Medicines & Healthcare products Regulatory Agency

MHRA Board (in public session)

MINUTES OF THE MEETING

23 April 2018

Present:

The Board

Professor Sir Michael Rawlins GBE Kt	Chairman of MHRA
Mr Martin Hindle	Deputy Chairman
Dr Ian Hudson	Chief Executive
Mr Jon Fundrey	Chief Operating Officer
Dr Barbara Bannister MBE	Non-Executive Director
Mr Matthew Campbell-Hill	Non-Executive Director
Mr Stephen Lightfoot	Non-Executive Director
Ms Deborah Oakley	Non-Executive Director
Dame Valerie Beral	Non-Executive Director

Others in attendance

MHRA executive and supporting officials

Mr Jonathan Mogford	Director of Policy
Ms Rachel Bosworth	Director of Communications
Mr John Wilkinson OBE	Director of Devices
Dr Samantha Atkinson	Director, Business Transformation
Dr Christian Schneider	Director of the National Institute of Biological Standards & Control
Stephen Lee	Senior Regulatory Policy Manager - IVD
Gavia Taan	Senior Regulatory Policy Manager
Louise Loughlin	Head of Science Strategy
Natalie Richards	Deputy Head of Directorate
Jude Thompson	Executive Assistant to the Chairman

Legal Services

Mr Paul Wright	Deputy Director, MHRA, Nutrition and EU Team, DH Legal Advisers, Government Legal Department.

Item 1: Introductions and Announcements

1.1 Apologies were received from Professor Bruce Campbell, Non-Executive Director, Professor Sir Alex Markham, Non-Executive Director, Professor David Webb, Non-Executive Director, and Mrs Carly McGurry, Department of Health and Social Care.

1.2 The Chairman welcomed everyone to the meeting.

Item 2: Declarations of interest

2.1 One declaration was made:

(i) *Professor Sir Michael Rawlins:* Professor Sir Michael advised that he is a member of Council for Newcastle University, who own the Intellectual Property for Rubraca (rucaparib), which is discussed in the Chief Executive's report.

Item 3: Minutes of the public Board meeting of 15 December 2017

3.1 The minutes of the last public Board meeting, which the Board adopted in February 2018, were noted.

DISCUSSION ITEMS

Item 4: Brexit

4.1 Jonathan Mogford gave an oral update on Brexit-related work to analyse the best options and opportunities available for the safe and effective regulation of medicines and medical devices in the UK. There are three key areas of work Mr Mogford provided updates on: the work on the withdrawal agreement and the Implementation Period (IP); the work on the future relationship with Europe; and the wider work which is ongoing alongside the negotiations. With regards to the withdrawal agreement and the IP; there has been an agreement within the EU for an IP from March 2019 to 2020. Work is ongoing to check the details of the IP and what that means in relation to specific activities such as batch release, the UK's position as co-rapporteur, and to confirm that UK Notified Bodies will continue to be able to issue CE marks for medical devicecs during the IP.

4.2 Mr Mogford detailed the ongoing discussions regarding the future relationship between the UK and the EU; the UK government position remains to seek associated membership of the EU pharmaceuticals framework and alongside this develop a set of mutual recognition agreements covering various areas including medical devices. MHRA continue to work with industry who are supportive of this associative membership work. MHRA continues to develop fallback options if the EU does not agree to an associative option, such as targeted assessment or standalone models.

4.3 It was noted that a full set of Statutory Instruments are being worked up at high levels of development for the legal underpinning of operations in a no-deal scenario. The MHRA also recently undertook a business continuity exercise to prepare for Brexit. Work continues to prepare IT systems for Brexit day 1 and for the future.

