MHRA Board meeting (part 1: in public session)

11 April 2016

CHIEF EXECUTIVE'S REPORT FOR THE MONTH OF MARCH 2016

1. HEADLINES for March 2016

Annual lecture 2016 – Dr Margaret Chan, Director General of the World Health Organisation (WHO), delivered the agency's annual lecture. The event was at full capacity and received very positive feedback from key stakeholders who attended. These included senior representatives from industry, trade bodies, academic institutions, professional regulators and others from across the health and care system. On the night our social media engagement reached just under 3 million unique views, a record for the agency. We filmed the event and have produced the following:

- Short promotional video can be viewed here.
- Full video of the lecture can be viewed here.
- Key excerpts of the lecture and stakeholder feedback can be viewed here.
- View photos from the evening here.

Sodium Valproate - Agency colleagues worked with Sanofi and stakeholders from professional bodies and voluntary organisations to develop package of materials to aid communication of risks of valproate in pregnancy to health professionals and patients. This was based on the outputs of the EU wide review of neurodevelopmental disorders associated with valproate use in pregnancy which completed in 2014.

The toolkit consists of a patient card, a healthcare professional booklet, a patient guide and a checklist for prescribers and was communicated to health professionals on 8 February to coincide with International Epilepsy Day. Following previous work with patient organisations, in January 2016 the agency established the Valproate Stakeholder Network (VSN) comprised of relevant patient groups that represent epilepsy, migraine, bi-polar, mental health and sexual health issues; as well as the main valproate campaign groups.

The VSN has worked in partnership with MHRA to support the introduction of the toolkit and its member organisations have committed to assist the agency through a range of opportunities that they will have to promote the communication measures during 2016. For example: during National Epilepsy Week to be held in May 2016, through inclusion in regular newsletters and magazines distributed to patients and supporters or at relevant conferences and other events.

On 15 April the agency will host a multi-stakeholder meeting to bring together the VSN groups with those professional and regulatory organisations that have participated in the ministerial roundtable, in order to collectively agree the metrics for a dashboard to measure the impact of the toolkit over time.

Social media was used to promote the Valproate toolkit as linked to Purple Day, World Epilepsy Day. This included a quotograph featuring Dr June Raine, Director of Vigilance and Risk Management of Medicines (VRMM).

Adrenaline auto-injectors - In 2014 the Medicines and Healthcare Products Regulatory Agency (MHRA) published its findings from a review of adrenaline auto-injectors (AAIs) – devices carried by patients for "on the spot" administration of adrenaline in the event of anaphylaxis, a life-threatening severe allergic response. The review was conducted on the recommendation of a coroner's report into the death of a patient with anaphylaxis who failed to respond to such a device. The investigation highlighted a lack of robust evidence for injection of adrenaline into muscle tissue, accepted to maximise the likelihood of a successful treatment outcome. Shortcomings in product information with regard to mode of use were addressed immediately at a national level by strengthened warnings and clarified instructions, implemented by variation applications. The public and healthcare professionals were notified of these changes via a wave of communications including a Press Release, Drug Safety Update Article and a Dear Healthcare Professional letter.

Outstanding uncertainty over the reliability of AAIs to deliver adrenaline into muscle tissue in all patients, led the MHRA to request a Europe-wide safety review under Article 31, the recommendations from which were embodied in European legislation by the European Commission last year. The Article 31 review concluded that AAIs are in the main effective and do save lives but there was a need for improvement to provide greater assurance of performance. Mandated improvements include revisions to the product information so that warnings implemented by the UK at a national level are now reinforced and rolled out across Europe, together with advice to carry two AAIs in case of a failure to respond to the first injection. Improvements in the quality and availability of training materials for patients, carers and prescribers, will also be implemented, the Risk Management Plan being the vehicle to ensure this.

