-to-day operational engagement, the Group has well-established strategic relationships with regulators and law enforcement partners across the globe. These relationships are managed primarily through participation in intergovernmental forums, including those established by the World Health Organisation, Interpol, the Council of Europe and the European Commission, and enforcement-specific forums such as The Permanent Forum on International Pharmaceutical Crime. Each forum is built on the shared objectives of removing international barriers to information and intelligence exchange, as well as prioritising the protection of public health.

17. Working with partners, regulatory interventions at points of entry into the UK are an important component in the Group's overall response strategy. MHRA intelligence has contributed to the domestic seizure of substantial quantities of product at ports and borders in recent years. Such seizures not only directly reduce the availability of unlicensed and falsified medicines on UK markets, but also chip away at the viability of the criminal enterprises responsible. As installing an impenetrable ring of steel around the UK against illegal medicines is unachievable for a trading nation, the Group also recognises the value in a more strategic approach to interdiction. Upstream activity to prevent consignments from leaving their countries of origin can yield even greater returns on investment.

18. However the UK begins 2021 following the end of the transition period, the Group will continue to provide the same protections to the UK public. Fruitful intelligence sharing relationships with international partners outside the EU will serve as a template for those within, as third countries already provide more than half of the overseas intelligence received by the Group. Whatever the new relationship with the EU looks

like, the intention of the Group is to continue collaboration with all international partners in the interests of protecting the UK public.

From strategic to tactical – collaboration with Indian authorities

19. The Group's proactive relationship-building in India is a strong example of how this kind of strategic influence overseas can be achieved by building trust and confidence bilaterally. Led by an intelligence assessment that identified the subcontinent as one of the primary sources of unlicensed medicines entering the UK, the Group worked hard to establish and develop a meaningful strategic relationship with Indian authorities.

20. In July 2018, following bilateral coordination and negotiation, Indian Border Force officials conducted their first ever internal postal hub exercise to identify and intercept medicines leaving India bound for the UK. This exploratory operation resulted in the inspection of 2448 parcels and the seizure of more than 350,000 doses of medicines. Importantly, it also validated the nascent strategic relationship between the two countries.

21. This strengthened strategic relationship has also resulted in improved tactical intelligence sharing with the MHRA. In December 2018 this led directly to the identification of unlicensed medicines valued at £1.24m prior to the consignment's arrival in the UK. Fast-time intelligence shared by Indian customs resulted in the interception and seizure of more than one million doses of medicines, including controlled substances, destined for illicit UK markets.

22. The Group's strategic and operational relationship with Indian partners has continued to strengthen, with work underway to develop a formal memorandum of understanding between the MHRA and Indian Customs.

Conclusion

23. In comparison with most similar UK and global government regulators, the MHRA has a mature enforcement function with class leading specialist capabilities and a clear understanding of the threat posed by the illegal domestic and trans-national trade in medicines. The impact on public health of these capabilities is optimised through meaningful relationships with partners overseas and within the UK. This combination affords strong protections to the UK public. Since April 2020, 7.9 million doses of illicit, potentially harmful medicines have been either removed from UK circulation or stopped from entering it. Nine months into the year, this already exceeds the total of 5.3 million doses removed during 2019/20.

24. The Group understands that the prevention and disruption of offending at a strategic level are equally important and can bring about lasting and sustainable reductions in the threat. Since April 2019, using financial investigative powers, the Group denied those involved in the illegal sale and supply of medicines access to £4.65m of criminal profits. This reduces the reward from offending and disrupts the criminal network's ability to run their enterprises. The Group's ground-breaking work in asset denial has won praise from peers across the law enforcement community this year.

25. The overall threat to the public interest from medicines crime will inevitably evolve in the years ahead, reflecting changes in supply and demand and prevailing regulatory regimes at home and abroad. The most committed offenders are known to actively seek out new ways in which to defeat regulation and avoid detection. The Group recognises the importance of flexing its approach accordingly. Further strengthening strategic efforts at home and overseas, adopting a more systems-based approach to threat reduction and optimising the impact of day-to-day operational relationships will ensure the Group's understanding and response to the threat are equal to the challenges of 2021 and beyond.