4.4 The Chairman thanked Mr Mogford for the update and invited comments from the Board. These centre on the following areas:

- *UK presence at European Committee meetings such as CHMP and PRAC during the IP* - The Board asked whether the UK would still be able to be present at European meetings such as CHMP and PRAC; Mr Mogford explained that the exact details are still being worked up; it is reasonable to expect the UK will be present at these meetings however it is not clear what the UK's voting rights will be.
- *IT preparations* – The Board asked if IT preparations are being made for data transfer in the case of a hard Brexit; Mr Mogford noted that preparations are being made to ensure that both in legal and in IT terms the UK is ready to continue the work of the organisation moving forward seamlessly.
- *Delays to market* – The Board asked whether Europe would have the capacity to stop delays in getting a product to market, once the UK has left the regime. It was

noted that the EMA has undertaken a capacity review to understand how they will be impacted in future. The EMA and the European Commission are briefing companies to be prepared for this eventuality.

4.5 The Chairman then invited questions from the staff and public observers; none was offered.

Item 5: Chief Executive Officer's report

5.1 Dr Hudson presented highlights from the Chief Executive Officer's (CEO) report. These centred on the following areas:

- *Hormone Pregnancy Tests (HPT)* – the recommendations of the Expert Working Group are being taken forward; a Cross-Sector Steering Group chaired by Lord O'Shaughnessey has been set up. MHRA has set up a Cross-Agency Group on the Safety of Medicines in Pregnancy; this repots up to the Cross Sector Steering Group.

- *Raxone* – a patient-focused meeting to consider Raxone and the Early Access to Medicines Scheme (EAMS) in light of the recent negative CHMP opinion on this product was held on 23 March; it provided the CHM members and Licensing colleagues with insight to the likely impact on patients should Raxone no longer be available through EAMS.

- *International work* – meetings were held with Health Canada and the USA Federal Drugs Administration recently to discuss future working. Dr Hudson met with Health Canada and the Australian Therapeutic Goods Authority in the margins of a recent ICMRA meeting. Work continues on updating the Memorandum Of Understanding (MOU) with India and taking forward the recently signed MOU with China.

- *Central Alerting System (CAS)* – the CAS system has been successfully transferred from the DHSC platform to the MHRA platform following a very short outage period.

- *Innovation Office* – to mark the 5th anniversary of the Innovation Office, a meeting was held with the major UK funders of academic research to raise awareness of the support offered by the Innovation Office and to gain feedback from the funders on how future efforts should be focused to bring together the research community and regulatory authorities.

- *MHRA Relocation Move* – the MHRA's move to 10 South Colonnade in Canary Wharf continues to progress; the physical move will take place in June 2018 and the next public MHRA Board will take place at the new building.

5.2 The Chairman then invited questions from the Board, which centred on:

- *Baroness Cumberlege Review* – the Board enquired as to the progress of the review into how the NHS responds to safety concerns raised by patients about medicines or medical devices led by Baroness Julia Cumberlege. The Chairman informed the Board that the Agency has been in touch with the organisers to offer the Agency's help to support this work.

- *Agency events programme* – the Board commented that the Agency's events programme has been a significant achievement for the Agency and demonstrates how valued the Agency's training events are to industry.

Questions from staff and public observers

5.3. The Chairman then invited questions from the staff and public observers, which centred on:

- A member of the public asked if any more insight could be given in to the impending announcements regarding valproate; Dr Hudson noted that the press release will be published on Tuesday 24th April.

Item 6: Horizon scanning

6.1 Dr Christian Schneider gave an oral update on horizon scanning. The Agency has started a horizon scanning initiative with a dedicated resource to systematically review new technologies; a strong network within the Agency and across the wider health family in the UK and beyond is essential for this initiative. Staff across the Agency have reported potential signals to the Horizon Scanning Strategic Lead; once a signal is identified, a report is generated which is taken to the CET for information. Dr Schneider gave an example of a recent horizon scanning signal of transplantation factors of the human gut natural microbiome. A research stream has been set up at NIBSC in this area; once this product has therapeutic intent, standardisation, manipulation and industrial manufacture, the principle active substance may be classified as a medicine.