Crucially, the European review endorsed the need for dedicated studies in human volunteers of the rate and extent of adrenaline penetration into the blood stream, when delivered by auto-injector devices, and whether adequacy to treat anaphylaxis can be inferred. The potential need for provision within the product information to vary the site of injection, or to provide brand recommendations, according to patient physique, will also be considered as a component of the clinical study. As mandated, clinical study protocols for all authorised devices have been submitted for review under a series of Worksharing procedures, assessment of which is being contributed to by all the involved Member States. Once the protocols are approved, the studies must be conducted and submitted within a specified time frame. The legal requirement for submission of clinical studies applies to existing and prospective holders of Marketing Authorisations for AAIs across Europe.

Throughout, the MHRA has listened carefully to the concerns and real world experiences of patients, and affected family members, to help inform amendments to patient and prescriber information material and the training material recommendations. Together with the new regulatory requirement for robust, dedicated, studies of AAIs in humans, these will help to ensure consistent and reliable performance of these vital life-saving devices in the treatment of anaphylaxis and may also instruct improvements in the design of the devices themselves.

Early Access to Access to Medicines Scheme (EAMS) – scientific opinions:
The aim of the Early Access to Medicines Scheme (EAMS) is to provide earlier availability of promising new unlicensed medicines to UK patients that have a high unmet clinical need. To dated there have been 7 EAMS scientific opinions awarded,

including medicines for treating lung cancer, melanoma and heart failure. The scientific opinion describes the risks and benefits of the medicine and supports the prescriber and patient in making a decision on whether to use the medicine before its licence is approved. The EAMS opinion lapses at the time of the grant of a marketing authorisation (drug licence). Four have expired.

There are three current EAMS scientific opinions, allowing earlier patient access.

- EAMS scientific opinion: pembrolizumab for non-small cell lung cancer. (15 March 2016 Decision)
- EAMS scientific opinion: nivolumab for renal cell carcinoma. (11 February 2016 Decision)
- EAMS scientific opinion: nivolumab for non-squamous non-small cell lung cancer (NSCLC) (5 February 2016 Decision)
- https://www.gov.uk/guidance/apply-for-the-early-access-to-medicines-scheme-eams

An Independent review of Early Access to Medicines Scheme (EAMS) was published on the 22 March 2016 (PWC). The Office for Life Sciences has commissioned Strategy & to conduct an independent review of the UK's EAMS. The review meets the government's objective to assess the performance of the EAMS within two years of launch and aims to address three key questions

https://www.gov.uk/government/publications/independent-review-of-early-access-to-medicines-scheme-eams

- Conclusions include: MHRA have provided good signposting of the EAMS application process and applicants to the EAMS interviewed commented that they have found the application process to be simple, clear to understand, and relatively straightforward. In particular, industry praised the MHRA for the guidance documentation provided on the EAMS webpage and for the accessibility of its staff to discuss the benefits and risks of entering the scheme.
- Recommendations to improve the scheme include providing updated guidance on the benefits and entry requirements of EAMS, provide easier industry access to MHRA, NICE, NHS and the devolved administrations and offer funding via application

2. PRODUCT RELATED ISSUES

Medicines issues

Pyrrolizidine alkaloids contamination - Pyrrolizidine alkaloids (PAs) are a group of naturally occurring alkaloids produced by plants. In February this year MHRA issued a precautionary recall of six batches of St John's Wort tablets as a precaution because of product contamination with PAs.

Clinical Trials in France: Involvement in cross-agency incident groups - On 15 January 2016, MHRA became aware that five participants in a French first-in-human clinical trial of the fatty acid amide hydrolase (FAAH) inhibitor BIA 10-2474 showed severe symptoms, with one participant reported as brain-dead. This subject died on 17 January 2016. The product has not been tested in any UK clinical trial and there

are no ongoing UK trials with compounds with a similar mechanism. The Agency is working through the available documentation to consider any implications for clinical trial approvals in the UK.

