AESGP Euro OTC News

Issue 290 | March 2017

Medicines

53rd AESGP Annual Meeting

30 May – 1 June 2017, Vienna

Self-care in a changing world

More information available on page 28 and on www.aesgp.eu/53

Food

Medical devices

WSMI General Assembly 2017 | The Economics of Self Care
hosted by the Australian Self Medication Industry (ASMI) and the New Zealand Self Medication Industry (NZSMI)

Sponsorship opportunities are available.

Interest should be directed to ASMI (david@asmi.com.au).

AESGP Euro OTC News
Monthly news update by the Association of the European Self Medication Industry
Self-care: the first choice in health care

7 avenue de Tervuren, 1040 Brussels, Belgium
Tel.: + 32 2 735 51 30
Fax: + 32 2 735 52 22
E-mail: info@aesgp.eu
http://www.aesgp.eu

AESGP © 2017 | All rights reserved

Medicines

Pharmacovigilance

- 2016 Annual report on Eudravigilance

On 16 March 2017, the 2016 Annual report on Eudravigilance for the European Parliament, the Council and the Commission was published.

The annual report is called for by the article 24(2), paragraph 2 of the Regulation (EC) No 726/2004. It summarises the activities performed in 2016 related to EudraVigilance, *the European database for adverse drug reaction reports*.

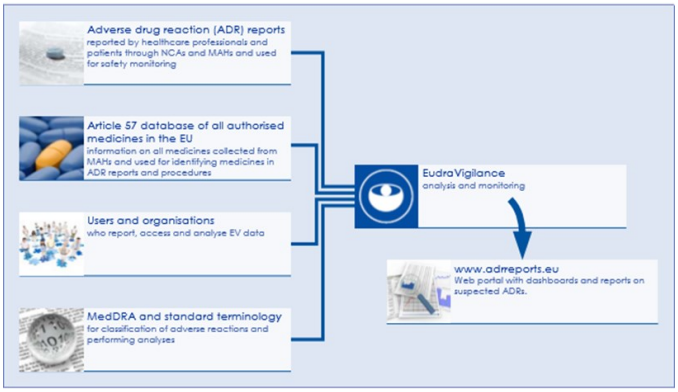


Figure 1: Eudravigilance actors and data sources

- Maintaining and updating a database of information on all medicinal products authorised in the EU allows for identification of medicines in reports of suspected adverse drug reactions, as well as supporting the management of pharmacovigilance procedures (signals, PSURs, referrals) and facilitates the administration of pharmacovigilance fees. It also allows Marketing Authorisation Holders (MAHs) to easily update details of the qualified person responsible for pharmacovigilance (QPPV) and the pharmacovigilance system master file (PSMF) without the need for submission of variations.

-The number of adverse drug reaction (ADR) reports collected and processed by EudraVigilance in 2016 was 1% higher than the previous year (1,238,178 reports received in 2016). The number of reports received originating from the EEA decreased by approximately 6% (339,544 reports received in 2016). The number of reports submitted directly by European patients and consumers through the NCAs and MAHs (47,238) was similar to but slightly lower than in 2015.

-2016 featured ongoing data quality activities, which included developing standards and guidance, detecting and managing duplicate reports, review and feedback to reporters on the quality of reports they submitted, and quality review and corrections of data on authorised medicinal products.

-The provision of 22,429 data analysis reports to the EU network monitoring EudraVigilance data on medicines safety (electronic reaction monitoring reports - eRMRs) and the provision of data analyses to support assessments in pharmacovigilance procedures. EudraVigilance monitoring is performed in collaboration between the National competent authorities (NCAs) and the Agency. NCAs monitor EudraVigilance data for potential signals (i.e. drug-event pairs, potential safety issues or associations between medicines and adverse reactions detected from screening of the EudraVigilance database, the medical literature, or information from other regulatory authorities etc.) relating to substances used in nationally authorised products.

- Review of potential signals for centrally authorised products EMA staff led on monitoring these and this resulted in 2,076 potential signals reviewed by the Agency, of which approximately 83% originated from analysis of ADR reports received in the EudraVigilance database, reflecting the central role of EudraVigilance for ADR data monitoring.

- Supporting the central role of the Pharmacovigilance Risk Assessment Committee (PRAC) in assessing and monitoring the safety of human medicines in the EU, including prioritising and assessing safety signals (94 confirmed signals previously validated by the Member states and the Agency were prioritised and assessed by the PRAC in 2016). Approximately 30% resulted directly in an update of product information, providing prescribers and patients with information aimed at minimising

the risks from these adverse drug events (ADRs). Others were to be monitored in the context of the PRAC's assessment of periodic safety update reports (PSURs) or in four cases handled via an EU referral procedure. The PRAC assessed the available evidence and where necessary, made timely recommendations to minimise the risks and provide information to patients and prescribers.

- Training activities, many of which were open to all stakeholders. Five training sessions on the EudraVigilance Data Warehouse and Analysis System were delivered, training 74 experts from 16 NCAs within the EU network on activities related to pharmacovigilance analysis of ADR report data, screening electronic reaction monitoring reports and aiding PSUR assessments. Additionally, 16 training sessions on EudraVigilance data submission and 7 training sessions on the XEVMPD were organised in 2016 and 263 users underwent training on XEVMPD via its e-learning platform.

- Development of Introduction to EMA's training offering as well as a comprehensive set of training materials, delivered ahead of time to support EudraVigilance stakeholders and partners in their preparation for new EudraVigilance functionalities.

- Delivering enhancements of the EudraVigilance database, internal and stakeholder testing and implementing fixes. This prepares the way for an independent audit in 2017 with the aim of bringing enhanced functionalities into operation. These functionalities will simplify ADR notifications by MAHs through centralising reporting to EudraVigilance and rerouting of the reports to NCAs in EEA Member States. Furthermore, new functionalities will give unprecedented stakeholder access to ADR data including healthcare professionals, patients, academia but also MAHs to the extent necessary to fulfil their pharmacovigilance obligations. Improved data quality and better data analysis is being achieved through the use of the internationally agreed ISO/ICH E2B(R3) ICSR standard and the Medical Dictionary for Regulatory Activities (MedDRA). Adverse reaction reports from within the EU will be delivered directly and in a faster way from EudraVigilance to the World Health Organization (WHO) Uppsala Monitoring Centre.

The development of EudraVigilance continued in collaboration with the Member states throughout 2016, with successful completion of user testing in preparation of its independent audit in early 2017. The enhanced functionalities are planned to become operational in late 2017 subject to a successful audit outcome.

In relation to this, new hands-on training courses on the new EV system and the electronic reporting of individual case safety report (ICSRs) in the ISO/ICH E2B(R3) format are now available.

■ Updated EURD list & Patient Registries Workshop Report - October 2016

On 28 February 2017, a revised version of the List of European Union reference dates and frequency of submission of periodic safety update reports (EURD List) was published.

The EURD list is maintained by EMA for medicines containing the same active substances or combinations of active substances. It allows the single assessment of PSURs as Marketing authorisation holders are required to submit PSURs according to the PSUR submission dates specified.

The updates are highlighted in the document. The following modifications are worth noting:

- the amendment of the PRAC rapporteur for ambroxol
- the amendment of the PRAC rapporteur for dexlansoprazole, lansoprazole
- the amendment of the PRAC rapporteur and next DLP for ibuprofen / pseudoephedrine
- the amendment of the PRAC rapporteur for methyl salicylate / levomenthol
- the amendment of the PRAC rapporteur for methyl salicylate / levomenthol / DL-camphor

In addition, the report on the Patient Registries Workshop, held on the 28 October 2016 was also posted on the EMA website.

The workshop was set up to better understand the challenges and barriers to collaboration between stakeholders. The perspectives of multiple stakeholders including registry holders, patients, the pharmaceutical industry, health technology assessment representatives and regulators were explored in the workshop. The report sets out participants' observations and recommendations in five theme areas: benefits of patient registries and obstacles to be overcome, benefits and

challenges of collaborations, technical considerations, governance, and sustainability. It recommends activities for EMA to undertake, in cooperation with the cross-committee task force, to improve stakeholder collaboration and optimise the use of registries to support regulatory decisions, taking account of feedback from the workshop. These include:

- exploring mechanisms for regulators and marketing authorisation applicants to systematically consider the need for registries and interact with registry holders;
- sharing and disseminating information on patient registries in specific disease areas;
- recommending governance principles and standards for stakeholder interactions;
- making recommendations on core data elements and quality standards acceptable for regulatory decision-making;
- identifying registry holders' needs for methodological and technical guidance;
- investigating what patient-reported outcomes registries should collect;
- exploring further measures to improve the sustainability of registries.

