Medicines and Healthcare products Regulatory Agency

24 April 2017

CHIEF EXECUTIVE'S REPORT FOR THE MONTH OF MARCH 2017

1. HEADLINES for March 2017

The Strengthening Collaborations for Operating Pharmacovigilance in Europe (SCOPE) - Joint Action Stakeholder Event took place on 20-21 March 2017 in London. The event brought together SCOPE's key stakeholders from National Competent Authorities, patient organisations, healthcare professionals, pharmaceutical industry and academia. The event provided an opportunity to raise awareness of the Joint Action and over the two event days, participants discussed SCOPE Joint Action's outputs and further tested and explored the project's findings. There was an open forum for the exchange of views and ideas for building on SCOPE to develop pharmacovigilance.

Algorithms Data and Regulation Meeting - on 23 March, the Chairman and CEO attended a workshop on Algorithms Data and Regulation, held at the British Academy chaired by Sir Mark Walport, Government Chief Scientific Advisor. Other colleagues from The Clinical Practice Research Datalink (CPRD) and Devices also attended the workshop. NHS England, the Department of Health, the MHRA and GO-Science jointly hosted the workshop.

The Drug Information Association (DIA) Euro-meeting in Glasgow - on 29 March the CEO and a number of agency staff attended the Drug Information Association (DIA) Euromeeting in Glasgow, where the CEO was co-Chair of the whole event. The DIA EuroMeeting goal is to bring together key healthcare stakeholder groups, such as industry, regulators, pharmacovigilance, and patient advocates to discuss and share insights. Agency staff participated in numerous sessions; including chairing a joint MHRA/NICE session on "Certainty versus access: unmet need and the decision maker's dilemma"; co-chairing session on "From Disruptive Technologies to Empowering Technologies in Healthcare in the opening plenary"; chairing a session on the International Coalition of Medicines Regulatory Authorities (ICMRA) - a global coalition of medicines regulators; and delivering a presentation on "Hurdles/Support from Regulatory Processes" in a session covering "Creating a Framework for Innovation: Incentives and Regulatory Frameworks". Other sessions at which the Agency was represented included, on Brexit, pharmacovigilance, device/borderline and CPRD/clinical research topics.

2. PRODUCT RELATED ISSUES

Medicines issues

Hormone pregnancy tests (HPTs) and a possible association with birth defects - A Sky News documentary on Primodos was aired in the House of Commons by the All Party Parliamentary Group (APPG) on HPTs and on Sky TV on 21 March 2017. This was attended by a number of MPs who had taken part in the last debate, and representatives from the MHRA (Vigilance and Risk Management of Medicines (VRMM), Press Office and Patient and Pubic Engagement). The story was picked up by many national newspapers.
The Guardian, The Independent, Sunday Telegraph and the Daily Mail reported that families have believed for decades that the drug might have been responsible for serious birth defects, including missing limbs, brain damage, heart defects and spina bifida.

Maloff public consultation – This month we launched a consultation into the reclassification of an anti-malarial medicine Maloff (atovaquone/proguanil) from Prescription only medicines to Pharmacy (POM to P). This was supported with promotion across our social media channels.

Viagra public consultation – We launched a consultation into the reclassification sildenafil from POM to P which generated interest and was covered in the Daily Mail, The Mirror and The Sun, and highlighted our commitment to widening access to medicines.

Dovonex: A public consultation was launched for a proposal for P availability of Dovonex Psoriasis 50 microgram/g Ointment for the treatment of mild to moderate plaque psoriasis.

Emollients and risk of fire - The use of emollients and the risk of fire again became prominent. Work is underway to agree new label warnings for these products, the majority of which are now medical devices rather than medicines.

Devices issues

Silicone breast implants and risk of Anaplastic Large Cell Lymphoma (ALCL) – The US Food and Drug Administration (FDA) announced that they will be updating their guidance on breast implants acknowledging the link with the rare cancer ALCL. We were contacted by the Metro and Comms provided a statement.

Medical Device Alerts - There were two alerts in March 2017

Number	Title
MDA/2017/004	eFilm Workstation and eFilm Lite radiology PACS software – risk of incorrect measurements for certain types of images.
MDA/2017/005	Comprehensive Reverse Titanium Shoulder Tray (specific lots) - risk of device fracture.

