HIGHLIGHTS

The EMA has now issued the first revision of the GVP Module VI on ADR Management, which brings changes to the requirements for the management and reporting of suspected ADRs in non-interventional studies.

The FDA has announced that it has reopened the comment period on the two social media guidelines it published for consultation in June. Following the publication of a Final Rule in June, the FDA will soon hold a meeting to discuss the electronic submission processes and formats for ICSRs.

The EMA will make publicly available the clinical reports included in applications for central marketing authorisations from 01-Jan-2015. The EMA has expanded the ADR website launched in 2012 to include information on suspected side effects for all drugs approved nationally in the EU. As part of a pilot project at EMA, patients will now be invited to bring their views into the benefit-risk evaluation of medicines.

PROTECT has made available a new version of its Adverse Drug Reaction database, which provides the list of all ADRs presented in the SPC of medicinal products authorised in the EU.

We hope you like the new design and structure of Safety Observer !! Please feel free to use the icons above and get in touch to provide comments and suggestions for improvement.
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1. REGULATIONS, GUIDELINES AND OTHER STANDARDS

1.1 Newly Applicable Standards

1.1.1 EudraVigilance issues revised Important Medical Event Terms list (08-Sep-2014)

The EudraVigilance Expert Working Group (EV-EWG) has released the update of the Important Medical Event Terms (IME) list, which is based on MedDRA version 17.1. The IME list was first made available in 2009 for guidance purposes only and to facilitate the seriousness assessment of suspected adverse reactions.

→ Link to EudraVigilance Page

1.1.2 ANSM issues revised notice to Applicants for Temporary Use Authorisation (09-Sep-2014)

The French Agency has issued a new version of its Notice to Applicants for Temporary Use Authorisation (ATU), which corresponds to Compassionate Use. It describes the regulations on labelling, import, prescribing, delivery and Pharmacovigilance. The corresponding protocol templates have also been updated.

→ Link to ANSM Page (in French)
→ Link to ANSM’s Notice to Applicants (in French)

1.1.3 ANSM issues revised notice to Applicants for Marketing Authorisation (11-Sep-2014)

The French Agency has issued a new version of its Notice to Applicants for Marketing Authorisation. It summarises the regulations in France, including for Pharmacovigilance and associated procedures. New forms and procedures concern PSUR and variation submission, including Urgent Safety Restrictions.

→ Link to ANSM Page (in French)
→ Link to ANSM’s Notice to Applicants (in French)

1.1.4 EMA updates training and guidance on submission of medicines information (12-Sep-2014)

The EMA has released new guidance to support MAHs updating the information on authorised medicines that they have submitted in accordance with Article 57(2) of the 2010 pharmacovigilance legislation. MAHs are required to update information on their authorised medicines by 31-Dec-2014, which includes completing additional data elements included in the new data submission format and checking the quality of the information in line with the updated reporting requirements.

The new guidance includes step-by-step guides for each of the activities that MAHs have to perform, including the update of an authorised medicinal product and the entry of a Pharmacovigilance System Master File (PSMF) Location. The XEVMPD data-entry tool User Manual has been updated together with the free e-learning course available on the EMA website.

→ Link to EMA Data Submission Training Page

1.1.5 EMA issues revised GVP Module VI on ADR Management (15-Sep-2014)

Following the consultation initiated in June 2013, the EMA has now released the much awaited Good Pharmacovigilance Practices (GVP) module VI (Rev 1) – Management and reporting of adverse reactions to medicinal products.

The main changes relate to the requirements for the management and reporting of suspected ADRs in non-interventional studies, which have proved difficult to implement. The revision brings more flexibility in the type of Adverse Events that need to be actively collected by the study sponsor, which should all be clearly defined and justified in the study protocol. Other revisions concern the definition of the clock start date, the use of languages, etc. The comments received during the consultation and a version with tracked changes are also available. The Introductory Cover Note of the GVPs has been updated accordingly.
This document is replacing the initial version of this module from June 2012. It is important to note that the new requirements for non-interventional post-authorisation studies will become mandatory for any new study started after 01-Jan-2015, whereas implementation for studies started before that date is optional.

1.1.6 EMA issues revised GVP Module III on Inspections (15-Sep-2014)

A Minor revision of the GVP module III on Pharmacovigilance inspections has also been issued by the EMA, which includes reference to the new Union procedures for pharmacovigilance inspections. This document is replacing the initial version of this module published in December 2012.