26. Specifically, and subject to additional funding, in 2021 the Group plans to significantly enhance its online threat reduction capabilities and to put in place a small team to develop innovative, non-criminal justice prevention and disruption interventions. In order to ensure that existing and putative capabilities continue to point in the right direction, the Group is currently refreshing its strategic intelligence picture, from which an unambiguous and risk-based set of priority threats for 2021 will be distilled. These priority threats will drive the work of the unit throughout 2021/22.

27. The Board is invited to review this document and to challenge the assurance provided, if more evidence is required, to ensure that the Agency can protect patient health by working with domestic and global partners in a timely, collaborative and effective manner.

Medicines & Healthcare products Regulatory Agency

Board Meeting

23 November 2020

WHAT ASSURANCE CAN BE PROVIDED BY THE AUDIT & RISK ASSURANCE COMMITTEE ON THE CURRENMT RISKS FACING THE MHRA AND THEIR PROPOSED MITIGATIONS?

Issue: The Audit & Risk Assurance Committee met on 2nd November 2020 with the aim of providing assurance to the Board.
Action required by the Board and by when (timings): The Board is asked: a. To note the Agency's likely end of year financial position and endorse the need for sustained implementation of the necessary changes which the Shape and Size review is likely to recommend so that the MHRA remains an effective and highly respected regulator but also becomes financially resilient. b. To consider the recommendations to strengthen further the Agency's approach to risk management and provide any other suggestions drawing on their wider experience. c. To support the work underway to better align fees to the Agency's costs and endorse the need for a clear fee strategy which is periodically reviewed by the Board to enhance accountability and governance.
Implications for patients and the public: The Audit & Risk Assurance Committee will provide assurance to the Board that the Agency has the necessary systems, controls and governance to manage risk 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? All and particularly Organisational Excellence / Efficiency. **If relevant, which Business Plan strategic activity does it support?**
Author (s): Michael Whitehouse
Board Sponsors: Michael Whitehouse

ARAC Meeting
2nd November 2020

Chair's summary of key outcomes

1. This report sets out ARAC's response to two actions assigned to it at the 26 October Board meeting and summarises key outcomes from ARAC's meeting on 2 November.

Action 1: Review the Corporate Risk Register and ensure that COVID-19 risks to the Agency have been appropriately articulated and mitigated.

2. ARAC reviewed both the corporate risk and the specific COVID-19 risk registers, received a separate paper on how the Agency is responding and sought assurance from Dr Sam Atkinson, Interim Chief Quality & Access Officer.

3. ARAC was assured that:

- the independence of the Agency's approval of vaccines was being maintained through the MHRA's Internal Vaccine Deployment Oversight Group chaired by the Agency's Chief Scientific Officer to ensure that any authorisation is entirely independent from any industry influence;
- the Agency has the capacity and flexibility to expedite the approval of safe vaccines and therapeutic drugs through targeted deployment of staff and running parallel assessments;
- risks to patient safety were being managed, for example, through NIBSC's control over batch release of vaccines (a statutory requirement), the prioritisation of vaccine inspections and planned enhanced safety reporting;
- the need to respond quickly to the pandemic had not resulted in any weakening of the Agency's internal controls;
- the wellbeing of the MHRA's people is paramount as they continue to work in challenging circumstances; and
- the Executive remained very focused on supporting all those working for the Agency.

4. The Committee emphasised the need to continue to manage the risk of the Agency's other key responsibilities being displaced because of the prioritisation of the response to COVID-19. The full cost of the Agency's COVID-19 activities is required to ensure that proven innovations and improvements in regulatory approach can be embedded in the future operating model and associated budgets.

5. Further detail on the review of the corporate risk register is provided further below.

Action 2: Draw up scenarios to stress-test the agreed MHRA governance framework to ensure that the structure is robust when something goes wrong.

6. In the coming weeks, the Agency will agree its new future operating model as a stand-alone national regulator. This will define the organisational structure of the Agency from which will flow new enhanced ways of working. It is proposed that the new governance framework is tested against different scenarios to understand potential weaknesses in the controls framework and agree mitigating actions to avoid adverse consequences. ARAC has also asked internal audit to independently review the new governance structure and report to ARAC before next March.

Other issues covered by ARAC:

Financial performance and fees

7. The Agency is predicting a financial deficit for 2020/21 of £15 million compared to a budgeted deficit of £6 million. Trading income is less than budget. This is mainly due to reduced income for the Regulator from the EU exit and partly explained by COVID-19 for NIBSC. Change costs are lower than budget and the Committee recommended that the rate of spend should increase for the rest of the year.