3. REGULATION AND POLICY

European issues

Medical Devices and in-vitro diagnostics (IVD) Regulations - The new EU Regulations for medical devices and IVD have been formally agreed by the Council and are to be adopted and enter into force around May 2017, triggering 3 and 5 year transition periods respectively. MHRA is taking a lead role with other European agencies and the Commission to agree priorities for a consistent implementation across Europe, to strengthen and utilise our influence for as long as possible. The first public stakeholder meeting was successfully held in Brussels on 9 March.

Falsified Medicines Directive - Work continues on plans for implementation of the 'safety features' element of the Falsified Medicines Directive – due for full implementation by 9 February 2019. Following the Minister's agreement to continue with our implementation plans, work has progressed towards a formal public consultation later in the spring. The draft impact assessment has been sent to the Regulatory Policy Committee (RPC) for their evaluation and initial drafts of the consultation document and statutory instrument have been prepared. A number of further meetings have taken place with the organisations impacted by Article 23 derogation (wholesalers decommissioning products on behalf of others) and have been helpful in mapping out how this will work in practice in the context of a complex

UK supply chain. Further editions of the newsletter have been published providing additional information to stakeholders on implementation and will be supported by a single guidance document to be published alongside the consultation. The Agency is continuing to work with colleagues in other Member States to ensure that the IT software at a cross-European level fulfils the requirements set out within the Regulation and allows us sufficient access to the data particularly for pharmacovigilance and pharmacoepidemiology.
The Agency also continues in its supervisory role overseeing the work of SecurMed (the UK repository), who are moving closer to completing the formal tendering process identifying a software provider.

UK ISSUES

Patient Safety and Vigilance Strategy – Work has continued on the strategy to pursue a common excellence model for patient safety and vigilance for both medicines and devices. An update on progress was given to the Corporate Executive Team (CET) in March. The strategy is now fully in the delivery phase and progress is being made in a number of areas. Project Team 1 is in discussion with Government Digital Services about the technical platforms for reporting of all incident types and is working to develop methodologies for device signal generation. Work is also starting on a device information standard for incident reporting. Project Team 2 has completed a mapping exercise on how post-marketing/ post-authorisation safety signals are handled in Devices and VRMM Divisions and the findings were discussed at the March CET. More work will be done to deliver a common approach to post marketing signal assessment for medicines and devices. Project Team 3 is continuing to prepare for a Health Summit of health organisations to discuss improving the impact of safety messaging in the healthcare sector and is developing a 6-month pilot to send Dear healthcare professional communications (DHPCs) electronically by MHRA compared to being sent by industry by post, as they are now. Now that the project is in delivery mode, an Agency team has taken on the Programme Management of the strategy.

Innovation - The last Director's meeting on Innovation took place on 21 March. There was an update on the Agency's Innovation Plan which is being re-written from the 2016 draft to update on the Brexit context and technological developments – this will be sent to DH by Easter subject to consultation with industry and the Department for Business, Energy & Industrial Strategy (BEIS) and DH are aware of our timelines.
There was a further update given on the activities of The European Commission's Expert Group on Safe and Timely Access for Medicines to Patients (STAMP) from 2015-2016 and its forward look on repurposing of medicines and off-label use.

Electronic cigarettes - Over 36,000 product notification submissions were received by the end of the financial year with receipts of £3M and over 18,000 products listed on the MHRA website. Processing is on track for completion by the end of the transition period in May 2017.

Partnership - We continue to build and embed partnership working with relevant bodies across Government, the health sector and industry. In particular, work towards new partnership agreements with Health Improvement Scotland, Care Quality Commission (CQC) and Public Health England (PHE) is close to finalisation, and we are progressing discussions with the Food Standards Agency. There was a very constructive meeting of the Cross-UK group on 5 April, and we have agreed that the next quarterly meeting will be hosted in Northern Ireland. The next Medicines Industry Liaison Group meeting has been arranged for 26 April.

Herbal Medicinal Products - We are exploring actions to address commitments for MHRA in the Government's response to Professor Walker's report - in particular, engaging with the

herbals sector to take action to remove from use potent or toxic ingredients, building on engagement already underway on ingredients with inherent pyrrolizidine alkaloids (PAs).

Patient and public engagement strategy 2017 is being considered by CET in April. The refreshed strategy is in response to a number of external factors that, collectively, have increased both Government and public expectation for patient involvement throughout the development and delivery of medicine, particularly in relation to innovative treatments and products. Most recently, these include the recommendations of the Accelerated Access Review.