1.1.7 CMDh updates information on PSUR Submission for NAPs (19-Sep-2014)

The European CMDh (Co-ordination Group for Mutual Recognition and Decentralised Procedures – Human) has issued updated guidance document describing National Competent Authorities (NCAs) requirements for PSUR submission, which applies to products authorised via MRP, DCP and National Procedures, and whatever the PSUR assessment procedure. The update relates to Portugal, where the PSUR submission is no longer required via the national web portal.

1.1.8 EMA updates EURD list (06-Oct-2014)

The EMA has published an updated EURD list, which provides the EU Reference Dates, frequencies for submission of PSURs and related data lock points for a list of active substances and combinations. As communicated earlier, the EMA intends to start the single assessment of active substances contained exclusively in nationally authorised medicines by the end of 2014. Consequently the EURD list includes those substances when their data lock point falls after 31-Aug-2014. Those with a data lock point before that date are available on the separate PSUR work sharing list published by the CMDh.

The changes to the EURD list are highlighted and include 93 new products and a number of amendments. Please note that as specified in the cover note, the “Publication Date” is not revised for all types of amendments and this column cannot be used to filter all amended substances in Excel.

1.2 Developments to Watch

1.2.1 ICH issue report of June 2014 Meetings in Minneapolis, USA (17-Sep-2014)

As already reported in our previous issue, The ICH Steering Committee met in June and the corresponding meeting report is now available.

As reported earlier, Heath Canada and Swissmedic are now Steering Committee members. A new Expert Working Group is developing an Addendum to E6, Good Clinical Practices (GCP), which should facilitate innovative approaches to GCP. The resulting Final Guideline (Step 4) is planned in November 2016. ICH has also launched a Call for Tender for the maintenance and support of MedDRA, which is currently contracted to the Maintenance and Support Services Organisation (MSSO).

Link to ICH Press Release
Link to ICH SC Report
1.2.2 FDA consults on REMS Standardization (23-Sep-2014)

The FDA has published a draft report entitled “Standardizing and Evaluating Risk Evaluation and Mitigation Strategies (REMS)”. This report describes the Agency’s findings concerning strategies to standardize REMS in order to reduce the burden of implementing REMS on practitioners, patients, and others. Following stakeholder engagement, the Agency selected priority areas and the report presents the design and the proposed workplans of the resulting four designated projects: (1) Providing benefit/risk information to patients, (2) prescriber education, (3) pharmacy systems, and (4) practice settings.

The FDA is publishing this report to allow the public to provide comments, which are expected by 24-Nov-2014.

→ Link to Federal Register Notice
→ Link to FDA REMS Report

1.2.3 FDA reopens comment period on Draft Social Media Guidelines (29-Sep-2014)

The FDA has announced that it has reopened the comment period on the two social media guidelines it published in June, and comments can now be made until 29-Oct-2014.

In the meantime, some comments have already been posted by stakeholders, including PhRMA (Pharmaceutical Research and Manufacturers of America) and BIO (Biotechnology Industry Organization) who have raised concerns with the draft guidelines, highlighting that the way the FDA uses social media currently would not be accepted from the industry under the current draft guidelines.

As a reminder, the draft guidelines cover the presentation of Risk and Benefit Information in media where there is limited space (e.g. Twitter), and how companies can correct misinformation disseminated by independent third parties on the Internet or through social media.

→ Link to FDA Page
→ Link to Docket Folder (Presenting Risk and Benefit in Limited Space)
→ Link to Docket Folder (Correcting Misinformation)
→ Link to FierceBiotech article
→ Link to The Hill article

1.2.4 FDA to hold Industry Meeting on electronic ICSR reporting (01-Oct-2014)

The FDA has just announced an industry meeting entitled “FDA Electronic Postmarket Safety Reporting Updates”, which purpose is to review changes in FDA postmarket safety reporting regulations, electronic submission processes and formats for ICSRs for drugs, biologics and vaccines. The meeting will take place on 27-Oct-2014 in Silver Spring MD, USA.

This follows the publication of a final rule in June, which requires the submission of postmarketing safety reports to FDA in an electronic format from 10-Jun-2015. Associated draft guidance documents were also published for consultation for drug and biological products, and separately for vaccines.