Together with the cross-committee task force, EMA will develop an implementation plan to support the delivery of these activities. The task force will adapt its governance structure, strategy and communication activities to reflect changes in its role. In 2017, EMA will organise two stakeholder workshops on patient registries in specific disease areas, to provide recommendations on details such as data elements, protocols, consents, registry governance and interoperability. These will act as models for best use of patient registries in other disease areas.

i

In 2014, the EMA commenced a Registry Initiative aiming to optimise the use of registries in supporting medicines authorisations. Establishing a strategy of early engagement between marketing authorisation applicants and registry holders and a task force to support activities, a pilot phase was undertaken aiming to understand the barriers and enablers in using registries to support marketing authorisation applications and to inform the development of recommendations to optimise their use. More information is available on the dedicated patient registries webpage on EMA.

CMDh *Co-ordination Group for Mutual Recognition and Decentralised Procedures-Human*

■ CMDh Report-February 2017

The CMDh has recently published the report from its meeting held on 20-22 February 2017, which includes:

Update of the Best Practice Guide on the submission of high quality national translations

The CMDh has agreed an update of the BPG on the submission of high quality national translations. Marketing authorisation applicants must now submit high quality national translations of their SmPC, PL and labelling and mock-ups for new marketing applications, extensions and renewals within seven calendar days instead of 5 calendar days after the marketing authorisation procedure.

The same change is applicable to other CMDh guidance documents and will be gradually included in the relevant documents with the next revision. The link to the Guideline *"Excipients in the label and package leaflet of medicinal products for human use"* has also been updated. In addition, the guide now states that national translations of PRAC recommendations on signals and PSUSAs should also be used.

- CMDh Best Practice Guide on the submission of high quality national translations (Clean/ Track version)

Regulation (EC) No 1234/2008 on variations

Article 5 of the variation regulation provides the basis for a marketing authorisation holder (MAH) or a competent authority of a Member State (NCA) to request CMD(h)/ CMD(v) for nationally authorised products or EMA for centrally authorised products to deliver a recommendation on classification of an unforeseen variation (i.e. a variation not listed in Annex II of the Variation Regulation (EC) 1234/2008 or the classification guideline). The CMDh agreed that the proposed change ("*Deletion of one manufacturing process of the drug product manufacturing processes*") should be submitted as a type IA variation provided that at least one previously authorised manufacturing process remains and the deletion should not be due to critical deficiencies concerning manufacturing.

- CMDh Recommendation for classification of unforeseen variations according to Article 5 of Commission Regulation (EC) 1234/2008

The CMDh has agreed an update of the Questions and Answers on Variations [*Track version*]. A new Q&A 1.8 on the update of SmPC following a renewal further to a repeat-use procedure has been added. Q&A 2.11a was deleted as it is considered obsolete. Q&As 2.10-3.28 have been reviewed by CMDv and specific answers related to veterinary medicinal products have been added, where applicable.

Update of Q&As on QP declaration

The CMDh agreed an update of the Q&A document on QP declaration. Question 7 has been added to clarify the need for QP declaration (s) in support of certain changes to a Marketing Authorisation, to confirm that the active substance is manufactured in accordance with the detailed guidelines on good manufacturing practice for starting materials.

Update of Q&As on QP declaration (Clean/Track version)

Revision - Urgent Safety Restriction - Member States' Standard Operating Procedure

The CMDh agreed a revision of the Member States' Standard Operating Procedure on Urgent Safety Restrictions. The document has been updated to bring it in line with the changed legislative environment since the last revision.

- Urgent Safety Restriction Members States' Standard Operating Procedure (Clean/Track version)

The update now states that '*before a USR is initiated, it should be carefully considered whether another existing pharmacovigilance tool would be more appropriate*'. The definition of Article 2(8), "Urgent Safety Restriction" was amended. It is now defined as meaning '*an interim change in terms of marketing authorisation due to new information having a bearing on the safe use of the medicinal product.*' In the event of a risk to public health, in the case of a centralised marketing authorisation, the Agency rather than the commission should be notified. References to the pharmacovigilance Working Party (PhVWP) have been replaced with the Pharmacovigilance Risk Assessment Committee (PRAC). It also now states that urgent safety restrictions and variations shall be implemented within a time frame agreed by the holder and the competent authority of the reference Member State, in consultation with the other relevant authorities. In addition, the list of references and the annexes (particularly the flow chart for the 24 hour USR procedure) have been updated. Other changes include updated article numbers. No procedural changes have been included.

Recommendations on submission dates for Applicants of the MRP

Following the recent amendment of the MRP/RUP timetable, the CMDh has adopted an updated guidance document with the timetables for MRP applications to be submitted in 2017.

- Recommendation on submission dates in 2017 for Applications of the Mutual Recognition Procedure (Clean/Track version]

Summary of CMDh Activities in 2016

The CMDh has published on the website, for transparency reasons, a Summary of the main activities in 2016 carried out by the CMDh and its working groups/working parties in 2016. A list of new and revised CMDh documents published by the CMDh in 2016 is included as an Annex to the document.

The CMDh finalised in 2016 its "Strategy to 2020", and further developed a Multi Annual Work Plan (MAWP) to bring the overarching strategy into operation. The CMDh continued working on the improvement of MRP and DCP procedures. The CMDh continued to work in close collaboration with PRAC and EMA on all pharmacovigilance procedures and how to implement the outcomes of the procedures after CMDh position. The CMDh started the discussion on how the Art. 57 database can be used to reduce variations which will continue in 2017. The CMDh extended the pilot for splitting MRPs/ DCP procedures and the outcome of the merging pilot will be assessed in 2017 once all procedures have been finalised. The CMDh started 4 waves of worksharing for the assessment of paediatric studies submitted in accordance with Article 45 of Regulation (EC) No 1901/2006, concerning 9 active substances/ combinations of active substances. The CMDh position paper on the use of Quick Response (QR) codes (*) was updated to include information on the use of QR codes in combination with safety features as per the Falsified Medicines Directive. The CMDh discussed potential candidates for a list of products for which a harmonised SmPC should be drawn up in 2016. No product for SmPC harmonisation, in accordance with Article 30(2) of Directive 2001/83/EC could be identified and the CMDh will revisit the situation in 2017. The CMDh's activities on e-submissions, transparency, interaction with the CMDv, EMA scientific committees and working parties, HMA and interested parties and summary statistics are also described.

A list of new and revised documents developed and published by the CMDh in 2016 are included as an annex.

(*) *A Quick Response (QR) code is a two-dimensional bar code that is used to provide easy access by patients and/or Health Care Professionals to information through a smartphone*

Falsified Medicines Directive

Following the receipt of several queries on the implementation of the Falsified Medicines Directive over the last year, the CMDh has agreed to publish, for transparency reasons, the feedback given to those queries.

- CMDh clarifications on questions received on the implementation of the Falsified Medicines Directive

These Q&As, based on several queries received over the past year, clarify requirements on the implementation of the Falsified Medicines Directive. A new QRD template version (*) was introduced to account for the Falsified Medicines Directive from the European Commission - Directive 2011/62/EU which introduces obligatory "safety features" to allow the verification of the authenticity of medicinal products subject to prescription and certain non-prescription products. The new safety features introduced by the Directive are a unique identifier (a 2-dimension barcode) and an anti-tampering device, to be placed on the packaging of most medicines for human use.

As a consequence, the new QRD template impacts the outer packaging, where two new sections were added, to include the new unique identifier information: section 17- unique identifier, 2D barcode and 18- unique identifier, human readable data. The implementation of the anti-tampering device is not expected to impact the product information. However, if this device is placed on the immediate packaging (because there is no outer packaging) and affects the container and its closure system, this should be taken into consideration in Module 3, particularly section 3.2.P.7 of the Notice to Applicants Volume 2B, and the necessary variation should be submitted.