8. Without fundamental readjustment, the Agency will remain in deficit for years to come. The Board has approved a change programme to enhance how the MHRA regulates to ensure patient safety while also supporting innovation in the life sciences sector to deliver wider public health benefits. This and associated projects such as the review of fees, reduction in corporate costs, legacy system replacement and focus on being a more data-led organisation should enhance the Agency's performance and enable it to operate at a reduced cost. While these changes require careful management, the speed with which they are implemented will determine how quickly the MHRA becomes financially resilient. Consideration should be given to whether we differentiate between one-off investment costs that enable future efficiency e.g. legacy systems replacement and the reduction of the Agency operating costs through reduction in staff, streamlining services, improving efficiency and better use of data. Focus, pace and delivery are now imperative.

9. ARAC reviewed the work presented on fee structures. It noted that the current fees do not recover the full cost of the services delivered. ARAC recommended that a more holistic approach to fee setting is developed that enables the Agency to cover its costs for delivering all its services e.g. inspections, enforcement activities essential to assure public health.

10. The new fee structure will require consultation with industry, understood to take c.18 months. It is important for industry to have confidence that fees reflect broadly accepted levels of efficiency if the UK is to remain competitive. Once the work on fees is sufficiently advanced, it should be used to formulate a transparent pricing strategy which can be approved by the Board. This should make it easier to set and review fees as the Agency develops new services and strengthens accountability and governance. The strategy should be principle based and in full compliance with Managing Public Money. It may cover, for example, how development costs of innovation could be recovered and criteria which Agency will apply in determining there is a clear case for charging a fee.

External and internal audit

11. External audit confirmed that planning for 2020/21 was underway with the formal plan and fee to be approved by ARAC at its next meeting. Four internal audit reports were considered: Financial controls (moderate assurance); CPRD disposal of data (moderate); Non-Executive Director onboarding (advisory review) and IR35 compliance (limited). ARAC was assured that appropriate action is being taken to implement recommendations. The remaining internal audit programme covers patient engagement, replacement of digital legacy systems, business planning, implementing reforms to device regulation and wider review of governance following the implementation of the new management structure. ARAC is assured that once completed this programme would provide sufficient comprehensive assurance for 2020/21.

12. The Committee identified one systemic issue concerning whether the Agency consistently ensures that there is adequate second level of internal challenge or review in implementing new initiatives or significant changes to ways of working. ARAC will seek further assurance on this as it reviews the new governance framework.

Risk

13. The Agency's approach to recording, assessing and managing risks has improved considerably. There are 21 high level Agency risks recorded on the register - two have recently been removed. ARAC was assured that there are no obvious omissions.

14. Risks reflect 8 broad groups: ensuring that the Agency effectively supports the drive to tackle COVID-19; can fulfil its regulatory responsibilities effectively after the end of the Brexit transitional period including ensuring continuity of drug supply and maintaining patient safety; implementing the recommendations of the Cumberlege Report and strengthening patient engagement; financial resilience; implementing the change programme and realising its intended benefits; supporting innovation and realising the benefits of data exploitation and sharing; internal capability; and legacy system replacement.

15. ARAC made the following recommendations:

- **Top-level risks, controls and actions should be aligned with the four strategic objectives of the Agency.** The divisional risk registers are still a key part of the controls process and allow a bottom up and top down approach to be balanced. Risks will need to be assigned and owned within the new governance structure so there is clarity on who is responsible for escalating when there are early signs of something going wrong. ARAC will review the ongoing development of the risk register and how the Agency's internal assurance framework supports this.

- **Risks should be further aggregated so that the interdependencies are more transparent.** For example, how the different elements contribute to maintaining public trust, sustaining a regulatory environment which both helps ensure patient safety but also promotes innovation and the UK's competitiveness, and the wider role of the Agency in the health system in promoting public health.

- **Ongoing clarity of what it means to be an effective regulator from the perspective of different stakeholders and understanding their expectations is also important**. The risk mitigation actions are comprehensive, but they should be more precise and where practicable time limited which would help determine whether the action has had a positive impact and whether a risk remains relevant after a certain period.

16. ARAC noted two areas where action is required immediately the development of a work force plan and the replacement of legacy digital systems. ARAC was assured that the size and shape review will include a workforce plan. Planning for digital replacement and enhancement is being finalised and tendering will then commence.