→ Link to FDA Meeting Page
→ Link to Final Rule
→ Link to FDA Draft Guidance (drug and biologics)
→ Link to FDA Draft Guidance (vaccines)

1.2.5 EMA to start publication of clinical reports on 01-Jan-2015 (02-Oct-2014)

The EMA has decided to publish the clinical reports that are used to support the decision-making on medicines. Following consultations with all stakeholders, the EMA Management Board adopted the new policy that will come into force on 01-Jan-2015. It will apply to clinical reports contained in applications for centralised marketing authorisations submitted after that date and the reports will be released after the decision on the application has been made. The policy will be extended to applications for line extensions and extensions of indications of already approved medicines submitted after 01-Jul-2015.
The EMA also plans to make available individual patient data in the future, which will be the subject of a new consultation to address various legal and technical issues, including data privacy. This will bring transparency to a new level and enable academics and researchers to re-assess data sets. The publication of clinical reports will also help to avoid duplication of clinical trials, foster innovation and encourage development of new medicines. The EMA has published a large volume of information related to this decision, which is all available from the links provided in the Press Release. This includes the EMA Policy itself, a Questions and Answers document and the comments received during the consultation.

→ Link to EMA Press Release

### 1.3 Beyond the Scope of Safety Observer

This section includes announcements collected through our secondary sources, which originate from authorities that we do not monitor systematically. For more information, please check our Q&As.

#### 1.3.1 Swissmedic implements ELViS to support electronic exchange of ICSRs (29-Sep-2014)

Swissmedic has just implemented a new Electronic Vigilance System (ELViS), which allows the E2B electronic exchange of post-marketing ICSRs and represents an alternative to the Swissmedic PV Gateway for the electronic exchange of ICSRs. Swissmedic has issued a guidance document that describes the conditions for MAHs to participate, the registration process, and the main functionalities of the ELViS platform.

The Swissmedic guidance describing Drug Safety Reporting Duties in Switzerland has been updated to reflect the implantation of the ELViS electronic reporting platform.

→ Link to Swissmedic ELViS Guidance

→ Link to Swissmedic Guidance on Drug Safety Reporting Duties

### 1.4 The Safety Observer Tracker

This section includes a cumulative list of the future implementation and consultation deadlines. For your convenience, a link is provided and we also specify the issue where the corresponding article can be found.

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<th>What?</th>
<th>Issue</th>
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<td>FDA consultation on Social Media Guidelines (Link)</td>
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2. PRODUCT SAFETY ANNOUNCEMENTS

2.1 Agomelatine (Valdoxan/Thymanax)
EMA confirms positive benefit-risk with new Risk Minimisation Measures (26-Sep-2014)

Following a recent benefit-risk assessment of Valdoxan/Thymanax by the PRAC, the EMA has concluded that the benefits of this anti-depressant medicine approved in 2009 continue to outweigh the risks, although new measures should be put in place to minimise the risk of liver toxicity.

A patient booklet will be distributed to all patients which describes the risk and associated symptoms, and to stress the importance of monitoring liver function. An observational study exposed a considerable level of non-compliance with the recommended liver monitoring programme and the product information will be revised to emphasise that liver function tests should be performed both before and during treatment.

The CHMP did not follow the PRAC’s recommendation to contraindicate the product in patients aged 75 years and above considering that the current warning regarding these patients was sufficient.

→ Link to EMA Press Release

2.2 Omalizumab (Xolair)
FDA approves label describing higher cardiovascular and cerebrovascular risks (26-Sep-2014)

Following an Early Communication about an Ongoing Safety Review issued in 2009, the FDA has announced that it completed a review of safety studies which suggests a slightly elevated risk of cardiovascular and cerebrovascular serious adverse events in patients treated with the asthma drug Xolair. The review also resulted in uncertain findings regarding a potential risk of cancer. The FDA Drug Safety Communication includes a Data Summary which provides more details about the results of the review. This new information has been included in a revised version of the product label.

→ Link to FDA MedWatch alert

2.3 Cefepime (Axepim and generics)
ANSM stresses the need to adjust posology in case of renal insufficiency (01-Oct-2014)

Following the notification of fatal adverse reactions associated to this antibiotic in elderly with renal insufficiency, the French Agency issued a reminder that posology should be adapted to the renal function. The product is exclusively eliminated by renal route and serious neurological adverse reactions including encephalopathy have been observed in this population.

→ Link to ANSM Press Release (in French)

2.4 Human normal immunoglobulin (Kiovig)
Baxter initiates batch recall due to safety concerns (03-Oct-2014)

The MHRA has announced that Baxter Healthcare Limited is recalling batches of its biological product as a precautionary measure due to an increased number of reports of allergic reactions associated with these lots.