Regulatory Excellence
We are in the process of collating our annual Business Impact Target (BIT) return to government. Under BIT we are required to report and quantify any initiative that has resulted in a reduction in burden for industry by completing individual Qualifying Regulatory Provisions (QRP) assessment templates. There are a few promising contributions which will need to be validated by the Department of Health (DH) Better Regulation Unit before going to the Regulatory Policy Committee no later than 28 April.

In addition, we are seeking Medicines Liaison Group (MLG) members' input on the post-implementation review of the Human Medicines Regulations. We have drafted a questionnaire seeking to understand the impact of the Pharmacovigilance Directive, Cross Border Prescriptions and Repeal of Section 10(7) legislation.

Going forward in 2017/18, the Regulatory Excellence programme will explore how to ensure the Agency has a robust model for regulatory policy for the post-Brexit environment.

Agency Business Plan 2017/18 - Next year's Agency Business Plan was endorsed at the CET and Board meetings in March, subject to a few amendments. A final version will go to the DH imminently with publication expected in early April. In parallel, Policy Division continues to seek input from DH on the likely content of the DH single delivery plan and formal remit letter from DH to the Agency, which we understand will be quite high level and strategic.

House of Commons Science and Technology Committee Inquiry into Genomics and Genome Editing - There is currently an inquiry by this select committee into genomics and genome editing. The MHRA contributed to the wider Department of Health written evidence for the inquiry in January 2017 with contributions from across all centres and divisions. MHRA is expected to be called for oral evidence on regulatory aspects of genomics in April/May 2017. The committee will produce a report on the human aspects of genetic technology in the summer of 2017.

Regulatory Advice Service for Regenerative Medicine (**RASRM) Survey** - We undertook a survey of customers and stakeholders that had used the RASRM, so that we could understand more about their experience of the service. Results indicate high satisfaction with the service with a number of respondents providing contact details so that we could get in touch about developing endorsements of the service.

British Pharmacopeia (BP) International strategy - Two international strategy workshops were held between BP and TSO (The Stationery Office), the most recent focusing on the Chinese market. The workshops aim to highlight the knowledge BP and TSO have of the markets and share it with each other in a structured way.

The Medical Device Safety Officers WebEx event took place at the beginning of March, with over 40 attendees. The agenda included Implementation of barcoding and medical

equipment management at Adenbrookes, GS1 and use of barcoding in Field Safety Notices and protection of patient identifier data.

The UK Stem Cell Bank has set up a new collaboration with the Department of Science and Technology at the University of Suffolk. This collaboration aims at ensuring that the University's MSc Regenerative Medicine and BSc (Hons) Bioscience courses are informed by the highest standards in the industry and research areas relating to Regenerative Medicine and Stem Cell Research. As part of this collaboration, final year BSc (Hons) Bioscience students recently visited the UK Stem Cell Bank (UKSCB), with the aim of furthering students' appreciation of the operational complexity associated to high-speciality laboratories in the area of stem cell banking and Good Manufacturing Practice (GMP). During the visit, students enjoyed a series of interesting talks presented by scientists at the UKSCB.

Standardisation of Genomic Amplification Techniques (SoGAT) - An Agency colleague in Virology led a team organising the first UK workshop for Standardisation of Genomic Amplification Techniques (SoGAT) which took place on 24 March. Recognising the needs of clinical diagnostic labs from across the UK (from feedback of those attending the International SoGAT meeting that The National Institute for Biological Standards and Control (NIBSC) coordinates), the team at NIBSC worked with partners in the Royal College of Pathologists (RCPath), Institute of Biomedical Science (IBMS), External Quality Assessment (EQA) providers, UK Accreditation Service (UKAS) and the British Standards Body (BSI) to produce a programme that educated clinical diagnostic laboratory staff on how to use quality control reference materials and frameworks to improve quality assurance of testing and address the requirements of the newly introduced standard ISO15189. The meeting was booked to capacity and more than 70 people attended. The meeting was held in a room at Department for Business, Energy & Industrial Strategy (BEIS) in Victoria Street, and in spite of the major security alert, resulting in the temporary lock down of the building, feedback has been very positive and requests to organise similar meetings both in London and across the country have been received.