6.2 The Chairman thanked Dr Schneider for his report and sought the Board's views. These centred on the following areas:

- *International collaboration* – The Board enquired whether international collaboration is undertaken as a formalised process; Dr Schneider noted that the Horizon Scanning Strategic Lead contributes to an International Collaboration of Medicines Regulatory Authorities (ICMRA) workstream on horizon scanning with input from across the globe.

- *Research vs regulation* – The Board asked how decisions will be made on how much effort should be put in to new areas of research compared to areas which already exist which require funding for regulation. Dr Schneider commented that the primary focus would be on public health; if a new area of work is identified which would be beneficial for public health then the Agency would liaise with funding bodies.

6.3 The Chairman then invited questions from the staff and public observers; none was offered.

Item 7: NIBSC – Highlights

7.1 Dr Schneider presented a summary of the NIBSC highlights against its activities in 2017/18. The Standards Programme Board (SPB) reported on the standards accepted at the WHO Expert Committee for Biological Standardisation held in October 2017, with 23 physical standards accepted, 17 of these being new (i.e. 1st) WHO International Standards or WHO Reference Reagents. It was noted that some of these standards will have significant impacts on public health. One standard Key Performance Indicator (KPI)

target was missed by 0.1 days; it was noted this was due to an issue outside of NIBSC control.

7.2 The Control Programme Board (CPB) met all the targets for batch release and workbench reviews. Batch release activity is being monitored by CPB, noting that there has been a decrease in batches provided to NIBSC over the year and there is indication that this drop will continue due to Brexit. It was noted that it is important to retain a close link with Licencing division to understand when new vaccines are due to be licenced, to NIBSC can help with the licencing or batch release process when the licence has been authorised. The Research Programme Board (RPB) reported that within 2017, Institute staff were authors or co-authors on 75 papers published in the year, a slight reduction again from the previous year.

7.3 The Regulatory Science Research Unit (RSRU) reported that funding has been granted by DHSC for another 5 years; this has been defined in to 6 workstreams:

a. Assuring Access to Monoclonal Antibodies as Biological
b. The threat of Global Infectious Diseases
c. Regenerative and Cell Based therapies - Accelerating access to treatment for Neurodegenerative Disease
d. Using Biologics to overcome Anti-Microbial Resistance
e. Stratified Medicine and Genomics
f. Humanised Mouse Models for evaluating Biologics

7.4 This year's round of applications for PhD studentships to commence in 2018 received 13 applications; 3 of these have been granted for research in to a novel vaccine for Bordetella pertussis; a glyco-conjugate vaccine against Group A Streptococcus; and influenza haemagglutinin. In the virology division, successful work has been ongoing in provision of vaccine candidate strains and potency reagents to support timely supply of influenza vaccines for both Northern and Southern Hemispheres. Good progress has been made on the work towards the global polio eradication programme. There has ALSO been good progress in the work around Emerging Infections, e.g. Ebola, Zika, MersCoV. A member of NIBSC has been appointed as a member on the Coalition for Epidemic Preparedness Innovation. In Technology, Development and Infrastructure (TDI), a new Nuclear Magnetic Resonance (NMR) spectrometer was installed, validated and is now supporting safety and efficacy of conjugate vaccines for batch release in line with the Quality System; this will establish NIBSC as a centre for excellence of use of technology. Funding for the UK Stem Cell Bank is currently being secured.

7.2 The Chairman thanked Dr Schneider for his report and sought the Board's views. These centred on the following areas:

- *Bill and Melinda Gates Foundation* – The Board asked whether there was opportunity for further development of years funding by the Gates Foundation; Dr Hudson noted that the Agency has recently received support from the Gates Foundation and from the World Health Organisation to support the launch of antimalarial drugs and tuberculosis treatments; there is also interest in supporting African drug safety networks.