It is possible to implement the new QRD template (including section 17 - unique identifier – 2D barcode and 18- unique identifier - human readable data) and the antitampering device separately, using the appropriate regulatory procedures as described in the implementation plan. The implementation of safety features can also take place before approval (independent of the procedure with which it is notified) in line with the process for type IA variations, provided that no other changes are made on the mock-ups at the same time and it has no impact on the overall readability of the mock-up.

(*) The QRD Template provides guidance on how to present the SmPC, Labelling and Package Leaflet for a marketing authorisation application

MRP/DCP statistics in 2016

- 2016 - Statistics for New Applications (MRP/DCP), Variations and Referrals

There were 249 MRP and 1133 DCP finalised procedures for new applications (regarding 475 and 2337 products respectively) from 1st January 2016 to 31st December 2016. Four out of a total of 249 MRP procedures related to Traditional herbal medicinal products and 24 related to well-established use applications. Thirty-five out of a total of 1133 DCP procedures related to Traditional herbal medicinal products and 72 related to well-established use applications. Nineteen of the 249 MRP procedures related to non-prescription medicines, and 86 of the 1133 DCP procedures related to non-prescription medicines.

Out of 270 MRP started procedures (regarding 525 products), 27 related to well-established use and 5 related to Traditional herbal medicinal products. Out of 1264 DCP started procedures (regarding 2568 products) 78 related to Well established use, and 2 related to Traditional herbal medicinal products. Twenty two of the 270 started MRP procedures related to non-prescription medicines, and 108 of the 1264 started DCP procedures related to non-prescription medicines.

An EU ASMF number request form for ASMF worksharing procedures has also been uploaded on the CMDh website.

i

As the same version of an Active Substance Master File (ASMF) may be submitted in different European procedures (Centralised, Decentralised, Mutual Recognition and national procedure), the Working Group on Active Substance Master File Procedures has established a worksharing procedure for the assessment of ASMFs, including a centralised EU numbering system for ASMFs and a centralised repository for the ASMF assessment reports. The aim is to harmonise the assessment of ASMFs, reduce the frequent updates of ASMFs, and reduce the resource and regulatory burden on Competent Authorities, ASMF and Marketing authorisation holders.

- Report to the European Parliament and the Council on the summary of product characteristics and package leaflets

The Report to the European Parliament and the Council on the summary of product characteristics and package leaflets has been published. This report was prepared pursuant to Article 59(4) of Directive 2001/83/EC1 according to which the Commission shall present to the European Parliament and the Council an assessment report on current shortcomings in the summary of product characteristics and the package leaflet and how they could be improved in order to better meet the needs of patients and healthcare professionals.

Two external studies carried out by 'NIVEL' provided the supporting information for this report.

1. Study on the Package Leaflets and the Summaries of Product Characteristics of Medicinal Products for Human use ("PIL-S Study") to assess the readability and comprehensibility of the SmPC and the PL as sources of information on prescription and non-prescription medicines for patients and healthcare professionals
2. Study on the feasibility and the value of a possible "key information section" in patient information leaflets and summaries of product characteristics of medicinal products for human use ("PILS-BOX Study")

AESGP, together with the innovative and the generic trade industry associations, provided a joint response on the above mentioned NIVEL reports to the European Commission in January 2016.

Based on the above-mentioned assessment the following outcomes and recommendations have been identified by the European Commission:

It should be noted that "the current EU legislation on medicinal products for human use allows for enhancement of the statutory medicines information to support the safe and effective use of medicinal products. The report therefore suggests that recommendations should be primarily taken forward by improvements of the existing regulatory guidelines, templates and other non-legislative means."

Room for improvement of PL rather than of SmPC

The assessment found that patient's comprehension of the PL and its readability can be improved. The language used is often too complex and the design and lay-out are not always user-friendly. On the other hand, less problems were identified with regard to the SmPC although improvements can still be made especially with regard to the readability of the SmPC. Representatives of healthcare professionals generally judge the quality of the SmPC as reasonable and value most of the current topics addressed in the SmPC as being important.

Recommendation: Generally, there should be more focus on improving the PL rather than the SmPC. However, for any potential improvement of the PL it should be also considered whether a corresponding or related change of the SmPC would be appropriate.

Amendments of Guidelines and QRD templates to enhance readability of PL

Content and layout-related issues were identified in the PIL-S Study. Small font size, narrow line spacing and the length of the PL were identified as the main issues. The QRD template should rely on principles of good information design and pay attention also to the needs of some specific groups of patients, such as elderly, young people or people with mental illnesses; together with the guidelines they were considered too restrictive in some aspects. They should allow for more flexibility to adapt the PL to the specificities of each product whilst respecting the limits provided by the legislation.

Recommendation: It should be considered to revise the existing guidelines, in particular the Readability Guideline, the Packaging Information Guideline and, where appropriate, the SmPC Guideline to include principles of good information design and consider allowing more flexibility in the information recommended in the QRD template, as long as the relevant legislation allows it. These revisions should also include introduction of guidance on translations that go beyond the principle of faithful translations. The aim should be to ensure that the lay language introduced through user testing in the original language version is not lost during translation.

Improving patient input in developing and testing of PLs, to e.g. gain a greater understanding on how to present risk-benefit information for a particular medicine

The assessment recognised the usefulness of patient involvement and the importance of user testing of the PL. It is equally important that methodology for such testing is well defined. The assessment further identified the need for strengthening the input from the patient perspective which could also help in getting more understanding on how to present risk-benefit information for a particular medicine.

Recommendation: The input from patients during the process and the related methodology should be further improved, for example, by considering the requirement to make the user testing process more iterative and to ensure that a sufficiently mature version of the PL is user-tested. This iterative user-testing would be coordinated by regulatory authorities in parallel to the assessment in a way that does not disrupt the whole marketing authorisation process. The iterative testing should focus on the content of the PL, rather than the format and layout, to ensure that information is clear and written in a way which is easily understood by patients. Potential amendments of the Readability Guideline could be considered in this respect taking also into account the use of structured benefit-risk approaches and visual representations to communicate benefits and risks to different stakeholders in different situations, including those approaches developed by the European Medicines Agency in the context of the Benefit-Risk Methodology project and by the Innovative Medicines Initiative (IMI) Pharmacoepidemiological Research on Outcomes of Therapeutics by a European ConsorTium (PROTECT) project.

Promotion and exchanges of best practice of user-tested examples of the PL/SmPC and their development process to facilitate and improve development

The assessment concluded that good, user-tested examples of the PL and to some extent also the SmPC as well as their development process could be promoted more by regulators to facilitate and improve the development of these documents.

Recommendation: Best practice examples of aspects of the PL (and the SmPC) design could be made available for pharmaceutical companies on a platform that would be suitable for that purpose and that could be regularly updated. These examples should include not only the end products, but also information on the process of development, where possible. The selection of these examples should be evidence-based.

Electronic SmPC/PL formats bring new opportunities for SmPC and PL to provide the information to individual EU-citizens in accordance with the existing legislation (e.g. in terms of presentation, format or use of multiple languages).

The assessment acknowledged the new opportunities brought up by electronic format for PIL and SmPC and the increasing access to information technologies. It nonetheless concluded that electronic PL formats should be complementary to paper PLs that are required by the legislation and should not replace them at this stage in order to ensure availability of the information for all patients.

Recommendation: It is recommended to explore the use of electronic media to provide the information included in the SmPC and PL in the future. It should be further explored what opportunities new technologies offer to optimize the presentation and design of SmPC and PL. In this context, the opportunities for the information included in the SmPC and the PL to be more easily used as an integrated part of the care process should be explored. For example, developing mechanisms through electronic tools to inform patients and healthcare professionals on changes in the SmPC and PL should be considered. The exploratory work in this area should be based on and further develop the existing work done by the European Medicines Agency in this area and should follow a multi-stakeholder approach involving also the pharmaceutical industry, patients, consumers, healthcare professionals, the Member States and the Commission. The aim will be to develop the key principles for the use of electronic SmPC and PL formats. The results of this exploratory work should be submitted to the Commission for any follow-up action as appropriate.

This is fully in line with the joint industry response concerning non-prescription medicinal products (conveying AESGP position) which states that "Non-prescription medicinal products OTC" products) need to be regarded separately. As the patient may have no or little interaction with a healthcare professional, information provided directly with the pack will continue to be required but could be complemented by possibly a more user-friendly electronic information." For prescription-only medicines, the industry position stated that "paper could stepwise be replaced by electronic information".