Zika Virus - MHRA has set up an incident group with personnel across the agency. We are actively involved in responding to this emergency with offer of help with early phase clinical trials, scientific advice and rapid evaluation of both clinical trials and the development of vaccines. The incident group has established contacts and interactions with the WHO, the European Medicines Agency, ICMRA (International Coalition of Medicines Regulatory Authorities) Zika Network and the EU wide group for Zika.

Within MHRA, the NIBSC has responded immediately to the WHO request to develop and evaluate reference preparations for Zika. NIBSC is currently working with the WHO and colleagues from other WHO designated collaborating centres to produce materials for and undertake international collaborative studies that will result in the production of:

- an international standard for Zika virus RNA to enable accurate diagnosis of active infection
- an international standard for Zika virus antibodies to enable accurate diagnosis for those exposed to the virus
- an international standard for Zika antigen for use in rapid point of care assays

The standards being created by NIBSC will help researchers, product developers, and regulatory authorities benchmark the multiple diagnostic tests for Zika that are currently under development. It is hoped that this work will accelerate the creation of vaccines or treatments.

MHRA is also taking action as the regulator of medicines. We've worked where necessary to remove from sale an unregistered homeopathic medicine claiming to be a treatment for Zika.

Inhaled corticosteroids and risk of pneumonia - The Pharmacovigilance Risk Assessment Committee (PRAC) completed a review (led by UK) into the latest evidence on the known risk of pneumonia associated with inhaled corticosteroids used in chronic obstructive pulmonary disease (COPD). The review concluded that COPD patients treated with inhaled corticosteroids are at increased risk of pneumonia but that the benefits of treatment continued to outweigh the risks. The review also looked to see if there was any difference between products in the level of risk of pneumonia and did not find conclusive evidence of a difference and concluded that all inhaled corticosteroids should have consistent warnings about the risk of pneumonia in the product information for healthcare professionals and patients.

Idelalisib (Zydelig) and serious and fatal adverse events - At its March meeting, the PRAC issued provisional advice for doctors and patients using Zydelig (idelalisib), which is authorised to treat chronic lymphocytic leukaemia (CLL) and follicular lymphoma pending review of data which showed a higher rate of serious adverse events in three clinical trials among patients receiving Zydelig compared with placebo. A letter will be sent to healthcare professionals advising close monitoring of patients on Zydelig and use of antibiotics to prevent pneumonia. PRAC will consider a review of all available data at a future meeting .

Direct acting antivirals and hepatitis B reactivation - Following the discussion at the February Pharmacovigilance Risk Assessment Committee (PRAC) about emerging data that raise concern about hepatitis B re-activation in patients treated with direct-acting antivirals for hepatitis C, the European Commission has initiated an Article 20 referral. The review will explore possible mechanisms, clinical consequences, risk factors and also the need for measures to further minimise the impact of potential reactivation of hepatitis B virus .

Gadolinium containing contrast agents and brain deposition - A referral on the issue of brain deposition of gadolinium containing contrast agents, used during MRI scans, was initiated at the March PRAC. A previous referral which finished in 2010 considered the risk of nephrogenic systemic fibrosis (NSF), a serious and life threatening syndrome involving fibrosis of the skin, joints and internal organs, and concluded that the gadolinium contrast agents could be categorised into high, medium and low risk for NSF. Risk minimisation measures implemented following that referral seem to have been successful in reducing the risk of NSF; however, concern has remained about the potential for accumulation of gadolinium in other tissues following administration of these agents. The current referral has been initiated following publications which have indicated the accumulation of gadolinium in the brain after administration of gadolinium containing contrast agents. The referral will consider the extent to which gadolinium is deposited in the brain following administration of the different products and the clinical consequences of the deposition. The referral will also consider the impact of this new information on the overall safety profile of gadolinium containing contrast agents .

Hearing aid batteries – The Agency issued a press release regarding defective hearing aid batteries, in support of a Medical Device Alert.