→ Link to MHRA Alert
2.5 OTC NSAIDs

Australia consults on actions to take to address safety issues (07-Oct-2014)

The Australian TGA has launched a consultation on two reviews which cover the cardiovascular safety of non-steroidal anti-inflammatory drugs (NSAIDs) and the safety of diclofenac. These reviews identified some risks associated with over-the-counter (OTC) NSAIDs and the TGA has proposed four alternative options to address the situation, which range from no action to rescheduling. Interested parties should respond by 06-Nov-2014.

→ Link to TGA Announcement

3. DEAR DOCTOR LETTERS AND SAFETY NEWSLETTERS

3.1 MHRA Dear Doctor Letters

The letters sent to Healthcare Professionals are routinely posted on the Agency’s website. The following letters were sent by the MHRA in August:

- Rienso (intravenous iron): Contraindicated in patients with drug allergy, including hypersensitivity to other parenteral iron products
- Prolia & Xgeva (Denosumab): Risk of osteonecrosis of the jaw and hypocalcaemia.

→ Link to MHRA Page

3.2 ANSM Dear Doctor Letters

Dear Doctor Letters sent in September 2014 are now available on the French Agency’s website (all in French). Letters associated to safety concerns include the following:

- Basiliximab (Simulect): caution when using after cardiac transplantation (Off-label use)
- Interferon beta: risks of thrombotic microangiopathy and nephrotic syndrome in patients with Multiple Sclerosis

→ Link to ANSM Page

3.3 New issues of MHRA “Drug Safety Update” Bulletin

The June issue of Drug Safety Update (Volume 8, Issue 2) was published on 25-Sep-2014. It includes the following topics:

- Ferumoxytol: Risk of serious hypersensitivity reactions – New recommendations
- Denosumab: Risk of osteonecrosis of the jaw & hypocalcaemia – Updated recommendations
- Nitrofurantoin: Revised contraindication in patients with eGFR of less than 45 ml/min
- Domperidone: Risk of cardiac side effects – no longer available without prescription
- MHRA updates Yellow Card reporting guidelines for ADRs in children

→ Link to MHRA Newsletter Page

3.4 New issue of Australian “Medicine Safety Update”

The Australian Therapeutic Goods Administration (TGA) has issued the new edition of Medicines Safety Update (Volume 5, Number 5, October 2014). The contents include:

- Bupropion and serious cardiovascular adverse events
- Methylphenidate and priapism
- Propranolol – prescribing to patients who may be at risk of self-harm
- Valproate – fetal exposure and cognitive impairment

→ Link to Medicines Safety Update
3.5 New issue of WHO Pharmaceuticals Newsletter

The latest edition of the WHO Pharmaceuticals Newsletter (N°4, 2014) is now available. Prepared in collaboration with the Uppsala Monitoring Center, it includes a section on Regulatory Matters and Safety of Medicines. The newsletter also includes signals based on the information available in the WHO Global database VigiBase and the corresponding responses from MAHs:

- Agomelatine – Hypotension
- Dronedarone – Polyneuropathy
- Finasteride – Convulsions
- Roflumilast – Pneumonia

→ Link to WHO Pharmaceuticals Newsletter (N°4, 2014)

3.6 New issue of WHO Drug Information

The latest edition of the WHO Drug Information, Vol. 28 No 3, is now available. The Safety and Efficacy section provides the latest information on safety signals and reports of adverse drug reactions, with other news from around the world, including labelling changes and alerts:

→ Link to WHO Drug Information

3.7 New FDA Drug Safety Podcasts

The FDA Drug Safety Podcasts provide emerging safety information about drugs in conjunction with the release of Public Health Advisories and other drug safety issues. Both Podcasts and Transcripts are posted on the FDA website and the following communication has been recently added:

- FDA approves label changes for asthma drug Xolair (omalizumab) describing slightly higher risk of heart and brain adverse events

→ Link to FDA Page

4. OTHER PUBLICATIONS BY REGULATORY AGENCIES

4.1 US Food and Drug Administration (FDA)

4.1.1 FDA updates information on Potential Safety Signals

The FDA has updated the information posted on its website regarding drugs with potential safety signals, as required by the 2007 FDA Amendments Act. Drugs that appear on the list are identified based on reports from the FDA Adverse Event Reporting System (FAERS).