- *NIBSC challenges* – The Board asked if there were any negatives form the last year of work; Dr Schneider noted that it is sometimes difficult to balance research standardisation and control in to staff workplans; often senior staff are required to spend a lot of time on administrative duties which could be improved. NIBSC are developing a generic system to address these issues to reduce administrative time for scientists.

- *Physical standards* – The Board queried the proportion of standards WHO approved were developed by NIBSC; Dr Schneider indicated that NIBCS standards contributed approximately 90%. NIBSC is a world leader in this area. It was noted there are some emerging competitors for example in the Chinese market; this keeps NIBSC expertise and technological skills prevailing.

7.3 The Chairman then invited questions from the staff and public observers which centred on:

- A member of the public asked whether the Agency considered whether safety regulations and controls of new medicines in the UK hampered new treatment of patients; Dr Hudson noted that in the lifecycle of a medicine, there are many challenges to bringing a product to market. Disease research and drug development is a complex field and products must be developed safely in a manner which protects subjects who partake in clinical trials. Patients need access to treatments as soon as possible and regulation is very flexible in relation to this. The Agency has various schemes which allows medicines to be accessible to patients before they are licenced, such as the Early Access to Medicines Scheme – this takes in to account areas of unmet medical need or lack of alternative treatments. Conditional licenses are also available to hasten patient access to medicines.

7.4 In conclusion, the Board endorsed the update and congratulated NIBSC on the vast amount of work undertaken in the last year.

Item 8: Building and maintaining academic relationships – update

8.1 Christian Schneider presented an update on building and maintaining academic relationships. 4 areas have been identified to focus on:

1. Regenerative medicine
2. Clinical Trial Design
3. Supporting emergency response to disease
4. Use of Real World Data

Each of these areas will be led by a CET member. The Board noted the updates on each of these areas. With regards to the functioning of the academic relationships network, previously CET had recommended that an informal network would work more successfully than a formal academic relationships network. This area of work is led by the Horizon Scanning Strategic Lead. A recommendation was made for MHRA staff to undertake academic lecturing and training on an ad-hoc basis as this would consist of a large amount of resource.

8.2 The UK Stem Cell Bank will bring along a number of academic relationships which will need to be supported; it was noted that the UKSCB is an important resource which is not for profit and which requires continual funding; which the Agency is currently investigating options for.

8.3 The Chairman thanked Dr Schneider for his report and sought the views of the Board, which centred on the following areas:

- *Clinical trials* – The Board noted that for very low risk studies, a notification scheme was set up, yet this has hardly been used; it was suggested that a piece of work should be undertaken by MHRA staff to promote this notification scheme.

Questions from staff and public observers

8.4 The Chairman invited questions from the staff and public observers which centred on:

- *UK Stem Cell Bank* – a member of the public asked how the international banking of stem cells or any other tissues may be affected by Brexit. Dr Schneider noted that the majority of clinical grade stem cell lines in the UKSCB come from UK resources. The UK would be able to host stem cells from international partners post Brexit; it was noted the impact on the UKSCB from Brexit is expected to be minimal as the UKSCB is a worldwide resource rather than a European resource.

8.5 In conclusion, the Board endorsed the paper and noted the update.

Item 9: Genomics and Companion Diagnostics

9.1 Stephen Lee presented an update on genomics and companion diagnostics, following a previous report to the Board in 2017. Genomics and companion diagnostics are an important area for the Agency to work in as they are new and innovative technologies which help with the diagnosis for rare and degenerative conditions, and help patients understand their treatment options. In the context of the new In-Vitro Diagnostics Regulations (IVDR) implementation, the new regulations provide a different framework for control of these technologies. To help guide companies during the implementation of the IVDR, MHRA has published a number of draft guidance documents for consultation on the website. This consultation runs until March 2019 to ensure health institutions have time to review and understand the new requirements.

9.2 Bioinformatics were discussed; there are particular challenges with regards to the use of open source software and Artificial Intelligence. Bioinformatics are considered essential for the safe and effective use of companion diagnostics; notified bodies will be required to review the clinical evidence, and a medicines authority will need to give an approval of a notified body. Headway is being made on obtaining EU agreement in getting this to practice.