Potential key information section in the SmPC and PL to e.g. allow patients and healthcare professionals to rapidly identify key safety messages

The key information section is not

specifically envisaged in the existing EU legislation on medicinal products for human use. The outcome of the assessment is that more experience and evidence needs to be gathered and that currently testing can be considered as a means to further determine the potential usefulness of the inclusion of a key information section in the SmPC or PL.

Having 'essential information' in a black box on leaflets was indeed part of the two Commission's proposals to strengthen and rationalise the EU system of pharmacovigilance. This was hence discussed at EU level and opposed by a great majority of stakeholders. The provision was abandoned early on in the legislative debate and did not make it to the final respective Pharmacovigilance Directive and Regulation.

Recommendation: More evidence would need to be gathered before considering introduction of a key information section in the Product Information. It is suggested to continue further exploratory work on the use of such key information in the PL as well as the possibility to use Quick Response (QR) codes as another way to make available information to patients. Appropriate testing (e.g. user testing) could be a way to demonstrate the clear evidence of the usefulness and added value to patients to introduce a key information section in the PL. In this respect, the work currently being undertaken by EMA as part of its strategy to improve information on benefit risk to patients and healthcare professionals could be taken into account. In particular, the planned testing of adding a 'key information section' to the 'EPAR summary' for each centrally authorised medicinal product could be used for this purpose. This may help to decide on the type of information that should be provided in the PL and the category or type of medicines where such a key information section could be useful and appropriate.

The report concludes that: "The Commission and the European Medicines Agency will work towards implementation of the above-mentioned recommendations in order to improve certain aspects of the SmPC and PL and to better meet the needs of patients and healthcare professionals. The work will be taken forward in close collaboration with the Member States. It will be ensured that the key stakeholders, in particular representatives of patient organisations, healthcare professionals, industry representatives, national regulators and other relevant parties will be duly consulted and involved as appropriate with regards to the respective proposed possible actions."

This report was awaited by the industry association task force (IATF) on product information composed of representatives from AESGP (Jennifer Collins, GSK and Anita Finne-Grahnén, LIF who participates in the different workstreams and Christelle Anquez-Traxler, AESGP), EFPIA and MfE. The IATF particularly looks into readability, layout and content of the product information/ QRD templates and e-leaflet and updates on the progress of the IATF are given at each AESGP Regulatory affairs committee (RAC) meeting.

EMA

- Important EMA note for registered products: THMPs expected to be in XEVMPD due to EudraVigilance access

The EMA has uploaded an important Note for clarification on pharmacovigilance requirements and the process for obtaining access to adverse reaction reports in EudraVigilance for Traditional herbal medicinal products (THMPs) and Simplified registrations for Homeopathic medicinal products.

Simplified registration application for homeopathic medicinal products (Article 14 of Directive No 2001/83/EC);

Homeopathic medicines are eligible for the simplified procedure on the condition that they are administered orally or externally (i.e. not by injection, for instance); no specific therapeutic indication appears on the labelling or in the patient information; they present a sufficient degree of dilution to guarantee the safety of the medicinal product.

Those products which do not comply with these criteria need to be authorised will require a general marketing authorisation.

Traditional use registration application for herbal medicinal products (Article 16a of Directive No 2001/83/EC);
This applies to Herbal medicines with a long tradition of use (at least 30 years, including 10 years in the EU) that do not fulfil the requirements for a marketing authorisation. Applications for registration have to fulfil the same quality and safety requirements as applications for a marketing authorisation, but they do not have to prove efficacy – the traditional indications must simply be 'plausible'.

It clarifies that pharmacovigilance requirements apply to *authorised* homeopathic medicinal products but do NOT apply to *simplified registrations of* homeopathic medicinal products. This means that registration holders of registered homeopathic medicinal products are exempt from reporting suspected adverse reactions and of Periodic Safety Update Reports (PSUR) submission (unless this is laid down as a condition in the registration or requested by the Competent Authority). Pharmacovigilance requirements (including reporting obligations) apply to both authorised and traditional herbal medicinal products with the exception of PSURs (unless this is laid down as a condition in the registration or requested by the Competent Authority).

With the coming into force of Eudravigilance, pharmaceutical companies will no longer receive reports of suspected adverse reactions through National competent authorities but via Eudravigilance.

In order to comply with pharmacovigilance reporting requirments and to obtain access to reports of suspected adverse reactions in EudraVigilance, holders of traditional use registrations for herbal medicines should submit the information for these medicines using the electronic format referred to as Article 57 format or eXtended EudraVigilance Product Report Message (XEVPRM) format. Registration holders should also ensure that the information is kept up to date. As pharmacovigilance reporting requirements do not apply for simplified registrations of homeopathic medicinal products, this is no need for registration holders to submit this data (although they can if they wish on a voluntary basis as the system allows for this).

However, NO fees will be charged for submission of data in the Article 57 database as Regulation (EU) No 658/2014 as on fees payable to the European Medicines Agency for the conduct of pharmacovigilance activities in respect of medicinal products for human use, does not apply to traditional herbal medicinal products, nor to homeopathic medicinal products registered through the simplified procedure.

The Article 57 database owes its name to a legal provision in Regulation (EC) No 726/2004, namely Article 57 (2), one of the key measures of the new pharmacovigilance legislation. According to this Article, marketing authorisation holders have to submit to EMA medicinal product-related data to the eXtended EudraVigilance Medicinal Product Dictionary (XEVMPD database) using the eXtended EudraVigilance Medicinal Product Report Message (XEVPRM) electronic format. Medicinal products falling out of scope of Article 57(2) legal obligation (namely traditional herbal medicinal products, and simplified registrations of homeopathic medicinal products) may be submitted on voluntary basis in line with the requirements and business processes described in Chapter 3.II: Extended EudraVigilance product report message (XEVPRM) user guidance. Please refer specifically to question 1.2 of the document "Electronic submission of Article 57(2) data Questions & Answers (Q&As)"

■ European and US regulators agree on mutual recognition of inspections of medicines manufacturers

The European Union (EU) and the United States (US) have put in place a Mutual recognition agreement (MRA) on good manufacturing practice (GMP) inspections. The aim of the agreement is to encourage greater international harmonisation, make better use of inspection capacity and reduce duplication. Under the new agreement, EU and US regulators will rely on each other's inspections in their own territories. In future, the need for an EU authority to inspect a production site located in the US to ensure compliance with good manufacturing practice (GMP) or vice versa, will be limited to exceptional circumstances.

The EU and US signed the MRA on GMP inspections in February 2017, which enters into force on 1 November 2017. The agreement is a sectoral annex of the broader EU-US MRA, signed in 1998 between the EU and US authorities. The text of the updated MRA is available on the European Commission's website. As the US Food and Drug Administration (FDA) will assess each EU Member State authority individually, a transition phase will be in place until July 2019. Imported products still need to be batch tested until this requirement is waived after the transition phase.
The EU-US MRA covers:

- finished pharmaceutical forms of human medicines;
- intermediate (in the EU) and in-process (in the US) products;
- certain marketed biological products for human use;
- active pharmaceutical ingredients.

It excludes medicines derived from blood or blood plasma, human tissues and organs and veterinary immunologicals. The MRA normally covers pre-approval inspections, although special provisions apply during the transition phase, which EMA and FDA may review. The press release, together with all related documents, are available on the EMA website.

■ Regulatory information – adjusted fees for applications to EMA from 1 April 2017

The EMA has published a reminder on its website for applicants and marketing authorisation holders that adjusted fees for all applications, except for pharmacovigilance procedures, will be coming into effect on Friday 1 April 2017.

Every year, the Agency adjusts its fees on 1 April, in line with the European Union (EU) inflation rate for the previous year. The European Commission is currently in the process of adopting a regulation adjusting the fees payable to the Agency by 1.2% in line with the 2016 inflation rate.

The rules for the implementation of Council Regulation (EC) No 297/95 on fees payable to the European Medicines Agency and other measures – revised implementing rules to the Fee Regulation as of 1st April 2017 was adopted by the EMA Management Board at their March 2017 meeting.