CPRD contribution to the Wellcome Trust initiative 'Understanding Patient Data' - Reassuring the public of the value of using health data for vital public health research is crucial to fostering public confidence in data sharing. CPRD relies on the goodwill of GPs and the public to share anonymised patient data for public health research purposes.
In 2016, the National Data Guardian for Health and Care, Dame Fiona Caldicott, published the Review of Data Security, Consent and Opt Outs, emphasising the importance of engaging the public in a positive conversation about how their information is used and safeguarded, and the benefits of data sharing. Dame Caldicott recommended that an initiative be set up to improve public engagement and trust in the use of patient data.
Following Dame Caldicott's recommendations, the Wellcome Trust has launched the initiative 'Understanding Patient Data' (UPD). UPD aims to support discussions with the public, patients and healthcare professionals about uses of health data. The initiative will develop tools and resources to aid conversations about patient data, and advocates who can champion responsible data usage. UPD is supported by a wide range of organisations including Association of Medical Research Charities, British Heart Foundation, Cancer Research UK, Information Governance Alliance, Involve and NIHR. Initial work has been carried out to look at the vocabulary used to talk about patient data and to find words that are accurate but also accessible and meaningful. The results have been published on the UPD website, together with a set of case studies highlighting the benefits of access to patient data for research.
CPRD is a strong supporter of the UPD initiative and has been working closely with members of the UPD team. The CPRD logo features on the UPD website and CPRD has contributed case studies where CPRD-enabled research has informed clinical guidance and

best practice. CPRD will continue to support and contribute to UPD and align communications material with the recommendations from UPD research findings.

Mutual Recognition with USA on inspections - At the start of March the EU and US regulators agreed to recognise inspections of manufacturing sites for human medicines conducted in their respective territories. The agreement (which is linked to Transatlantic Trade and Industry Partnership (TTIP)) negotiations, will for the first time enable EU regulators and the FDA to rely on each other's inspections to enable better use of resources to conduct more inspections in countries where medicines and active ingredients are increasingly being manufactured and sourced, such as in India and China. The Inspectorate played a leading role in the assessments and in the negotiations leading up to the subsequent agreement.

4. MINISTERIAL AND PARLIAMENTARY PRIORITIES

Parliamentary Questions (PQs): the target for 2016/17 is to meet DH deadlines in at least 90% of cases. The Agency answered **nine** PQs in March of which one was counted as late. The PQs were on a number of subjects including:

- Primodos and the ongoing review (4 PQs)
- Reclassification and regulation of dermal fillers (2 PQs)
- The sale of antibiotics online
- Transposition of the EU Medical Devices Directives into UK law
- Potential effects of Ibuprofen on the heart

Private Offices Cases (POs): the target for 2016/17 is to meet DH deadlines in at least 90% of cases. Performance for the month was 100%. The Agency led on **five** responses in March on subjects including:

- Sodium Valproate (2 POs)
- Labelling of medicines
- Packaging of medicines
- Importation of a medicine from Japan for personal use

Submissions: One submission was sent to Ministers in March about making Viagra available over the counter.

FOI Response Time Compliance: the target for 2016/17 is to ensure that 100% of requests receive responses within statutory limits (20 working days; or exceptionally within 40 days where an extension is required to complete a complex public interest test).

As at 28/02/2017	**FOI Requests Received 2016/2017**					
	Q1	**Q2**	**Q3**	**Jan**	**Feb**	**Total**
Received	161	134	153	52	33	**533**
Replies sent on time	158	132	152	52	33	**527**
Replies not yet due	0	0	0	0	0	**0**
Breaches	3	2	1	0	0	**6**
Compliance %	98.1%	98.5%	99.4%	100.0%	100.0%	**98.9%**

5. COMMUNICATION

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

Ovarian Cancer Awareness (OCA) Month - This month our most successful tweet was a promotion of OCA Month and the work by the Early Access to Medicines Scheme getting innovative medicines to patients. The tweet was seen by more than 7,500 people and retweeted more than 32 times including by key stakeholders including CCGs around the country and NHS Choices @NHSChoices has more than 204,000 followers.

Pharmafocus – A pharmafocus article was published following an interview with Lynda Scammell, IE&S Senior Policy Advisor, for a monthly life science publication. She discussed her role at the MHRA, the #FakeMeds campaign and the Falsified Medicines Directive.

GP communications - We are refreshing the existing flyer targeted at CPRD-naïve GP practices (including positive quotes from GPs and examples of public health impact) and are working with Royal College of General Practitioners (RCGP) on draft text for a flyer promoting the benefits of participating in the RCGP/Quality Improvement project. We are also exploring with Clinical Research Network (CRN) the possibility of Jonathan Sheffield (CRN CEO) writing to GPs to encourage them to join CPRD.