Board Action

17. Over a period of significant change and external challenge for the Agency, ARAC is pleased to report the good level of assurance which we have received. Inevitably there is more to do but the Agency has a sound base to build on and the foundations for its new future operating model are becoming much clearer.

18. The Board is asked:

a. To note the Agency's likely end of year financial position and endorse the need for sustained implementation of the necessary changes which the Shape and Size review is likely to recommend so that the MHRA remains an effective and highly respected regulator but also becomes financially resilient.

b. To consider the recommendations to strengthen further the Agency's approach to risk management and provide any other suggestions drawing on their wider experience.

c. To support the work underway to better align fees to the Agency's costs and endorse the need for a clear fee strategy which is periodically reviewed by the Board to enhance accountability and governance.

Medicines & Healthcare products Regulatory Agency

Board Meeting held in public

23 November 2020

What are the strategic priorities for the new MHRA Corporate Plan (April 2021-March 2024) and the 2021/22 Business Plan?

Issue:

This paper aims to facilitate a Board discussion on the strategic priorities for the new MHRA Corporate Plan (April 2021-March 2024) and the 2021/22 Business Plan. At its meeting on 6 October, the Executive Committee (ExCo) discussed and agreed the need for the Agency's Corporate Plan to be refreshed early, given the significant change underway; and that business planning should be integrated, bringing together the outputs from the Change Strategy and incorporating workforce, financial and IT needs.

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

1. The Board is asked to approve the proposal for a 2-year Corporate Plan (and outline third year) focused on the Agency's Change Strategy, and a Business Plan focused on year one implementation of the Corporate Plan.
2. The Board is asked to review the issues identified in this paper and provide direction on the strategic priorities that should be used in the development of this new Corporate Plan.
3. The Board is asked to provide feedback and advice on the proposed planning process.

Implications for patients and the public:

The paper aims to support a discussion about how best to capture and deliver the Agency's strategic priorities which have a clear focus on patient and public need.

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

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

Author (s):

Policy Division

Chief Officer sponsor:

Jon Fundrey

What are the strategic priorities for the new MHRA Corporate Plan (April 2021-March 2024) and the 2021/22 Business Plan?

Purpose

1. This paper aims to facilitate a Board discussion on the strategic priorities for the new MHRA Corporate Plan (April 2021-March 2024) and the 2021/22 Business Plan. At its meeting on 6 October, the Executive Committee (ExCo) discussed and agreed the need for the Agency's Corporate Plan to be refreshed early, given the significant change underway; and that business planning should be integrated, bringing together the outputs from the Change Strategy and incorporating workforce, financial and IT needs.

Context

2. The agency Corporate Plan 2018-2023 sets out long-term strategy; but given significant change since the plan was drafted, there is a strong case for a refresh:
    a. EU Exit nearing finalisation, with the impact on the Agency becoming clear; and the resulting Medicines and Medical Devices Bill.
    b. Revitalised change strategy, with new Chair and governance being established.
    c. Independent Medicines & Medical Devices Safety (IMMDS) Review recommendations to strengthen patient involvement, safety reporting and medical device regulation.
    d. COVID-19 has created additional pressure but provided focus on our regulatory offer and expertise.
    e. Spending Review bid emphasises changes needed – in overall structure, to improve safety and to embed innovation, and support the Life Sciences sector.
    f. The current corporate plan was anyway a roll-over from the previous plan, because of the uncertainties created by the EU exit referendum: this is now the time to set out a new vision and approach.
3. Our Business Plan 20/21 focussed on ambitious strategic objectives. It was well received by DHSC and industry, and in specialist press. Next year's Business Plan will be, in effect, the first year of delivery of what will need to be a new Corporate Plan, incorporating delivery of the Agency's change strategy.

Strategic priorities and business priorities

4. The Corporate and Business Plan will start from the new strategic priorities.
5. The Board is invited to discuss what they see as the key business priorities that will sit underneath and deliver the strategic priorities. Proposed examples are below:
    a. Involving patients and the public in all our activities and delivery of actions to address the concerns of the IMMDS Review.
    b. Defining the regulatory approaches post-transition and post-standstill for medicines and medical devices, including capturing learnings from COVID-19; ensuring strong, clear regulation of new technologies; and developing further our new innovative and access licensing pathway.
    c. Strengthening safety regulation with integrated internal working between medicines and medical devices.
    d. A new business model for the Agency that is financially viable.

e. Ensuring a competitive proposition for the Agency's CPRD and other data services and for NIBSC work on standards and its research programme.

f. Operationalising of Agency partnership working nationally and internationally.