All applications received by 31 March will be charged at the current fee and reduction rates. Applications received after that date will be charged the adjusted fees and be subject to the revised reduction rates, where applicable. For scientific advice and protocol assistance, the cut-off date will be the date of validation of the request for advice. For annual fees the anniversary date defines the applicable fee and consequently any anniversary on or after 1 April 2017 will attract the new fee.

Fees charged for pharmacovigilance procedures in accordance with Regulation (EU) 658/2014 are expected to be updated from 1 July 2017.

■ Guidance on triggers for inspections of bioequivalence trials: Quick scan

Guidance on triggers for inspections of bioequivalence trials: Quick scan, adopted by Co-ordination Group for Mutual Recognition & Decentralised Procedures – Human (CMDh), has come into effect from March 2017, replacing the 2013 guidance.

The guidance is in the form of a checklist, designed to be used by assessors when reviewing bioequivalence studies. Missing documentation should first be solved through questions to the applicant. If triggers are identified, after the completion of the checklist, which potentially have an impact on the quality of the data, the assessor is advised in the first instance to have a discussion with their good clinical practice (GCP) inspectorate.
In case of an old bioequivalence trial, i.e. performed more than 5 years ago, before requesting an inspection it should be checked that the trial complies with current requirements.

Identification of other triggers not mentioned in the document is possible-this list is to be considered a quick scan. The topics listed in this document are intended to assist the assessor in deciding on whether to consult or to seek input from their GCP inspectorate on the need for a GCP inspection and on the best way forward. Where concerns appear, this may warrant a triggered study-specific or even a systems inspection.

■ 2016 Activity report of the Modelling and simulation working group (MSWG)+2017 work plan

The EMA has uploaded the 2016 Activity report of the Modelling and simulation working group (MSWG). The Modelling and Simulation Working Group (MSWG) was established in January 2013 to provide specialist scientific support to the SAWP, PDCO and CHMP in the form of feedback on technical issues around how companies propose to use modelling and simulation (M&S) in support of registration dossiers. It summarises its activities/ priorities in the following areas of interest:

- Modelling and simulation approaches (M&S) in dose -exposure-response characterisation and dose selection
- Projected PK (/PD) in children
- Population pharmacokinetics and PBPK in clinical pharmacology evaluations
- Dose exposure response analyses and/or PK/PD modelling to support SmPC claims mainly on posology section
- M&S as a method to support the life cycle management of medicinal products, e.g. new dose regimens, new formulations, route of administrations and the design of post approval studies.

The report also notes the following:

M&S was proposed in submissions as a tool to bridge efficacy data to a new route of administration, from non

-pregnant to pregnant women, to justify a biowaiver of a new oral formulation and to quantify the predictive properties of biomarkers. However, there is currently a very specific regulatory position on biowaivers and bioequivalence. Unless model based methods are qualified to support such uses, the report notes that it will be difficult to accept M&S in this context. Using M&S to support extrapolation between different populations is encouraged, however it is acknowledged that more experience is needed with the use of models to predict PK/PD in pregnant women.

It states that good progress was achieved in the areas identified from the 2016 work plan. Some activities are still ongoing (i.e. extrapolation, PBPK) due to the complexity of the issue or due to the fact that they have long term deliverables (e.g. assessors' guides and harmonisation of regulatory requirements on M&S).

The Work plan for the Modelling and Simulation Working Group (MSWG) for 2017 has also been uploaded.

■ Dual logo on the outer packaging of centrally authorised medicinal products in cases of co-marketing and co-promotion agreements

EMA has relayed an important communication concerning a change in policy of displaying the logo of companies on the outer label of centrally authorised medicines in cases of co-marketing/co-promotion agreements.

The inclusion of additional information on the outer packaging, such as co-promotion or co-marketing partners' logos, relates to additional information that is not required by Article 54 of Directive 2001/83/EC. As such, it must comply with the legal provisions of said Directive and, in particular, Article 62, which states that *"The outer packaging and the package leaflet may include symbols or pictograms designed to clarify certain information mentioned in Articles 54 and 59(1) and other information compatible with the summary of the product characteristics which is useful to the patient, to the exclusion of any element of a promotional nature*".

This is consistent with the main purpose of the provisions on the packaging of medicinal products, which is to facilitate medical doctors', and patients' understanding of the concerned leaflet and outer packaging. This objective was underlined in the ruling of the Court of First Instance in case T-179/00 *Menarini v European Commission* and also clearly expressed in Article 62.

Thus, the question of the possibility, under Article 62 of the Directive, to place the logos of both the marketing authorisation holder (MAH) and the co-promoter/co-marketer on the outer packaging of centrally authorised products depends on whether it would be useful to the patient and would not create confusion for patients. Having regard to the above considerations a new approach has been taken in relation to the above subject. In particular:

- In terms of co-promotion the inclusion on the outer packaging of the co-promoter's logo will no longer be allowed. Co-promoters are not responsible for the quality of the product, for the pharmacovigilance duties of a MAH, nor for placing the product on the market. Their main task is to lend their marketing force to the MAH to promote a particular medicinal product, whilst the MAH retains all other responsibilities. The co-promoter's logo would not seem to enhance consumer protection and, if present on the outer packaging, could even be regarded as potentially able to confuse patients.

- In terms of co-marketing, the display of the co-marketer's logo will be accepted only in cases where the co-marketing partner is also the local representative, as per the Menarini ruling. The logo of the co-marketer/ local representative can, therefore, only be included in the Blue Box of the outer packaging, next to its name and address.

In addition, in accordance with Article 62 of the Directive, trademark statements cannot be considered as useful to the patient, and could be regarded as an element of promotional nature. Therefore, in principle, such statements should not be included on the packaging, unless the non-inclusion of such trademark statement would constitute a breach of trademark law.
Similarly, statements on licencing relationships between companies, as also copyright statements, cannot be considered as useful to the patient, and consequently are not accepted on the packaging.

The new policy will be reflected in a revised Q&A document to be published on the EMA website. The new policy has no impact on the labelling of medicines authorised before this change.

■ Joint HMA/EMA taskforce on big data

The establishment of a Joint HMA/EMA taskforce on big data to explore how medicines regulators in the EEA can use big data to support research, innovation and robust medicines development in order to benefit human and animal health has been announced on the EMA website and the HMA website.

Thomas Senderovitz's Director General, Danish Medicines Agency had discussed the creation of this taskforce at AESGP's Conference with the Heads of EU Medicines Agencies (HMA) during the Maltese EU Council Presidency.

The term big data refers to extremely large sets of information which require specialised computational tools to enable their analysis and exploitation. These data might come from electronic health records from millions of patients, genomics, social media, clinical trials or spontaneous adverse reaction reports, to name just a few. The vast volume of data has the potential to contribute significantly to the way the benefits and risks of medicines are assessed over their entire lifecycle.

While creating huge opportunities, it is recognised there are also significant challenges in the use of these data. For example, there is a fundamental need to establish appropriate access to the data, to understand their strengths and limitations and to apply new analytical methods to integrate and analyse the heterogeneous datasets in order to generate conclusions which contribute to regulatory decision making. Importantly, compliance with data protection legislation, ensuring robust mechanisms to protect patient confidentiality is critical for securing patient trust. It is therefore important for EMA and HMA to gather information on the latest developments in the field of big data from the perspective of different stakeholders. This will begin to clarify how and when the multitude of data sources may contribute to medicinal product development, authorisation and surveillance.

The task force, chaired by Thomas Senderovitz, Danish Medicines Agency and co-chaired by Alison Cave, EMA, is composed of representatives from medicines regulatory agencies in the EEA. Their efforts will be complemented on an ad hoc basis by external experts in big data collection analysis.

The mandate of joint HMA/EMA Task Force on Big Data is to explore a number of issues regarding the emerging challenges presented by big data. The group has agreed a number of actions for the next 18 months. These include:

- mapping sources and characteristics of big data;
- exploring the potential applicability and impact of big data on medicines regulation and developing recommendations on necessary changes to legislation, regulatory guidelines or data security provisions;
- creation of a roadmap for the development of big data capabilities for the evaluation of applications for marketing authorisations or clinical trials in the national competent authorities;
- collaboration with other regulatory authorities and partners outside the EEA (FDA, Health Canada and other third country stakeholders, including ICMRA) to ensure bilateral insights on big data initiatives

■ Updated version of the EU eSubmission Roadmap v.2.0

An updated version of the EU eSubmission Roadmap v.2.0 has been approved by the the EU Telematics Management Board (EUTMB) and endorsed by the HMA.