Dermal fillers – ITN are conducting research for a consumer affairs programme due to be aired shortly about the cosmetic industry. We provided them with clarification on the regulation of dermal fillers in the UK and the requirements.

Online selling guidance – Updated guidance for online sellers of medicines was published and we proactively publicised this with a press release, social media and targeted stakeholder engagement. We briefed the Pharmaceutical Journal who published a balanced piece.

Dimethylamylamine (DMAA) - Following the BBC investigation into doping in amateur sports, we shared our messages around DMAA and repurposed visual infographics on the dangers of fake or unlicensed medicines and supplements

Buying medicines online – The Times contacted us for information about the reasons people buy prescription medicines online without a prescription. We have provided guidance around purchasing patterns seen through Pangea seizures, and the risks of buying prescription medicines online without a prescription.

CANVAS Study – The Times published a story following their request to us for information and comment on the CANVAS study of diabetes medicines in two clinical trials. We provided information on the safety of clinical trials in the UK and the approvals process by MHRA.

Repurposing of medicines: We met with Licensing and Policy to discuss ways to increase awareness, amongst the academic community, of MHRA's role in repurposing and the services it can offer. We identified relevant academic stakeholders and initialised engagement with the Anticancer Fund's researcher, the CADRe academic network at Birmingham University and academic contacts at Sussex University. We met with the Association of Medical Research Charities (22 March) to begin exploration of a jointly-hosted workshop for AMRC member charities and interested academics.

UK Stem Cell Bank - We published a press release on the UK Stem Cell Bank (UKSCB) at NIBSC releasing its first stem cell lines suitable for development into novel cell-based medicines to researchers wishing to bring new and innovative therapies to clinical trial.

Additional promotion included a number of updates on the NIBSC website, a news article on nibsc.org, and posts on Twitter and LinkedIn. Following this announcement we were contacted by Regulatory Affairs Professionals Society (RAPS) and biopharma-reporter.com and have provided additional comment and background.
Work continues on phase 2 of promoting the new stem cell lines, and creating an infographic.

British Science Week – We issued social media supporting British Science Week #BSW17, this month. These have both been liked by the British Science Week account and the British Science Association, who together have a total of 59.5K followers.

HPV vaccine – South West News Service published a story on a case study of a girl who claims the HPV vaccine Gardasil for made her wheelchair bound. Both MHRA and Public Health England (PHE) responded with our joint statement.

PUBLICATIONS

Defence Science and Technology Laboratory (Dstl) - Agency colleagues recently took part in some collaborative research with Defence Science and Technology Laboratory (Dstl) and demonstrated that abatacept is a robust and potentially credible drug to prevent toxic effects from Staphylococcal enterotoxin B (SEB) exposure. Their results were published in Journal of Immunology on 20 March 2017 (http://www.jimmunol.org/content/early/2017/03/18/jimmunol.1601525). Interference of the T Cell and Antigen-Presenting Cell Costimulatory Pathway Using CTLA4-Ig (Abatacept) Prevents Staphylococcal Enterotoxin B Pathology

Sarah J. C. Whitfield, Chris Taylor, Jane E. Risdall, Gareth D. Griffiths, James T. A. Jones, E. Diane Williamson, Sjoerd Rijpkema, Luisa Saraiva, Sandrine Vessillier, A. Christopher Green and Alun J. Carter (J Immunol March 20, 2017, 1601525; DOI: https://doi.org/10.4049/jimmunol.1601525)

PLOS-ONE (Public Library of Science) has just accepted the publication entitled 'Interleukin-10 and prostaglandin E2 have complementary but distinct suppressive effects on Toll-like receptor-mediated dendritic cell activation in ovarian carcinoma', authored by Dr Sandra Diebold from Biotherapeutics and co-authors,

The manuscript has been accepted for publication in Journal of Immunological Methods (now available online): '**Establishment of the First WHO International Standard for Etanercept, a TNF receptor II Fc fusion protein: report of an international collaborative study'** authored by Meenu Wadhwa, Chris Bird, Paula Dilger, Peter Rigsby, Haiyan Jia, Marie Emmanuelle Behr Gross and participants of the study.

Glyn Stacey, Orla O'Shea and Charlotte Chapman from the UK Stem Cell Bank were named authors and contributors to a publication in the journal "Stem Cell Research" on the rapid start-up of the EBiSC project in which the UKSCB was a key partner. The paper is entitled 'Rapid establishment of the European Bank for induced Pluripotent Stem Cells (EBiSC) - the Hot Start experience'.