Devices issues

Medical Device Alerts (3),

Number	Title
MDA/2016/002	Ambulatory syringe pumps (T34 and T60) and syringe extension sets used with the T34 pump, manufactured by Caesarea Medical Electronics (CME).
MDA/2016/003	All ZeniPower mercury-free hearing aid batteries – low risk of batteries exploding during use or if depleted.
MDA/2016/004	Estradiol immunoassays – interference from the drug fulvestrant (Faslodex®) may cause falsely elevated estradiol results.

3. REGULATION AND POLICY

European issues

The EMA launched their scheme for Priority Medicines (PRIME) on 7 March. PRIME aims to optimise the development and accelerated assessment of medicines of major public interest. Agency officials will be participating in the PRIME Oversight Group, which will begin in April.

In March, the working group on Pharmaceutical and Medical Devices began to discuss the Commission's proposal on removing the veterinary content from the Regulation (726/2004) and updating it to ensure it is consistent with the Lisbon Treaty. There was Member State concern over the proposition of delegated acts in some cases over implementing acts and further discussion is needed at the next meeting in April on the proposals around fees.

Medical Devices - EU Negotiations - Trilogue negotiations on the new EU Regulations on Medical Devices (MD) and in vitro diagnostic (IVD) Devices Regulations began in October 2015 following the agreement of a full Council General Approach. These continued into the 2016 Dutch Presidency and an informal political agreement before the end of their Presidency in mid-2016 is expected, although it is unlikely that final Regulations will be published before autumn 2016. We are working closely with other Member States and the European Parliament to ensure that the outcome of the trilogue discussions is in line with the UK's priorities

The 4th meeting of the European Commission Expert Group on Safe and Timely Access to Medicines for Patients (STAMP) took place on 10 March, and was attended by Agency officials. MHRA colleagues presented a paper on repurposing of established medicines/active substances and led a discussion. The MHRA was asked to maintain a lead in this area and will collate views and experiences of individual member states. Other areas discussed at the meeting included real world evidence data collection, compassionate use programmes and personalised medicines.

E-cigarettes – Agency colleagues have worked with the European Commission to develop guidance on the information and testing requirements for notification of e-cigarettes and refill containers and held a series of meetings with industry trade associations in March to discuss the guidance and their key concerns. VRMM and Policy Division also met a Swedish delegation to share experience of implementing the notification scheme.

We plan to transpose the Tobacco Products Directive 2014/14/EU (TPD) into UK law from 20 May 2016. Article 20 of the TPD introduces new rules for nicotine-containing e-cigarettes and refill containers. MHRA is responsible for implementing the majority of provisions under Article 20 and has been designated as the competent authority for the notification scheme in the UK.

The TPD introduces new rules which ensure:

- minimum standards for the safety and quality of all e-cigarettes and refill containers (otherwise known as e-liquids)
- that information will be provided to consumers so that they can make informed choices
- an environment that protects children from starting to use these products

From May 2016, the TPD introduces requirements for producers of e-cigarettes and refill containers to submit the information about their products to MHRA through a European Common Entry Gate (EU-CEG) notification portal. Initial information about the EU-CEG has been published by the European Commission.

When MHRA is satisfied that a product notification is complete and complies with the TPD, we will publish all non-confidential information. Producers will be able to specify information that they consider to be confidential when they submit a notification.

Further information about the notification scheme and what information will be required will be made publicly available in line with the European Commission's timetable.

The TPD does not cover nicotine-containing products that are authorised as medicines. Retailers do not need to submit information unless they also qualify as a producer.

The e-cigarette industry will be charged a fee to submit a notification to MHRA. An annual fee will also be charged from April 2017 unless a notification is withdrawn. MHRA consulted on the level of these fees in January 2016. Responses to the consultation are being considered and an announcement of fee levels will be made shortly

UK issues

Falsified Medicines Directive - The delegated regulation on the 'safety features' element of the Falsified Medicines Directive has now been adopted and published. The implementation deadline is 9 February 2019. We are working with DH on the joint implementation plan. The first meeting of the joint DH/MHRA implementation advisory board (this includes stakeholders from across the supply chain – industry, professional bodies and the devolved administrations) was held on 17 March, followed by another European Stakeholder Model (ESM) stakeholder meeting on 18 March.