9.3 The Chairman thanked Mr Lee for his report and sought the Board's views. These centred on the following areas:

- *Timing of licencing* – The Board asked how the timing of approval of the companion diagnostic and licencing of the drug is managed. Mr Lee noted that Licencing and Devices Divisions in the Agency work together to ensure the CE mark and the medicinal product licences appear on the market at the same time. It was noted that there may be a situation in the future when a generic version of the medicine will appear on the market; these companies would need ot have their own companion diagnostic or there would need to be a generic platform which also needs to be regulated; this will be a challenge for the future.

Questions from staff and public observers

9.4 The Chairman then invited questions from members of the public and staff. These centred on the following areas:

- *Mitochondrial disorders* - A member the public asked whether as part of genomics and pharmacovigilance of medicines, would the way genes be affected by medicines studied, such as mitochondrial dysfunction. It was noted that it is important for clinical researchers to understand the connections between adverse effects and medicines; the Centre for Drug Safety Science undertakes research in to adverse effects.

Item 10: Key changes introduced in the new EU Devices Regulations

10.1 Gavia Taan presented a paper on the key changes introduced in the new EU Device Regulations, following an action from the last public Board meeting where there was a request of an overview of the changes from the current directives and the new device regulations. Much of the implementation is currently ongoing at a European level; the UK is involved in most of the working groups to implement the European Implementation Roadmaps. The UK is leading on a number of deliverables – including the new devices Product Safety Update Report; development of guidance on equivalence; and joint action on market surveillance.

10.2 Work continues to prepare the Agency and stakeholders for the new regulations; including those who are new to the regulations such as importers and distributers who have now been brought in under the new regulations. Relationships are also being strengthened with existing stakeholders, and closer relationships are being developed with NHS trusts. In January 2018 guidance was published by the Agency for health institutions on how to apply for exemptions for new products; this guidance will run until March 2019. At a global level the Agency continues to be involved in a number of International Medical Device Regulators Forum (IMDRF) workstreams to harmonise definition of custom made devices and patient specific devices to work towards a global harmonised approach. One of the key areas in the Agency is the expanded market surveillance role, alongside the expanded role in general for regulation of medical devices. A key challenge from this relates to resourcing; the Agency is looking in to how to raise fees from industry to fund some of these changes.

10.3 The Chairman thanked Ms Taan for the update and sought the Board's views. The Board noted the update.

Questions from staff and public observers

10.4 The Chairman invited questions from members of the public and staff; none was offered.

Item 11: Any Other Business (AOB):

11.1 The Chairman and the Board thanked members of the public and staff for attending the meeting.

11.2 The Chairman then asked if there were any items of AOB. Comments from members of the public centred on the following areas:

- *Teratogenic reporting systems* – it was asked whether the MHRA is putting in place a teratogenic reporting system to go alongside the Yellow Card reporting scheme. Dr Hudson noted that the Expert Working Group on Hormone Pregnancy Tests identified a number of recommendations; a cross-centre expert group is currently being established to review drugs during pregnancy. This work will be taken forwards through this working group. It was noted that when new medicine dossiers are assessed, particular attention is given to any evidence of teratogenicity.

- *Hip replacements* – a member of the public enquired whether hip replacement products fall under MHRA's remit. It was noted that this does fall under MHRA's remit and the Agency monitors the safety of hip joints and any implantable

medical devices very carefully. An expert advisory group under the Devices Expert Advisory Committee exists to monitor the safety of hip joints, using data sources including a national joint registry.

- Prescribing practice – a member of the public noted that there seems to be practice of over-prescribing of medication which should be addressed. It was noted that the MHRA ensures that prescribers have access to the most up to date relevant information however the Agency has no jurisdiction over the medical profession.

Date of next public meeting: 22 October 2018