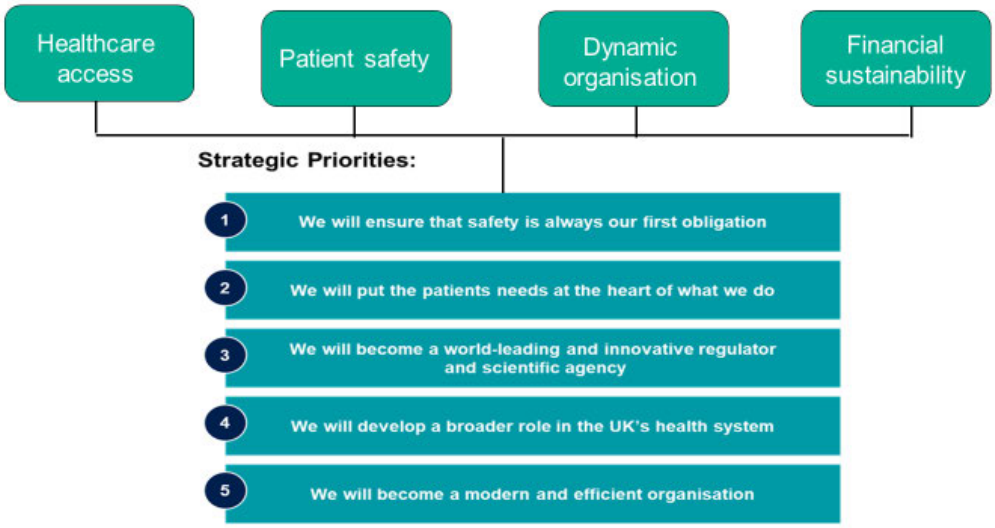
6. These are important objectives. To ensure we can deliver on them, we need to ensure we implement the Change Strategy, and through that, put in place a sustainable financial model for both capital investments and resources. All objectives also need to be underpinned by strong workforce planning and refreshed technology infrastructure.

7. It should be noted that, alongside implementing the change strategy, the Business Plan will need to give confidence that the Agency will resolve any outstanding uncertainties relating to EU Transition and will continue to address all the regulatory challenges posed by COVID-19, notably the assessment of new therapies and vaccines.

Corporate and business planning approach

8. The Board is asked to review the following overall approach:

a. Work will begin with this discussion by the Board to confirm the strategic priorities for the Corporate Plan.



b. Top down process: Using the Board's strategic priorities, the ExCo will determine the process; incorporate the size and shape work to set firm parameters for business areas so that the Chief Officers can be commissioned to populate plans for their areas, working closely with corporate support services. It should also reflect the items in the Agency's Spending Review bid.

c. The Corporate Plan should "bridge" from the agency's current state to the new operating model envisaged by the change strategy – it will set out at appropriate level the plan for implementing the transition. This means covering a shorter 2 year (and outline 3rd year) timeframe and being kept under closer review; after that initial period, there would be a new 5 year plan.

d. The Business Plan should set out the change implementation activities planned for the year. It should bring together strategic priorities (as the current one does) and set out our anticipated core activities, with outcome focussed KPIs to enable measurement and reporting.

e. The Business Plan should integrate a clear description of our objectives and how we will utilise our resources, namely workforce, finance and IT to achieve them.

It should also follow an agreed "Outcomes and Key Results" framework with metrics linked back to the Balanced Scorecard currently in development. All objectives will be costed and will need to be considered within the context of financial sustainability. We are working on developing more outcome focused business metrics to ensure impacts are more measurable and to facilitate decisions on prioritisation through the business cycle.

f. There should be a "clear line of sight" from the Corporate Plan to the Business Plan and the Annual Report, which would report back on the year with the same structure and thereby measure success – and account for it clearly and publicly.

g. Consultation with DHSC and stakeholders to ensure plans reflect wider priorities, (especially key HMG agendas eg COVID-19, IMMDS Review, Life Sciences etc); and engagement with staff to ensure the plans are owned by and drive the business.

Corporate and business planning outline timeline

9. The ExCo propose to work closely with the Board to deliver a more top down approach to the new Corporate Plan and welcome the Board's views on how to optimise the process.