Falsified medical products campaign - Following feedback from the Spend Control Panel (SPC) in February, we reviewed and revised our application to spend money for the campaign. Our application can now proceed to the next stage and some of the major preparatory work for the campaign can start, whilst we await sign off from the Minister and Cabinet Office. This includes starting the tender process to commission creative development, media planning and quantitative surveys.

We are halfway through our paid social media advertising to promote consumer awareness of the EU Common Logo. The Facebook advertising campaign is using carousel ads and promoted posts from the agency's main Facebook page to target online consumers of medicines, encouraging them to look for and use the EU Common Logo to identify if the website they are purchasing from is registered with MHRA. To date, this advertising has been seen 1.22 million times and resulted in an additional 12.5k members of the public who have visited the logo register of approved sellers.

Other ongoing campaign work includes: discussions with the Government Digital Service about hosting all of the online campaign content in a suitable place on GOV.UK that isn't the MHRA homepage; starting to develop content for the

campaign and generate PR coverage once we launch; continuing stakeholder engagement to ensure that we have the right partnerships in place to support the campaign. We have also started to consider how we can use the Yellow Card Scheme to generate higher calibre reports received via its 'Fake' button.

Framework Agreement - A Framework Agreement between MHRA and DH, agreed with HM Treasury, was signed by Ian Hudson and Will Cavendish on 24 February and published on 15 March 2016.

Corporate Plan Refresh and Agency Business Plan 2016/17 - Following discussions at the CET/Board in mid-March, both the Corporate Plan and the Business Plan will be published at the end of March / start of April

Regulatory Excellence (REGEX)- Regulatory Group has approved the reinvigoration of the Regex Working Group, with a renewed focus on the coherence and proportionality of the Agency's regulatory programme. A meeting is planned for 4 April. Refreshed Terms of Reference will be circulated prior to the meeting.

Innovation: Accelerated Access Review (AAR) - Publication of the final report is still expected in the near future, although the final date remains to be agreed. During March, the MHRA responded to final queries from clarifications from the AAR team. Some of the supporting evidence to the AAR – including the independent review of the Early Access to Medicines Scheme was published online in March. See: https://engage.dh.gov.uk/acceleratedaccess/supporting-evidence/

Joint Patient Safety and Vigilance Strategy – Work continues on the strategy to pursue a common excellence model for patient safety and vigilance for both medicines and devices. The Steering Group met for the third time in March and agreed the Terms of Reference and the Governance structure and heard outline deliverables from the Project Teams to take the strategy forward. The proposed deliverables will be presented to the CET in April and the Board will also be updated on progress.

4. MINISTERIAL AND PARLIAMENTARY PRIORITIES

Freedom of Information (FOI) requests

FOI Requests Received by Month 2015/2016													
	Apr-15	May-15	Jun-15	Jul-15	Aug-15	Sep-15	Oct-15	Nov-15	Dec-15	Jan-16	Feb-16	Mar-16	Total
Received	57	47	63	66	41	56	58	55	42	68	82	55	**690**
Replies sent on time	57	47	63	66	40	56	58	55	41	68	81	24	**656**
Replies not yet due	0	0	0	0	0	0	0	0	0	0	1	31	**32**
Breaches	0	0	0	0	1	0	0	0	1	0	0	0	**2**
% Compliance	**100%**	**100%**	**100%**	**100%**	**97.6%**	**100%**	**100%**	**100%**	**97.6%**	**100%**	**100%**	**100%**	**99.7%**

Please note that there is one reply outstanding from February. This is still compliant as the applicant was informed that the agency needed further time to consider the public interest test.