The new report covers the second quarter of 2014 and includes one new combination of Product / Signal:

- Everolimus (Zortress) – Pulmonary hypertension; Pulmonary arterial hypertension

→ Link to FDA’s Potential Signals Page

4.1.2 FDA meeting to discuss the evaluation of drug safety in pregnancy

As announced earlier, the FDA invited a public meeting entitled “Study Approaches and Methods to Evaluate the Safety of Drugs and Biological Products During Pregnancy in the Post-Approval Setting”, which took place on 28 and 29-May-2014. The purpose of the meeting was to discuss challenges in designing and implementing pregnancy registries and other methods of evaluating the post-approval safety profile of drugs and biological products in pregnant women. In addition to the webcasts and presentations of this meeting previously published, the transcripts are now available on the FDA website.

→ Link to FDA Event Page
4.1.3 FDA meeting on Evaluation of Cancer as an Adverse Outcome

As announced previously, the FDA invited a public meeting entitled “Methodological Considerations in Evaluation of Cancer as an Adverse Outcome Associated With Use of Non-Oncological Drugs and Biological Products in the Postapproval Setting”, which took place on 10 and 11-Sep-2014. The purpose of the meeting was to discuss challenges in designing and implementing postapproval studies to evaluate the risk of cancer associated with use of non-oncological drugs and biologicals.

The meeting material available on the FDA website includes the presentations used at the meeting.

→ Link to FDA Event Page

4.1.4 Drug Safety and Risk Management Advisory Committee: New material available

The Drug Safety and Risk Management Advisory Committee met on 17 and 18-Sep-2014 in a Joint Meeting with the Bone, Reproductive and Urologic Drugs Advisory Committee to discuss Testosterone Replacement Therapy and the associated potential for Cardiovascular ADRs.

On Day 1, the committees advised that the current indication should be revised to promote proper use of testosterone replacement therapy (TRT) and recommended that post-marketing studies be performed to assess cardiovascular risk.

On Day 2, the committees recommended further study for Rextoro, which is the first oral testosterone replacement therapy submitted. There are also concerns that the oral formulation of TRT could promote misuse and appropriate measures should be considered to control this risk.

The material available on the FDA website includes the slides presented during the meeting.

→ Link to FDA Page

4.1.5 Pediatric Advisory Committee: New material available

The Pediatric Advisory Committee met on 23-Sep-2014 to discuss pediatric-focused safety reviews for a number of products, which included everolimus, levofloxacin, and montelukast amongst other medicinal products and vaccines. The FDA has made available some material from this meeting, including the presentations used during the meeting.

→ Link to FDA Page

4.2 European Medicines Agency (EMA)

4.2.1 EMA issues new Pharmacovigilance Risk Assessment Committee (PRAC) material

The EMA routinely makes available the agendas, minutes and highlights of the Pharmacovigilance Risk Assessment Committee (PRAC).

→ Link to EMA PRAC Page

The minutes of the July PRAC meeting have now been published. The PRAC recommended the suspension and reformulation of oral methadone products containing povidone, whereas it recommended restrictions for bromocriptine in inhibiting post-partum lactation. In addition, the PSUR review also led the PRAC to recommend restrictions for the anaemia treatment Rienso (ferumoxytol) in order to better manage the risk of hypersensitivity reactions. The following new Safety Signals were discussed:

- Buprenorphine (transdermal patches) – skin depigmentation
- Sildenafil – increased risk of incident melanoma
- Rivaroxaban – spontaneous splenic rupture/haemorrhage

→ Direct link to PRAC Meeting Minutes (07 to 10-Jul-2014)

The agenda and highlights of the September PRAC meeting have been published. As communicated through a Press Release (see section 2), the PRAC recommended further measures to minimise the risk of liver toxicity.
with agomelatine (Valdoxan/Thymanax). According to the agenda, new Safety Signals have been identified for the following combination of Product / Signal:

- Latanoprost – increased number of eye disorders after change of formulation
- Natalizumab – neonatal haematological abnormalities (thrombocytopenia/anaemia)
- Paliperidone – accidental exposure of children to oral formulations
- Paroxetine – aggression
- Temozolomide – dehydration leading to renal failure
- Teriparatide – non-uraemic calciphylaxis
- Interferon and Peginterferon – pulmonary arterial hypertension
- Lithium salts – solid renal tumours
- Thiotepa – pulmonary arterial hypertension

→ Direct link to PRAC Meeting Highlights (08 to 11-Sep-2014)

### 4.2.2 PRAC recommendations on Safety Signals

The EMA now routinely issues the PRAC recommendations resulting from the assessment of safety signals. MAHs are legally obliged to monitor this information to keep informed about the PRAC recommendations concerning their products, which may require the submission of a Safety Variation.