10. Through the work on the future operating model, ExCo will determine business priorities and parameters for business areas which will provide a framework against which to develop the Corporate and Business Plans. This means aligning workforce and financial planning with the corporate planning process. A working group of key corporate leads is being established to support this process.

11. We normally publish our annual Business Plan every April to align it with the start of the financial year. This is not a statutory deadline, but we should seek to publish the new Corporate Plan, and the more detailed one year actions through the Business Plan, as close as possible to this date. However, we note the timeline for updating both plans will be very tight given wider pressures (eg Transition and COVID-19) and due to the dependency with the size and shape work, which is still underway.

12. An outline timeline is shown below:

    a. **End Nov / Dec** - Size and shape work concludes, ExCo sets change agenda for the Agency and moves into detailed design phases, balanced score card development underway; "user needs" analysis run in parallel.

    b. **Jan** - ExCo proposes the outline vision and key priorities, after consultation with the DHSC sponsor, for the Board to approve.

    c. **Jan** - Chief Officers develop priorities and deliverables for the year, to give an overall plan for their business areas using priorities within size and shape outputs (ie a clear picture of their staff headcount), working closely with corporate support services.

    d. **End Feb** - Outline plans produced in draft.

    e. **Mar** - External (DAs, industry, network, public etc) consultation and iteration.

    f. **End Mar** - Draft final plans cleared by DHSC Finance, EU/trade and Sponsor.

    g. **Apr** - final draft ready for Board and then ministerial approval; DHSC comms approval needed prior to plans being published.

Items for discussion

1. The Board is asked to approve the proposal for a 2-year Corporate Plan (and outline third year) focused on the Agency's Change Strategy, and a Business Plan focused on year one implementation of the Corporate Plan.
2. The Board is asked to review the issues identified in this paper and provide direction on the strategic priorities that should be used in the development of this new Corporate Plan.
3. The Board is asked to provide feedback and advice on the proposed planning process.

Medicines & Healthcare products Regulatory Agency

Board Meeting

23 November 2020

WHAT IS THE PROPOSED MEMBERSHIP OF THE BOARD ASSURANCE COMMITTEES AND THE SPECIAL RESPONSIBILITIES OF THE NON-EXECUTIVE DIRECTORS?

Issue: There is a need to agree the membership of the new Board Assurance Committees agreed at the last meeting following a series of individual discussions between the Chair of the Board, the Non-Executive Directors and the Executive Committee to establish personal preferences, special interests, skills and experience.
Action required by the Board and by when (timings): The Board is asked to approve the proposed membership of the Board Assurance Committees so that each committee can finalise their Terms of Reference in line with the MHRA Governance Framework and Assurance Map approved at the MHRA Board Meeting on 26 October 2020. The Board is also asked to endorse the proposed special responsibilities assigned to each Non-Executive Director.
Implications for patients and the public: The Patient & Safety Assurance Committee will provide assurance to the Board that the Agency has the necessary systems, controls and governance to enable patient engagement and patient involvement in the discharge of its statutory responsibilities on patient safety. The Audit & Risk Assurance Committee will provide assurance to the Board that the Agency has the necessary systems, controls and governance to manage risk 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? All and particularly Organisational Excellence / Efficiency. **If relevant, which Business Plan strategic activity does it support?**
Author (s): Stephen Lightfoot
Board Sponsors: Stephen Lightfoot

BOARD ASSURANCE COMMITTEES AND SPECIAL RESPONSIBILITIES OF NON-EXECUTIVE DIRECTORS

Background

1. The Board approved a Revised Governance Framework and Assurance Map at its last meeting on 26 October 2020 and this included the establishment of the following three Board Assurance Committees:
   - Audit & Risk Assurance Committee
   - Patient & Safety Assurance Committee
   - Organisational Development & Remuneration Committee

2. The Chair of the Agency Board has spoken to each of the Non-Executive Directors (NEDs) and the Executive Committee to establish personal preferences, special interests, skills and experience for which Assurance Committee they would want to be involved in before making the following proposals.

3. The intention is to build a Unitary Board Assurance Committee structure with an equal number of Executive and Non-Executive members. These committees will be chaired by a nominated Non-Executive Director, who will have a casting vote in the unlikely event that there is a significant difference of opinion between the members of the committee on the level of independent assurance that can be given to the Chief Executive and the Board.