5. COMMUNICATION

The main agency-related issues covered in the press in March are as follows:

- **Twitter Q&A -** Following the Twitter Q&A workshops, development of a project plan and Q&A document, we ran our first-ever Twitter Q&A. As part of the employer branding campaign, the focus was on answering questions on the role of the Pharmaceutical Assessor, using the hashtag #AskPharm, to help potential applicants understand more about the role and ask questions of Pharmaceutical Assessors directly. It yielded very positive results across a number of different areas; during the hour we earned 17.8k impressions (versus an average of 2.3k), received 29 questions, answered 17 then and there, and saw engagement in our posts exceed our averages. We received very positive feedback from the pharmaceutical assessors who participated and built relationships with the Academy of Pharmaceutical Sciences (APS), the European Industrial Pharmacists Group (EIPG), the Organisation for Professionals in Regulatory Affairs (TOPRA) and the Royal Pharmaceutical Society (RPS) who all supported us by reposting our tweets or submitting questions.

  The session was a good example of how we can utilise social media to positively reflect the work of the regulator. It was also an opportunity to iron out some of the common misunderstandings of what the role involves and engage with Potential candidates who were unsure of their suitability.

- **Joint MHRA/ The Association of the British Pharmaceutical Industry** (**ABPI**) **Conference "Making the case for Medicines Manufacturing" -** This was our first jointly branded conference with ABPI and focused on some areas that were relatively niche for ABPI, meaning the event attracted a smaller, different audience who participated fully in discussions in the pros and cons of medicines manufacturing in the UK. The event also brought to life two of our published case studies, with representatives from Eisai and AstraZeneca taking delegates through the detail. We were also able to promote the Innovation Office to delegates though the event channels - microsite and ABPI event app.

- **Meldonium –** BBC Sport covered Maria Sharapova's suspension from tennis for taking the banned medicine, Meldonium. MHRA was approached for comment and we issued our guidance for taking unlicensed medicines in the UK**.**

- **Botox parties –** BBC News Online carried an article on an investigation which uncovered the two men staging "Botox parties" in homes and beauty salons for people desperate to banish wrinkles. We are supporting IE&S who have launched an investigation as a result of the BBC story.

.

- **WEB-RADR –** The Agency facilitated an interview between Insights magazine and Mick Foy, VRMM, for a piece called 'The wisdom of social media crowds'. Mr Foy spoke about identifying the meaningful data.

- **Unlicensed drugs –** The Agency facilitated an interview between MHRA head of enforcement, Alastair Jeffrey, and BBC South on the issue of buying unlicensed medicines online.

- **Pharmaceutical Assessors –** The agency facilitated a profile piece on Marion Westwood, pharmaceutical assessor, as part of our Employer Brand campaign.

- **Droperidol –** The Sunday Express in Scotland ran a story on a drug which is used for severe post-operative nausea and vomiting and its withdrawal as an antipsychotic in 2001. We provided a briefing**.**

- **SSRIs and suicide** – The Daily Mail ran a story about a teenager who killed himself in 2013, weeks after being put on Prozac. The Agency provided a statement on the use of SSRIs in teenagers.

- **Reported adverse incidents** – The Agency provided the Sunday Express with the 2015 figures for adverse incidents relating to medical devices that have been reported across the UK and Scotland.

6. ORGANISATIONAL TOPICS

Regulatory Excellence - the Regulatory Group has approved the reinvigoration of the Regex Working Group, with a renewed focus on the coherence and proportionality of the agency's regulatory programme. Work continues to define the programme and agree refreshed terms reference for the working group.

Bilateral Meeting with Public Health England with Duncan Selbie Chief Executive for discussions of mutual interest. Followed by a meeting with Helen Gordon, Chief Executive of the Royal Pharmacueitcal Society (RPS) and their President, Ash Soni for a regular six-month bilateral.