The eSubmission Roadmap aims at establishing secure, consistent and efficient electronic submission processes for medicinal products for human and veterinary use across the European Medicines Regulatory Network (ERMN or "the Network"). Although electronic submission of applications within the Network has increased, the use of non-standard electronic submission formats, including NeeS, are still largely used as an alternative format for the submission of applications for medicinal products for human use.

A number of initiatives have been undertaken to enable and improve the added value of eSubmission within the Network. For instance, EMA has required mandatory eCTD for applications of Centrally Authorised Products (CAP) for human use from 2010, the Network developed structured electronic Application Forms (eAFs) and HMA set up a Common European Submission

Platform (CESP). However, the increase of regulatory requirements throughout the product lifecycle, introduced by legislation has put the Network under strain and interoperability of systems has become the key for efficient use of data and resources. There was a need for the Network to establish a clear roadmap that would enable pharmaceutical industry and regulatory authorities to plan for the necessary investments and organisational changes to cope with the increasing regulatory workload and the electronic processes resulting from the implementation of the eSubmission Roadmap.
Implementations listed in the eSubmission Roadmap utilise new technical opportunities to enable and facilitate new ways of collaborative business processes and the re-use of data throughout the medicinal product lifecycle. These measures will lead to improved efficiency, less administrative burden and increased transparency through sustainable, fully end to end, electronic processing of information, and the elimination of paper and physical electronic media. The eSubmission Roadmap is a high level strategic plan for business and technology change, typically operating across multiple disciplines over several years. It is a tool to align the plans of target groups and help National Competent Authorities (NCAs), EMA and pharmaceutical industry to prepare themselves to forthcoming changes. It clarifies objectives and activities to reach them. It sets a common timeline for development; and helps supporting strategic decisions and resource provisions behind implementation for the achievement of the eSubmission objectives. It is also incorporated into the EU Telematics Strategy.

The Roadmap has been updated to reflect achieved milestones and to include new and amended timelines for implementation of various telematics systems/standards.
The main updates compared to version 1.0 are as follows:

- **eCTD v4.0**
  A new timeline has been added for planning and preparation. The timeline for optional use was postponed and a caveat has been added explaining that the implementation timelines will be confirmed based on the outcome of the planning and preparation phase.

- **eCTD v.3.2 (current version)**
  New milestones were introduced for mandatory use in national procedures (NP); Q3 2018 for new MAA and Q1 2019 for all submissions

- **eSubmission Gateway, CESP, eAF and CESSP**
  The delivery of the mandatory, fully integrated, single submission portal has been postponed. Timeline has been added to introduce a stepwise replacement of the eAF by CESSP.

  A section on SPOR (Substance, Product, Organisation, Referential) has also been included in the Roadmap, reflecting the major role SPOR will play in the use and re-use of master data in eSubmission systems. Other changes and updates not affecting the timelines have been added to the eSubmission Roadmap and a number of editorial changes have also been made.

A visual representation of the milestones is available here and information on the main changes can be found in the release notes.

Further information is also available on the EMA website eSubmissions section.

■ EP plenary adopts mercury regulation

Following the interinstitutional trialogue negotiations reached by the Commission, Council and Parliament on 14 December 2016, endorsement by Coreper on 16 December 2016 and by the ENVI Committee on 12 January 2017, the text on the proposal for a regulation of the European Parliament and of the Council on mercury, and repealing Regulation (EC) No 1102/2008 [COM (2016)0039 - C8-0021/2016 - 2016/0023(COD)] was submitted for a first/single reading vote in the March 2017 plenary session.

The European Parliament legislative resolution of 14 March 2017 on the proposal for a regulation of the European Parliament and of the Council on mercury, and repealing Regulation (EC) No 1102/2008 (COM(2016) 0039 – C8-0021/2016 – 2016/0023(COD)) and the consolidated text of the position of the European Parliament adopted at first reading on 14 March 2017 with a view to the adoption of Regulation (EU) 2017/... of the European Parliament and of the Council on mercury, and repealing Regulation (EC) No 1102/2008 was approved with 663 votes to 8 and 28 abstentions.

The legislation will replace the 2008 Mercury Export Ban Regulation, while incorporating its provisions. It also restricts mercury imports, bans its use in artisanal and small-scale gold mining, and phases out its use in manufacturing processes such as the chlor-alkali industry. The legislation also aims to phase out the use of mercury in dental amalgam by 2030, and limits the maximum permitted period for temporary storage of waste mercury to five years, with a possible extension of three years. The European Commission will have to produce an inventory of contaminated sites within three years, based on the data provided by member states.

****

The debate proceeding the vote, was opened by Stefan Eck, rapporteur, on behalf of the Committee on the Environment, Public Health and Food Safety, who expressed his disappointment that the compromise that came about after the second trialogue is lacking in the ambitious positions that the draft report contained after the vote in the environmental committee. He would have liked to go to a third round of negotiations to defend the position of Parliament. He regrets that during the negotiations on the crucial issues, he did not receive the necessary support from the majority of the shadow rapporteurs.

Věra Jourová (Member of the Commission) expects that ratification by the EU and those Member States that have completed their required national procedures will take place before the end of June. She also draws attention to two statements by the Commission. The first one signals the Commission's continued engagement at international level, which will aim at further narrowing the remaining gaps between the level of protection guaranteed by the Minamata Convention and the stricter requirements that prevail in the EU. The Commission's second statement concerns the so-called 'no opinion clause' in comitology.

1. Commission statement on international cooperation on mercury

The Minamata convention and the new Mercury Regulation are major contributions to protecting citizens from mercury pollution globally and in the EU. International cooperation should be sustained to ensure successful implementation of the Convention by all Parties and further strengthen its provisions. The European Commission is therefore committed to supporting continued cooperation, in accordance with the Convention and subject to applicable EU policies, rules and procedures, inter alia undertaking work in the following areas:

- Narrowing the gap between EU law and the provisions of the Convention through the review clause of the list of prohibited mercury-added products;

- In the context of the provisions of the Convention on financing, capacity building and technology transfer, activities such as improving traceability of mercury trade and use, promoting certification of mercury-free artisanal and small-scale gold mining and mercury-free labels for gold, and increasing the capacity of developing countries including in the area of mercury waste management.

2/ Commission statement on comitology

The Commission underlines that it is contrary to the letter and to the spirit of Regulation 182/2011 (OJ L 55 of 28.2.2011, p. 13) to invoke Article 5 § 4, subparagraph 2, point b) in a systematic manner. Recourse to this provision must respond to a specific need to depart from the rule of principle which is that the Commission may adopt a draft implementing act when no opinion is delivered. Given that it is an exception to the general rule established by Article 5 § 4 recourse to subparagraph 2, point b), cannot be simply seen as a "discretionary power" of the Legislator, but must be interpreted in a restrictive manner and thus must be justified.

The following also spoke:

Michel Dantin, on behalf of the PPE Group, Massimo Paolucci, on behalf of the S&D Group, Julie Girling, on behalf of the ECR Group, Anneli Jäätteenmäki, on behalf of the ALDE Group, Merja Kyllönen, on behalf of the GUE/NGL Group, Bas Eickhout, on behalf of the Verts/ALE Group, Piernicola Pedicini, on behalf of the EFDD Group, Mireille D'Ornano, on behalf of the ENF Group, Peter Liese (PPE), Pavel Poc (S & D), Bolesław G. Piecha (ECR), Gesine Meissner (ALDE), João Ferreira (GUE / NGL), Julia Reid (EFDD), Pilar Ayuso (PPE), Susanne Melior (S&D), Norbert Lins (PPE), who also replied to a blue-card question (*) by Tibor Szanyi, Christel Schaldemose (S&D) and Jiří Pospíšil (PPE).

The following spoke under the catch-the-eye procedure (*): Eleftherios Synadinos (NI), Igor Šoltes (Verts / ALE), Ivan Jakovčić (ALDE), Doru-Claudian Frunzulică (S&D), Notis Marias (ECR) and Nicola Caputo (S&D).