6. ORGANISATIONAL TOPICS

MEETINGS

All Staff Meetings - The Agency held well attended all staff meetings in March. We had one in South Mimms on Thursday, 23 March and two in Buckingham Palace Road (BPR) on both Monday, 27 March and Tuesday, 28 March.

Colleagues attended the second **TOPRA** (The Organisation for Professionals in Regulatory Affairs) careers fair which presented an opportunity to showcase the opportunities within the MHRA and our investment in developing our staff. We conducted a survey of delegates which included students and professionals in the regulatory industry. Over 70% of people surveyed were aware that they could report medical devices through Yellow Card scheme.

Students from University of Leicester - Every two years, NIBSC hosts a visit from 2nd year undergraduate Biological Science students from University of Leicester. On 30 March, twenty students visited along with two of their professors, as part of a week-long field trip in which they visit different scientific organisations. This was the fourth time we have hosted their visit and they are always very appreciative and find the day very interesting. The programme consisted of an overview of NIBSC including a tour of the site and a specific tour and talk in the UK Stem Cell Bank, along with other presentations on: model systems to study human immunodeficiency virus (HIV) / Simian immunodeficiency virus (SIV) and emerging infections; Novel Vaccines to Prevent Enteric Bacterial Diseases; Diagnostic reference materials leading to precision medicines and Work of the Standards Processing Division.

Civil Service Positive Action Pathway (PAP) - A NIBSC employee from Virology, has been the only member of MHRA to be awarded a place on the Civil Service Positive Action Pathway (PAP). The pathway was developed from the talent action plan in 2015 with the aim of increasing diversity in the senior roles of the civil service and is run through Civil Service Learning. The aim is to make the civil service the UK's most inclusive employer by 2025.
She has been successful in gaining a place on the G6/G7 cohort and was the only successful applicant from the 13 members of staff that applied. A fantastic achievement in light of the numbers applying - there were 2200 applicants from across the whole civil service.

Colleagues from NIBSC Corporate Affairs attended University College London on 6 March for a Careers Event as part of the University's Life & Health Sciences **Themed Week 2017, Colleagues were part of a panel of five members from both public and** private sector organisations talking to students about our career histories and answering questions on the topic of Leadership & Governance in the Science and Health sector.
Continuing in the area of promotion around career opportunities, they also attended two different schools to promote the type of varied careers available in NIBSC and the wider MHRA.

7. OPERATIONAL PERFORMANCE

ASSESSMENT PERFORMANCE

New UK Marketing Authorisations (MAs) - New Active Substances - Two new drug substances were assessed in March. The overall average assessment time of new active substances from April 16 to March 17 is 50 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 2015/16.

Procedure	MAA Assessed This Month	MAA Assessed 2015/16 Average per month
National, UK-only	29	24
Decentralised, UK=RMS	24	28
Decentralised and MR, UK=CMS	39	45
Total	92	97
Procedure	MAA Determined This Month	MAA Determined 2015/16 Average per month
National, UK-only	43	19
Decentralised, UK=RMS	19	26
Decentralised and MR, UK=CMS	39	48
Total	101	93

The number (volume) of new MA applications assessed in March was lower when compared with the average number of assessments completed in 2015/16. The numbers of new MA applications determined in March was higher compared with the average monthly figures for 2015/16.

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 4592 UK ADR reports were received in March 2017, of which 720 were received from patients, parents and carers. A further 29,016 non-UK reports were received in the month. Results against key performance measures for fatal and serious reports were both 100%. 100% of UK spontaneous serious ADRs were sent to EMA and Marketing Authorisation Holders (MAHs) within the High Level Target of 11 days. For black triangle and established medicines 93% of signals generated were initially evaluated within 5 days. Of 222 general enquiries received, 98% were answered within 7 working days and 100% within 10 working days.

Devices adverse incidents - 1,675 Adverse Incident reports received in March (which compares with 1,593 for the same month last year), an increase of 5.2%.

Device clinical investigations - 100% of clinical investigations have been completed within 60 days and the average review time for the year to date is 51 days. 7 clinical investigations were completed in March and 70 have been completed this financial year.