Royal Colleges – the series of bilateral meetings continues. On 11 March the Chairman and I met with Dr Catherine Calderwood, Chief Medical Officer (Scotland) and Dr Rose Marie Parr, Chief Pharmaceutical Officer (Scotland) in Edinburgh. This was followed by an introductory meeting with Professor David Galloway, President Elect of Royal College of Physicians and Surgeons of Glasgow.

March all staff meetings - Over half of staff attended the six-monthly all staff meetings hosted at 151 BPR and NIBSC. At the NIBSC meeting, Director-designate Christian Schneider, shared with staff his initial impressions since joining the agency in early January. The staff meetings at BPR were led by Ian Hudson and Peter Commins.

Staff feedback following the meetings was generally positive, with over 80% of respondents from BPR saying they felt more or considerably more informed about the future direction of the agency as a result of attending a meeting. This figure was closer to 66% for NIBSC colleagues.

People Survey action plans - The centre/divisional and agency-wide People Survey action plans have now been developed and signed off by the Corporate Executive Team (CET). The focus for most colleagues will be on the actions outlined in their centre/divisional action plan and CET will be checking in on progress made in relation to these in the summer, when we will also provide a general update.

SCOPE - SCOPE (Strengthening Collaboration for Operating Pharmacovigilance in Europe) Work Packages have worked closely with Walkgrove, a design company, to help with the development of SCOPE training materials. The monthly Work Package Leaders teleconference focused on the project extension and project plan, journal publications and the sustainability plan development.

EU Medical Device Expert Group – a Vigilance meeting in Brussels. The Agency provided substantial input to the meeting including feedback on the progress of UK-led working groups/initiatives developing: Europe-wide systems for manufacturer reporting to a central database; device specific vigilance guidance for cardiac stents and standardised format for manufacturers' Field Safety Notices. In addition we proposed a number of changes to the existing European Vigilance Guidance document.

Information Management Division (IMD) – IMD has successfully completed the transition from a single supplier for infrastructure to a new supply chain consisting of different specialist suppliers. We have completed this transfer of infrastructure with no disruption to our services. This is a major achievement and will allow us to benefit from a 20% cost reduction for infrastructure, improved service levels, compliant contracts, greater delivery control, more security control, and crucially the ability to bring resources to bear on remediation and transformational activities.
A security incident with a ransom virus occurred, handled and lessons learned will be undertaken.

Recruitment is now completed for the 2016 PhD studentship program. All projects attracted a wide field of applicants, with many potential students of high academic calibre, from across Europe, and the three posts have now been filled with students of promising potential.

NIBSC Director - This month has seen the final stages of the transition to the new NIBSC Director, Dr Christian Schneider, who takes up his role as NIBSC Director on 1 April. The current Director Dr Stephen Inglis retires in early April following a very successful career at NIBSC since 2001.

7. OPERATIONAL PERFORMANCE

ASSESSMENT PERFORMANCE

New UK Marketing Authorisations (MAs) - New Active Substances - One new drug substance was assessed in March. The overall average assessment time of new active substances from April 15 to March 16 is 51 working days or 72 calendar days.

New UK Marketing Authorisations (MAs) - Existing Active Substances - The following tables give the numbers of new Marketing Authorisation applications assessed and determined (granted, refused, and withdrawn) during this month compared to the monthly averages for 2014/2015.

Procedure	MAA Assessed This Month*	MAA Assessed 2014/15 Average per month
National, UK-only	15	20
Decentralised, UK=RMS	5	23
Decentralised and MR, UK=CMS	83	41
Total	103	84

Procedure	MAA Determined This Month*	MAA Determined 2014/15 Average per month

National, UK-only	23	22
Decentralised, UK=RMS	41	28
Decentralised and MR, UK=CMS	42	42
Total	106	91

The number (volume) of new MA applications assessed in March has increased from April and is greater than the average numbers of assessments completed 2014/15. The higher assessment volume was driven by DCP CMS assessments for ivabradine. RMS assessments are lower reflecting lower receipts in January. The numbers of new MA applications determined in March was higher compared with the average monthly figures for 2014/15.