(*) *MEPs can hold up a blue card to indicate they would like to ask a question to another MEP holding a speech. If both the speaker and the President agree, then the Member will have half a minute to pose the question.*

(*) *In a typical debate, expect first to hear from the rapporteur (if the debate concerns a report from a committee), from Commission and Council representatives and from a round of representatives from all the political groups (plus a non-attached member). Subsequently, other interested members from across the House will intervene. Part of the debate speakers are selected on the "catch-the-eye" principle, whereby the President selects Members in the Chamber indicating the wish to speak. If this is the case, then the Member will have up to a minute to do a short speech. Normally the agenda sets aside five minutes for catch-the-eye, but President can choose to either shorten or extend this period.*

The following provisions from the consolidated text are worth noting:

(12) The mercury export ban laid down in Regulation (EC) No 1102/2008 should be complemented by restrictions on the import of mercury which vary depending on the source, the intended use and the place of origin of the mercury. Regulation (EC) No 1013/2006 of the European Parliament and of the Council [(5)] should continue to apply as regards imports of mercury waste, particularly as regards the powers of the competent authorities under that Regulation.

(21) The use of mercury in dental amalgam is the largest use of mercury in the Union and a significant source of pollution. The use of dental amalgam should therefore be phased down in accordance with the Convention and with national plans based in particular upon the measures listed in Part II of Annex A to the Convention. The Commission should assess and report on the feasibility of a phase out of the use of dental amalgam in the long term, and preferably by 2030, taking into account the national plans required by this Regulation and whilst fully respecting Member States' competence for the organisation and delivery of health services and medical care. Furthermore, particular preventive health protection measures should be taken for vulnerable members of the population, such as children and pregnant or breastfeeding women.

(22) Only pre-dosed encapsulated dental amalgam should be allowed for use and the use of amalgam separators in dental facilities in which dental amalgam is used or dental amalgam fillings or teeth containing such fillings are removed should be made mandatory, in order to protect dental practitioners and patients from mercury exposure and to ensure that the resulting waste is collected and disposed of in accordance with sound waste management and under no circumstances released into the environment. In this respect, the use of mercury in bulk form by dental practitioners should be prohibited. Amalgam capsules such as those described in European standards EN ISO 13897:2004 and EN ISO 24234:2015 are considered to be suitable for use by dental practitioners. Furthermore, a minimum level of retention efficiency for amalgam separators should be set. Compliance of amalgam separators should be based on relevant standards, such as European standard EN ISO 11143:2008. Given the size of economic operators in the dentistry sector affected by the introduction of those requirements, it is appropriate to provide sufficient time to adapt to the new requirements.

(30) In order to ensure uniform conditions for the implementation of this Regulation with regard to specifying forms for import and export, setting out technical requirements for the environmentally sound interim storage of mercury, mercury compounds and mixtures of mercury, prohibiting or allowing new mercury-added products and new manufacturing processes involving the use of mercury or mercury compounds and specifying reporting obligations, implementing powers should be conferred on the Commission. Those powers should be exercised in accordance with Regulation (EU) No 182/2011 of the European Parliament and of the Council [(13)] .

(33) In order to allow for the competent authorities of the Member States and the economic operators affected by this Regulation sufficient time to adapt to the new regime laid down by this Regulation, it should apply from 1 January 2018.

■ Draft European Union herbal monograph on Ribes nigrum L., folium (Blackcurrant leaf)

Further to its endorsement at the EMA Committee on Herbal Medicinal Products (HMPC) January 2017 meeting, the EMA has released the Draft European Union herbal monograph on Ribes nigrum L., folium for consultation.

The draft assessment report and draft list of references supporting the assessment of *Ribes nigrum L., folium* have also been published.

Members should send their comments on this draft monograph (and assessment report) by 10 May 2017.

Draft public statement on Glycine max (L.) Merr., semen (Soya-bean)

A Draft public statement on Glycine max (L.) Merr., semen which was adopted by the HMPC at their meeting on 30-31 January 2017, is now open for public consultation.

The HMPC/MLWP concluded that the following requirements for the establishment of a European Union herbal monograph on traditional or well-established herbal medicinal products containing *Glycine max (L.) Merr., semen* are not fulfilled:

- Well-established use marketing authorisation: the requirement laid down in Article 10a of Directive 2001/83/EC that the active substance has a recognised efficacy
- Traditional use registration: the requirement laid down in Article 16a(1) of Directive 2001/83/EC that the herbal substance has been used for at least 30 years, including at least 15 years within the EU

During the assessment of Glycine max (L.) Merr., semen, HMPC noted that it would be more appropriate to develop a separate monograph on soya lecithin (*Lecithinum ex soya*) and a separate monograph on soya oil (*Soiae oleum raffinatum*). Hence, this public statement excludes these herbal preparations.

The draft assessment report and draft list of references supporting the assessment of *Glycine max (L.) Merr., semen* have also been published.

Members should send their comments on this draft statement by 10 May 2017 using this template.

■ Draft public statement on Glycine max (L.) Merr., semen (Soya-bean)

A Draft public statement on Glycine max (L.) Merr., semen which was adopted by the HMPC at their meeting on 30-31 January 2017, is now open for public consultation.

The HMPC/MLWP concluded that the following requirements for the establishment of a European Union herbal monograph on traditional or well-established herbal medicinal products containing *Glycine max (L.) Merr., semen* are not fulfilled:

- Well-established use marketing authorisation: the requirement laid down in Article 10a of Directive 2001/83/EC that the active substance has a recognised efficacy
- Traditional use registration: the requirement laid down in Article 16a(1) of Directive 2001/83/EC that the herbal substance has been used for at least 30 years, including at least 15 years within the EU

During the assessment of Glycine max (L.) Merr., semen, HMPC noted that it would be more appropriate to develop a separate monograph on soya lecithin (*Lecithinum ex soya*) and a separate monograph on soya oil (*Soiae oleum raffinatum*). Hence, this public statement excludes these herbal preparations.

The draft assessment report and draft list of references supporting the assessment of *Glycine max (L.) Merr., semen* have also been published.

Members should send their comments on this draft statement by 10 May 2017 using this template.

Food

Health claims

- EFSA opinion on Stablor® and decrease in visceral fat while preserving lean mass

The EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA) published an opinion on the scientific substantiation of the Article 13(5) health claim related to Stablor® and decrease in visceral fat while preserving lean mass.

The Panel concludes that a cause and effect relationship has not been established between the consumption of Stablor® and reduction of visceral fat while maintaining lean body mass in the context of an energy restricted diet.

The Panel considers that Stablor®, a drink preparation with defined macro- and micronutrient composition and specific proportion of amino acids (tryptophan to neutral amino acids ratio), is sufficiently characterised.

The claimed effect proposed by the applicant is 'decrease in visceral fat while preserving lean mass'. The target population proposed by the applicant is 'overweight or obese subjects with abdominal fat and cardio metabolic risk factors'. The Panel considers that reduction of visceral fat while maintaining lean body mass in the context of an energy restricted diet is a beneficial physiological effect in the target population. Four human studies were considered by the applicant as pertinent to the claimed effect. The Panel considers that no conclusions can be drawn from three uncontrolled studies for the scientific evaluation of the claim. The Panel notes that one human intervention study does not show an effect of Stablor® on the primary outcome (reduction of visceral fat) in the primary (full analysis set (FAS)) analysis and that the per protocol (PP) analysis for the primary outcome is at risk of bias.

In the absence of evidence for an effect of Stablor® on reduction of visceral fat while maintaining lean body mass in efficacy studies in humans, the studies on the proposed mechanisms of action were not considered by the Panel for the scientific substantiation of the claim.

In weighing the evidence, the Panel took into account that one human study from which conclusions could be drawn for scientific substantiation of the claimed effect did not show an effect of Stablor® on reduction of visceral fat while maintaining lean body mass in the context of an energy restricted diet.

- EFSA to assess the safety of monacolins in red yeast rice

EFSA has accepted the Commission's request for a scientific opinion on the safety of monacolins in red yeast rice (EFSA-Q-2017-00138).

The Commission on its own initiative has initiated the procedure under Article 8 of Regulation (EC) No 1925/2006 for the intake of monacolins derived from red yeast rice as concerns have been raised by the Member States regarding a potential risk to consumers linked with the consumption of red yeast rice during discussions on the possible authorization of health claims related to monacolin K from red yeast rice. In accordance with Article 8(2) of Regulation (EC) No 1925/2006, the Commission has requested EFSA to provide a scientific opinion on the safety in use of monacolins derived from red yeast rice.