Parallel imports (PLPIs) – In March, 130 PLPI initial submissions were received, 69 were assessed and 90 were determined (80, 56 and 68 respectively in February).
Median time from submission to grant was 4.1 months (4.6 months in February).
844 PLPI variation applications were received, 594 were assessed and 706 were determined (830, 600 and 629 respectively in February).
Average time from submission to grant was 2.5 months (2.2 months in February).
The Unit has exceeded the income budget for 2016-17.
Five recent resignations have severely depleted the assessor resource and recruitment to fill the vacancies is under way. It is anticipated that service levels will be impacted in the next financial year.

Public Assessment Reports (PARs) - • 97.5% of UK Public Assessment Reports and Lay Summaries (39/40) completed in March 2017 were published within the 60-day high-level target time from grant of the marketing authorisation. There was one update to a PAR (Type II Medical) with non-safety variations of clinical importance completed in March 2017, completed on time.

Clinical Trial Authorisations (CTAs) - There were **12** Phase 1 applications processed in an average time of **12.9** days with **12/12 (100%)** within the 30 day target. In the year to date there have been **147** Phase 1 applications processed in an average time of **12.5** days.
Of all other CTAs, **69** were processed with an average time of **24.2** days and **68/69 (98.6%)** within the 30 day target. In the year to date there have been **808** non-Phase 1 CTA applications processed in an average time of **24.2** days.

Biological Standards – Total sales in March were at a value of £1,443k, up 44% from last month, and giving a total YTD sales figure of almost £9.5m, although slightly lower than at the same month last year. Flu sales in the month were £1,143k, up 85% from last month, making YTD sales £5,283,245 which is 10% lower than the same time last year. The total quantity of standards shipped was 15,352, lower than last month's figure of 35,210, which had been due to an increase in sales in several product areas including one shipment of 6000 ampoules to Baxter. There were no contract fills this month.

Biologics batch release – Test release certificates for vaccines and blood products were issued for 152 product batches in March, and for 191 plasma pool batches, both up from February. The target for timeliness of product testing was achieved in March.

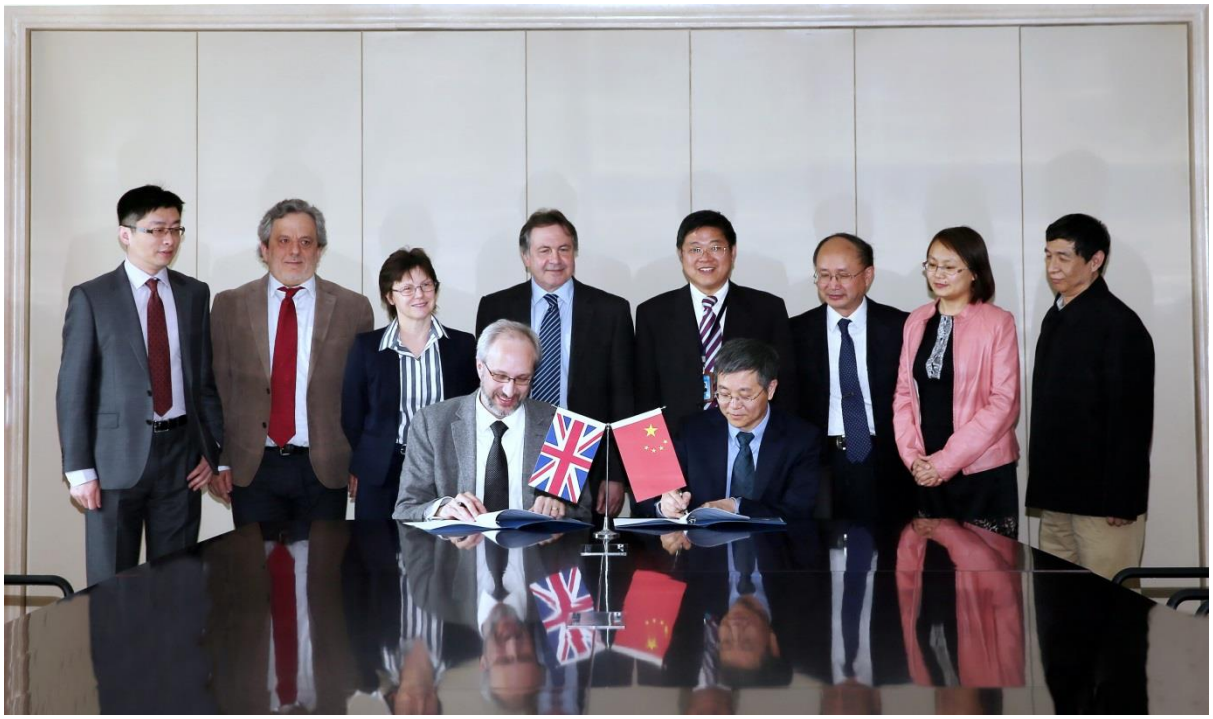
Information Management Division (IMD):-
- IPU hit all their stretch targets for the year again
- E-Business rollout remains at green for go
- DWP rollout of Office365 is in Beta for laptop rollout and office, alpha for team sites
- PA review required significant support and resources, but represented a good challenge
- Accommodation move remains technical strand remains a High risk given the lack of plans, certainty, and a target state
- Team morale is high and there is a buzz around delivery
- Good supplier engagement with key strategic suppliers on digital services
- Improvement on infrastructure suppliers is steady
- IMD IT business case has been completed and submitted