Pharmacovigilance Adverse Drug Reactions (ADRs) – During March the Division continued to meet all Agency targets related to the capture of ADR reports and signal detection. A total of 4,072 UK ADR reports were received in March 2016, of which 552 were received from patients, parents and carers. A further 25,527 non-UK reports were received in the month. Results against key performance measures for fatal and serious reports were both 100%. For black triangle and established medicines 91% of signals generated were initially evaluated within 5 days. Of 215 general enquiries received, 95% were answered within 7 days working days and 100% within 10 working days.

Device adverse incidents - 1,593 Adverse Incident reports received in March (which compares with 1,295 for the same month last year), an increase of 23.0%. Cumulative total for 2016 is 4,366, which compares with 3,790 in 2015, an increase of 15.2%.

Parallel imports – In March, 105 PLPI initial submissions were received, 113 were assessed and 142 were determined (109, 108 and 107 respectively in February). Median time from submission to grant was 4.0 months (4.6 months in February).
756 PLPI variation applications were received, 736 were assessed and 853 were determined (685, 636 and 534 respectively in February).
Average time from submission to grant was 2.5 months (209 months in February).

Public Assessment Reports (PARs) - 96.9% of UK Public Assessment Reports and Lay Summaries (31/32) completed in March 2016 were published within the 60-day high-level target time from grant of the marketing authorisation. There were three updates to PARs (Type II Medical) with non-safety variations of clinical importance completed in March 2016, all completed on time.

Clinical Trial Authorisations (CTAs) - There were 7 Phase 1 applications processed in an average time of 14.3 days with 7/7 (100%) within the 30 day target. In the year to date there have been 180 Phase 1 processed in an average time of 10.3 days.
Of all other CTAs, 103 were processed with an average time of 23.3 days and 103/103 (100%) within the 30 day target. In the year to date there have been 900 non-Phase 1 CTA applications processed in an average time of 18.2 days.

Device clinical investigations - 100% of clinical investigations have been completed within 60 days and the average review time for the year to date is [48] days. Three clinical investigations were completed in March 2016 and 58 have been completed year to date

Biological Standards – during March, total sales were 190% above budget at £1.704m, a new monthly record. Total sales YTD are £9.67m, 37% higher than last year, a new record for annual sales. Of these, £5.8m were influenza reagents.

Biologics batch release – Batches continue to be released from both the original BRIMS system and the new CT-LIMS whilst the final transfer between the two is taking place. Test release certificates were issued for 32 product batches from the old BRIMS system and 50 from CT-LIMS, giving a total of 82 product batches. Numbers of plasma pools were 40 from BRIMS and 177 from CT-LIMs giving a total of 217 plasma pools. Targets for timeliness of product testing were met.

8. OTHER INTERNATIONAL TOPICS

Meeting: 'Making the case for public standards' - The widespread introduction of the Biosimilarity route to Market authorization, in which a candidate biosimilar is compared directly with an reference product has led to uncertainty as to the relative roles of reference product and reference standard, with the possible outcome that the central role of WHO bioactivity standards is reduced in future regulatory approaches to biologicals. Recognising this threat a meeting was held on 11th March of representatives of key stakeholders in the public standards sector (WHO, EDQM, USP, FDA, PEI) to discuss and agree strategy in clarifying the role of WHO and other reference standards, and maintaining their status in the regulatory environment. The meeting was highly successful and will be used as the basis for developing public position statements.

USP peptide standards - The unites states pharmacopoeia is expanding and updating its program of reference standards for therapeutic peptides, and had been carrying out this work in partnership with NIBSC, over the last 2-3 years, making use of the high specification performance of NIBSC's standards production facility. NIBSC has just completed negotiations and agreed terms for the next three peptide standards, and will deliver these during the next 12 months, with significant revenue accruing to the organization as a result.

9. LITIGATION - no major activity to report in March 2016

Dr Ian Hudson
Chief Executive