4. The Chair of each Board Assurance Committee will be expected to prepare a written report after each committee meeting on the level of assurance that can be provided within its remit and then present that report to the Board at the next Board Meeting.

Proposed Assurance Committee Membership

5. The following membership has been proposed for each committee to achieve a fair balance of skills, experience, interest and workload:

Audit & Risk Assurance Committee
Michael Whitehouse (NED Chair)
Dr Barbara Bannister (NED Member)
Mandy Calvert (NED Member)
Dr June Raine (Chief Executive Officer)
Jon Fundrey (Chief Operating Officer)
John Quinn (Chief Technology Officer)

Patient & Safety Assurance Committee
Mercy Jeyasingham (NED Chair)
Professor David Webb (NED Member)
Professor Bruce Campbell (NED Member)
Lay Member (to be recruited)
Lay Member (to be recruited)
Dr Sam Atkinson (Chief Quality & Access Officer)
Dr Christian Schneider (Chief Scientific Officer)
Chief Safety Officer (to be recruited and Dr June Raine will cover this role until then)

Organisational Development & Remuneration Committee
Anne-Toni Rogers (NED Chair)
Mandy Calvert (NED Member)
Professor Liam Smeeth (NED Member)
Dr June Raine (Chief Executive Officer)
Jon Fundrey (Chief Operating Officer)
Director of Human Resources

6. The next step is for each committee to meet and finalise their Terms of Reference based on the key headlines in the approved MHRA Governance Framework and Assurance Map before submitting them to the Agency Board for approval at the earliest opportunity.

7. This membership list will be kept under review and amended when new Board Directors are appointed and as the transformation of the Agency progresses.

8. All Board Members will have an open invitation to attend and participate in any of the Board Assurance Committee Meetings as required.

Non-Executive Director Special Responsibilities

9. The following special responsibilities have also been proposed to provide further opportunities for Non-Executive Directors to collaborate and add value outside the schedule of Board and Committee Meetings:

Special Board Responsibility	**Non-Executive Director**
Deputy Chair of MHRA Board	Professor David Webb
Senior Independent Director of MHRA Board	Michael Whitehouse
NED Member of Conflicts of Interest Sub Committee	Dr Barbara Bannister
Chair of NIBSC Scientific Advisory Committee	Professor David Webb
Member of CPRD Executive Board	Anne-Toni Rodgers
Medical Appraiser for Senior Medics in MHRA	Dr Barbara Bannister
Raising a Concern Champion	Mercy Jeyasingham

10. This list of special responsibilities will be kept under review and amended as required.

11. Non-Executive Directors will be asked to present an assurance report on their responsibility to the Board on at least an annual basis and this can be done in conjunction with the relevant Executive Director to reinforce collaborative working across the Unitary Board. These assurance reports will be built into a rolling schedule of business to further strengthen the assurance received by the Board.

Medicines & Healthcare products Regulatory Agency

Board Meeting

23 November 2020

WHAT ARE THE PROPOSED 2021 DATES FOR THE MHRA BOARD MEETINGS?

Issue: There is a need to agree the 2021 dates for the MHRA Board Meetings, which will all be held in public.
Action required by the Board and by when (timings): The Board is asked to approve the proposed dates for MHRA Board Meetings in 2021 which have been selected to provide a regular schedule based on the third Tuesday in every month. Meetings will continue to be held virtually until Government Guidelines on COVID-19 allow face-to-face meetings to resume. However, when face-to-face meetings do resume, these dates avoid the need for travel on Monday mornings and Friday evenings. The proposed dates are: • Tuesday 19th January 2021 • Tuesday 16th February 2021 • Tuesday 16th March 2021 • Tuesday 20th April 2021 • Tuesday 18th May 2021 • Tuesday 15th June 2021 • Tuesday 20th July 2021 • Tuesday 21st September 2021 • Tuesday 19th October 2021 • Tuesday 16th November 2021
Implications for patients and the public: The MHRA wants to hold its Board Meetings in public to help highlight its critical role in protecting and improving patient health, whilst making the activities of its Board more transparent, accessible and accountable to patients and the general public.
Which of the theme (s) in the Corporate Plan 2019/2023 does the paper support? All and particularly Organisational Excellence / Efficiency. **If relevant, which Business Plan strategic activity does it support?**
Author (s): Stephen Lightfoot
Board Sponsors: Stephen Lightfoot