The list of signals discussed at the September PRAC meeting was published on 30-Sep-2014 and includes recommendations to update the product information for the following combination of Product / Signal:

- Androgen deprivation therapy – QT interval prolongation due to long-term use
- Chlorhexidine cutaneous solutions – Chemical injury when used in skin disinfection in premature infants
- Imatinib – Decreased estimated glomerular filtration rate
- Leuprolerin – Medication error - wrong technique in drug usage process

The cumulative list of all safety signals discussed at the PRAC since September 2012 has been updated accordingly. It includes links to the corresponding PRAC minutes and specifies whether a variation was recommended.

→ Link to EMA Page

### 4.2.3 EMA issues new CHMP Meeting Material

The highlights for the September meeting of the CHMP have been published. As communicated through a Press Release (see section 2), the CHMP reviewed the PRAC’s recommendations on the anti-depressant medicine Valdoxan/Thymanax and concluded that its benefits continue to outweigh the risks, although further measures should be put in place to improve monitoring of liver function during treatment.

The “Meeting Highlights” are presented in a tabular format, which allows users to view the main opinions adopted at the meeting, including on safety variations/PSURs.

→ Link to CHMP Meeting Highlights (22 to 25-Sep-2014)

### 4.2.4 EMA updates the list of Black Triangle Products

As described in GVP Module X, the EMA is publishing the list of medicines under additional monitoring, which must be identified by a Black Triangle (▼) throughout Europe. The list specifies the reason for a product to be subject to additional monitoring and 12 products have been added, including Numeta G16%E and dexamfetamine sulphate-containing medicinal products, for which a full list of products has been provided as Annex XI and XII. The lists of cyproterone-acetate / ethinylestradiol-containing products (Annex I) and hydroxyethyl starch (HES)-containing products (Annex V) have also been updated.

→ Link to EMA Page: Pharmacovigilance / List of Black Triangle Products
4.2.5 EMA website on ADR reports now includes Nationally Approved Products

The EMA has announced that the website launched in 2012 to present information on suspected side effects with centrally authorised medicines has now been expanded to include information about those medicines approved by national authorities in the EU, which represents an additional 1,700 active substances.

All the information made available through the public website comes directly from EudraVigilance and aggregated data can be viewed by age group, sex, type of suspected side effect and outcome.

The EMA has also published a leaflet in all official EU languages to encourage patients to report side effects. In the second year of operation of the new European Pharmacovigilance legislation, EudraVigilance received 35,600 patient reports compared to 21,600 in the year preceding the legislation.

→ Link to EMA Press Release
→ Link to EMA ADR website

4.2.6 EMA holds 8th stakeholder forum on new Pharmacovigilance legislation

The EMA hosted the eighth stakeholder forum on the implementation of the new Pharmacovigilance legislation on 15-Sep-2014, which was approximately a year after the previous forum and the third to take place since the new requirements came into force in July 2012. The objectives of this meeting were to discuss the current status of implementation and review future activities in the context of the new legislation.

Presentations covered the EMA literature monitoring service, Public Hearings and the involvement of Patients and Health Care Professionals in benefit-risk decision-making, amongst other topics.

The agenda and presentations from the meeting are available on the EMA website.

→ Link to EMA Meeting Page

4.2.7 EMA launches pilot project to engage patients in benefit-risk evaluation of medicines

As part of the pilot, patients will be invited to present their views on medicines for which there is an unmet medical need and where the CHMP has concerns or doubts. Patients may also be invited when the CHMP is considering whether to recommend the withdrawal, suspension or revocation of a marketing authorisation, or a restriction of indication.

The first medicine to be included in the pilot project contains the active substance afamelanotide, which is intended for the treatment of erythropoietic protoporphyria (EPP), a rare genetic blood disorder for which there is currently no authorised medicine. Two patients with EPP were invited at the September meeting of the CHMP, and their inputs will be considered as part of the assessment.

A document outlining the main principles of the project is available and the pilot will run for at least one year. A report will subsequently be presented to the CHMP to review the experience and make proposals for a full implementation of the project.