8. OTHER INTERNATIONAL TOPICS

Visit to Japan - Ian Hudson and Mark Birse, Group Manager of the Inspectorate, had a very productive meeting with senior officials from both the Pharmaceuticals and Medical Devices Agency (PMDA) and the Ministry of Health, Labour and Welfare (MHLW). This meeting was chaired by Dr Tatsuya Kondo, Chief Executive of PMDA.
As well as providing an opportunity for discussion on arrangements for the Summit of Heads of Medicines Regulatory Agencies and ICMRA meeting, being held in Osaka in October 2017, a number of bilateral issues of mutual interest were also discussed, including innovation, antimicrobial resistance and collaboration on GMP.
This meeting helped to enhance the strong relationship that exists between MHRA and PMDA/MHLW, which will contain to be nurtured through continued collaboration, particularly through ICMRA and membership of the Executive Committee. These meeting were followed by the 9th Asian Regulatory Conference where Dr Hudson was a member of the conference advisory council and chaired a session on innovative approaches to licensing, comparing the US, EU and Japanese approaches, and Mark Birse presented on inspections and harmonisation, including the ICMRA project.

China's National Institutes for Food and Drug Control (NIFDC) - NIBSC's Director, Dr Christian Schneider, travelled to Beijing at the end of March with colleagues to meet Dr Bo Li, Director General of China's National Institutes for Food and Drug Control (NIFDC) and his

team. This was an important visit to cement the existing strong relationship between the two Institutes and to discuss existing and future collaborations such as Sabin-IPV standardisation and the design of our next joint WHO International Standard for Enterovirus EV71 antigen. During the visit, Christian and Dr Li took the opportunity to sign a revenue share agreement to allow distribution by NIFDC of the World Health Organisation International Standard (WHO IS) for EV71 neutralising antibodies to Asian countries in return for sharing the resulting revenue with NIBSC. This WHO IS EV71 antibody standard was jointly developed by NIBSC and NIFDC, and is of particular relevance in Asia which has seen a number of EV71 epidemics. (see photo below)



Singapore: The MHRA Good Distribution Practice Inspectorate hosted a visit by a representative from the Health Sciences Authority (HSA), Singapore for a wide ranging training programme.

Also during March there was a two-week staff exchange between the British Pharmacopoeia (BP) and the **Chinese Pharmacopoeia** (ChP). The aim was to allow the ChP to better understand the working practices of the BP and UK regulatory requirements for medicines. Various MHRA groups presented and visits to the MHRA laboratories in Teddington and laboratories at Kew and University College London were given.

VSV-EBOVAC annual meeting in Camogli, Italy. – A member of NIBSC attended the VSV-EBOVAC annual meeting. - Vaccine safety and immunogenicity signatures of human responses to rVSV-ZEBOV - is a collaborative research programme aimed to characterize the immune response elicited in humans by the Vesicular Stomatitis Virus (VSV)-vectored Zaire Ebola vaccine (rVSV-ZEBOV). VSV-EBOVAC is a public-private consortium of 12 partners involving experts from academic institutions, scientists of the 3 main clinical sites (Switzerland, Gabon, Kenya), the vaccine manufacturer, small and medium-sized enterprises (SMEs) and research institutes.
VSV-EBOVAC started in March 2015, and is a 3 year project funded by the Innovative Medicine Initiative 2 Joint Undertaking (IMI 2 JU). NIBSC has been involved in this through

testing EBOLA vaccine sera for neutralising activity as well as supporting the standards work.

Dr Ian Hudson
Chief Executive