→ Link to EMA Press Release

4.3 UK Agency (MHRA)

4.3.1 MHRA issues Pharmacovigilance Expert Advisory Group summary minutes

The MHRA has published new summary minutes of the Pharmacovigilance Expert Advisory Group. On 02-Jul-2014, the committee met and discussed the following topics:

- Ivabradine: early results from a clinical trial
- Recombinant human erythropoiesis stimulating agents: analyses of clinical trial data
- Ferumoxytol: serious hypersensitivity reactions including fatal cases
- Bisphosphonates and strontium ranelate: risk of heart valve disorders
- Ibuprofen: risk of side effects in the stomach and gut

→ Link to Summary Minutes
4.4 French Agency (ANSM)

4.4.1 ANSM provides update on PRAC/CHMP meetings
Following the PRAC meeting of September, ANSM issued a French summary of the discussions and decisions together with ANSM positions and recommendations for Healthcare Professionals:

- Agomelatine: ANSM recommends HCP to monitor the liver function according to SmPC
  → Link to the ANSM synthesis following the PRAC meeting of September 2014 (in French)

In the same way, following the CHMP meeting of September, ANSM issued a French summary of the discussions and decisions. No specific ANSM positions or recommendations applied.
  → Link to ANSM synthesis of the CHMP meeting of September 2014 (in French)

4.4.2 ANSM issues guidance on variations for renin/angiotensin blocking agents
Following the decision of the European Commission dated 04-Sep-2014 to maintain the MA of the products with modifications, the French Agency requests that MAHs submit a type IB variations and provides some guidance about the procedure to follow.
  → Link to the ANSM guidance (in French)

5. QUALITY ASSURANCE, INSPECTIONS AND AUDITS

5.1 Health Canada issues Annual Inspection Summary Report
Health Canada has published a Summary Report covering all inspection activities conducted by Health Canada in the Fiscal Year 2013-2014 (i.e. April 2013 to March 2014).

Results and observations from inspection activities are summarized by type of inspection and chapter 5 is dedicated to Pharmacovigilance Inspections, which provides information resulting from 86 inspections conducted in the period (82 in previous year). A total of 268 observations were noted and only one establishment was considered Not Compliant.

The report presents examples of common observations, which include the inappropriate management of ADR reports, the lack of adequate safety data exchange agreements with third parties, the absence of procedures for conducting periodic self-inspections of Pharmacovigilance activities, and the preparation and submission of Annual Summary Reports.
  → Link to Health Canada Report

6. DRUG SAFETY AND LIABILITY RISK

6.1 Takeda and Actos
US state court orders Takeda to pay more than $2 Million to Actos user
Takeda was ordered to pay more than $2 million to a 79 year-old woman who claimed the diabetes medicine caused her bladder cancer in the latest of thousands of lawsuits involving the drug. The company intends to challenge this verdict.
  → Link to Bloomberg News article
7. OTHER NEWS AND RESOURCES

7.1.1 PROTECT provides updated ADR database
PROTECT (The Pharmacoepidemiological Research on Outcomes of Therapeutics by a European Consortium) has just made available a new version of its Adverse Drug Reaction database, which is intended to support signal detection and research activities. The PROTECT ADR database is a downloadable Excel file listing all ADRs listed in the SPC of medicinal products authorised in the EU according to the centralised procedure, based on MedDRA terminology.

→ Link to PROTECT ADR Database Page

7.1.2 UMC issues report on Thalidomide
Following extensive consultations involving the UK’s Thalidomide Trust, WHO and the Uppsala Monitoring Centre, experts have met to discuss the risks brought by the new uses of thalidomide, especially in countries with limited drug regulation and poor health communications. Key actions to develop standardised criteria for diagnosis of thalidomide embryopathy have been identified, which are presented in this new report.

→ Link to UMC Page

7.1.3 FDA agrees to revise label for Chantix
In a victory for Pfizer, the FDA has agreed to update the labeling for the Chantix smoking-cessation treatment to soften the warning about the risks of suicidal behavior. The changes reflect the results of various studies and the FDA has convened an Advisory Committee to review the latest data, which Pfizer hopes will lead to the removal of the Black Box Warning included in 2009. The meeting comes more than a year after the company paid $275 million to settle some 2,000 lawsuits over the psychiatric effects of Chantix.

→ Link to StarTribune article
→ Link to The Wall Street Journal article

7.1.4 New Study shows patients misjudge risks of medicines
A new study found that people tend to misjudge risks of medical treatments because they see a catastrophic outcome as less likely when it is presented alongside more benign risks.

→ Link to Bloomberg Businessweek article

7.1.5 FDA’s Mini-Sentinel to become fully developed project
The FDA’s Mini-Sentinel pilot project to evaluate the safety of drugs through the electronic Health Records of more than 175 million people is set to become a full initiative, even though challenges remain and the recent review of Pradaxa has sparked debate. The Harvard Pilgrim Health Care Institute was awarded a $150 million contract by the FDA to spearhead the program.

→ Link to Nature article
→ Link to The Boston Global article

7.1.6 New issue of MedDRA Messenger
The MSSO (Maintenance and Support Services Organization) has published a new “Messenger” Newsletter, which highlights the main changes introduced with MedDRA Version 17.1 in September 2014. The MSSO has also announced that it has successfully maintained its ISO 9001:2008 certification. Another article presents Swissmedic’s experience in switching from WHO-ART to MedDRA.

→ Link to MedDRA Messenger
8. CONFERENCES AND TRAINING EVENTS

EMA/DIA Events

→ EudraVigilance and Electronic Reporting of ICSRs in the EEA
  3 day-training course (see schedule for venues and dates)
→ Extended EudraVigilance Medicinal Product Dictionary (XEVMPD) Training Course
  2 day-training course (see schedule for venues and dates)
→ Joint MHRA/EMA Information Day – MedDRA in the Pharmacovigilance Regulatory Process
  December 08 in London, UK

DIA Events

→ Postmarketing Drug Safety & Pharmacovigilance
  October 20 – 21 in Horsham PA, USA
→ 5th DIA Cardiac Safety Workshop in Japan
  October 23 – 24 in Tokyo, Japan
→ DIA’s Annual Canadian Meeting
  October 28 – 29 in Ottawa, Canada
→ How to Prepare for Pharmacovigilance Audits and Inspections
  November 03 – 04 in Paris, France
→ Advanced Signal Detection - Tools, Triage, Evaluation, and Escalation
  November 03 – 04 in Washington DC, USA
→ Signal Management in Pharmacovigilance
  November 03 – 04 in Paris, France
→ Benefit / Risk Management
  November 10 – 11 in Barcelona, Spain
→ Risk Management and Safety Communication Strategies
  November 10 – 11 in Bethesda MD, USA
→ 11th Annual Meeting DIA Japan 2014
  November 16 – 18 in Tokyo, Japan
→ ICH endorsed Pharmacovigilance training course
  November 26 – 27 in Algiers, Algeria

DSRU Events

→ Risk Benefit Assessment in Pharmacovigilance
  October 15 – 16 in Southampton, UK
→ Case Narrative Writing for Reporting Adverse Events
  November 05 – 06 in Fareham, UK
→ Monitoring the Effectiveness of Risk Minimisation
  November 11 – 12 in London, UK
→ Pharmacovigilance in Products Subject to Licensing Agreements
  November 19 – 20 in London, UK
→ Introduction to Pharmacoepidemiology
  November 26 – 27 in Fareham, UK
Other Events

→ IFIS – Pharmacovigilance: Role, Missions and Responsibilities (event in French)
  October 16 - 17, November 07 in Paris, France

→ ISOP – 2014 Annual Meeting
  October 19 – 22 in Tianjin, China

→ ISPE – 30th Conference on Pharmacoepidemiology & Therapeutic Risk Management
  October 24 – 27 in Taipei, Taiwan

→ OMICS – 3rd Conference on Pharmacovigilance & Clinical Trials
  October 27 – 29 in Hyderabad, India

→ Management Forum – Essential Pharmacovigilance
  October 30 in Dubai, UAE

→ PIPA – 9th Annual Conference
  November 06 – 07 in Chesham, UK

→ RQA – 2014 RQA Annual Conference
  November 12 – 14 in Brighton, UK

→ IFIS – Drug Safety in clinical trials (event in French)
  November 14 in Paris, France

→ IFIS – Risk Management Plan (event in French)
  November 17 in Paris, France

→ Recunnect – Pharmacovigilance 2014
  November 18 – 19 in London, UK

→ RQA – Practical Pharmacovigilance Auditing
  November 18 – 20 in Old Windsor, UK

→ Faculty of Pharmacy, Paris V – Risk Management Plan (event in French)
  November 24 in Paris, France

→ IFIS – Pharmacovigilance: Role of the Responsible Pharmacist (event in French)
  November 24 in Paris, France

→ IFIS – Writing periodic reports in Drug safety
  November 24-25 in Paris, France

→ PIPA – First Steps in Pharmacovigilance: A Workshop for Administrators and Beginners
  November 25 in Chesham, UK

→ Arena – Pharmacovigilance, Drug Safety and Risk Management 2014
  November 26 – 27 in Brussels, Belgium

→ IFIS – The New EU PV legislation for Assistants (event in French)
  December 01 in Paris, France

→ IFIS – Pharmacovigilance for Assistants (event in French)
  December 09-10 in Paris, France