EFSA is also requested to provide advice on a dietary intake of monacolins from red yeast rice that does not give rise to concerns about harmful effects to health, for the general population, and as appropriate, for vulnerable subgroups of the population, including amongst others, pregnant women and children.

EFSA scientific opinion is to be delivered by 17 February 2018.

- Caffeine claims - Italian recommendations restricting their use

The Italian Ministry of Health has issued on 22 February a note restricting the use of caffeine claims for safety reasons.

i

The draft Regulation authorizing the following four health claims on caffeine (with specific conditions/restrictions of use) was rejected by the European Parliament last year:

- Caffeine contributes to an increase in endurance performance (only for foods targeting adults performing endurance exercise)
- Caffeine contributes to an increase in endurance capacity, (only for foods targeting adults performing endurance exercise)
- Caffeine helps to increase alertness (forbidden on foods targeting children).
- Caffeine helps to improve concentration (forbidden on foods targeting children).

Although the draft text was rejected by the Parliament, the caffeine claims covered by the draft are not rejected and therefore remain 'on hold'.

Health claims put 'on hold' can still be used until a Regulation is adopted that will accept or reject them, subject to the transition measures in Article (28)(5) of the Nutrition & Health Claims Regulation 1924/2006 (NHCR). This is commonly interpreted as meaning that they must comply with Articles 3,5,6,7 & 10 of the Regulation as well as other relevant national legislation.

According to this note from the Italian authorities, the following restrictions will apply in Italy:

- The intake of caffeine via food supplements should not exceed 200 mg/ day based on EFSA opinion of May 2015.
- The consumption of food supplements containing caffeine should not be recommended for children, pregnant women nor lactating women. The restriction should appear on the label of the products.
- The two caffeine claims on alertness and concentration can continue to be made. The labels of the products bearing the claims should however indicate that intake of caffeine from all sources should not exceed a daily intake of 400 mg.
- Claims related to endurance performance and capacity are not permitted in Italy. The reason for this is that the proposed conditions of use (3 mg/kg bw) would result in exceeding the maximum intake of 200mg /day for a person > 67 kg.

EFSA

- Public consultation on 2 draft guidance documents - the weight of evidence approach & biological relevance of observed effects

EFSA has launched a public consultation on two draft guidance documents – on the weight of evidence approach and biological relevance of observed effects –. These documents, together with the guidance on uncertainty assessment (see email below), will help to further harmonise methodologies across all the areas under EFSA's remit.

Draft Guidance for the identification of biological relevance of adverse/ positive health effects from experimental animal and human studies

EFSA's Scientific Committee has developed a draft guidance document providing generic issues and criteria to consider biological relevance, particularly when deciding on whether an observed effect is of biological relevance, i.e. is adverse (or shows a positive health effect) or not. The opinion clarifies a number of definitions and concepts, such as, responses of a biological system to exposure, mode of action and adverse outcome pathways, thresholds, critical effect, modelling approaches, biomarkers, which are central to biological relevance and in order to achieve that these concepts are used in a consistent way across EFSA areas of activity. Several case studies covering the various EFSA areas are referred to in the guidance and annexed to the opinion to illustrate the proposed approach.

Draft Guidance on The Use of the Weight of Evidence Approach in Scientific Assessments

EFSA's Scientific Committee has developed a draft guidance document on the use of the weight of evidence approach in scientific assessments for use in all areas under EFSA's remit. The guidance document addresses the use of the weight of evidence in scientific assessments using both qualitative and quantitative approaches. The guidance proposes a three-step approach for assembling, weighing and integrating evidence and defines reliability, relevance and consistency, in terms of their contributions to a weight of evidence assessment. Several case studies covering the various areas under EFSA's remit are annexed to the guidance document to illustrate the applicability of the proposed approach.

Written comments on these documents might be submitted to EFSA via the following links by 1st May 2017:

- Comments on draft Guidance on biological relevance of observed effects
- Comments on draft Guidance on the weight of evidence approach

AESGP members wishing to submit comments to these documents via AESGP, should submit them in line with the EFSA format (referring to the specific chapter/ section and line number of the text) by 12 April 2017.

Food additives

■ EFSA opinion on the re-evaluation of guar gum (E 412) as a food additive

EFSA published its scientific opinion on the re-evaluation of guar gum (E 412) as a food additive.

The Panel concluded that:

- there is no need for a numerical ADI for guar gum (E 412), and that there is no safety concern for the general population at the refined exposure assessment for the reported uses of guar gum (E 412) as a food additive. The Panel considered that for uses of guar gum in foods intended for infants and young children the occurrence of abdominal discomfort should be monitored and if this effect is observed doses should be identified as a basis for further risk assessment.

- the available data do not allow an adequate assessment of the safety of guar gum (E 412) in infants and young children consuming the foods for special medical purposes and special formulae.

i

Guar gum (E 412) is authorised according to Annex II of the Food Additives Regulation 1333/2008 as part of Group I in Food Supplements (Category 17) in all forms at *quantum satis* level with the following restriction in Food supplements supplied in a solid form (17.1): *E 412 may not be used to produce dehydrated foods intended to rehydrate on ingestion*

Regarding the general population, according to the conceptual framework for the risk assessment of certain food additives re-evaluated under Commission Regulation (EU) No 257/2010 (EFSA ANS Panel, 2014) and given that:

- adequate exposure data were available; in the general population, the highest refined exposure assessments calculated based on the reported data from the food industry were for infants (12 weeks–11 months) up to 812 mg/kg bw per day (brand-loyal scenario),•guar gum is practically undigested, not absorbed intact, but significantly fermented by enteric bacteria in humans,
- adequate toxicity data were available,

- no adverse effects were reported in sub chronic studies in rodents at the highest dose tested of15,000 mg guar gum/kg bw per day in mice and 18,000 mg guar gum/kg bw per day in rats,
- there is no concern with respect to the genotoxicity of guar gum,
- no carcinogenic effects were reported at the highest dose tested of 7,500 mg guar gum/kg bw per day in mice and 2,50 0 mg guar gum/kg bw per day in rats;
- oral intake of large amount of guar gum in (9,000–30,000 mg/person corresponding to 128–429 mg/kg bw per day) was well tolerated in adults. In most studies after consumption of around 15,000 mg per day in adults corresponding to 214 mg/kg bw per day, some individuals experienced abdominal discomfort which was considered by the Panel as undesirable but not adverse,
- in one interventional study with diabetic children abdominal discomfort was reported in 5 out of 22 children given 13,500 mg guar gum per day corresponding to 314 mg/kg bw per day,
- using the refined exposure assessment (non-brand-loyal scenario), the Panel noted that exposures for high level consumers (children and adults) would be below the level at which some abdominal discomfort was reported,
- no data on abdominal discomfort were available for infants and young children,

Concerning the use of guar gum (E 412) in 'dietary foods for special medical purposes and special formulae for infants' (Food category 13.1.5.1) and 'in dietary foods for babies and young children for special medical purposes as defined in Directive 1999/21/EC' (Food category 13.1.5.2), and given that:

- for populations consuming dietary foods for special medical purposes and special formulae, the highest refined exposure estimate (p95) calculated based on the reported data from the food industry are for infants (12 weeks-11 months) consuming dietary foods for special medical purposes and special formulae up to 1,555 mg/kg bw per day (brand-loyal scenario),
- infants and young children consuming these foods may be exposed to a greater extent to guar gum (E 412) than their healthy counterparts because the permitted levels of guar gum (E 412) in products for special medical purposes are 10-fold higher than in infant formulae and follow-on formulae for heal thy individuals,
- infants and young children consuming foods belonging to these food categories may show a higher susceptibility to the gastrointestinal effects of guar gum than their healthy counterparts due to their underlying medical condition,
- no adequate specific studies addressing the safety of use of guar gum (E 412) in this population under certain medical conditions were available,
- it was not possible to assess at which exposure level of guar gum the gastrointestinal effects developed in this specific population,

The Panel recommended that:

- the maximum limits for the impurities of toxic elements (lead, mercury and arsenic) in the EC specification for guar gum (E 412) should be revised in order to ensure that guar gum (E 412) as a food additive will not be a significant source of exposure to those toxic elements in food in particular for infants and children. The Panel noted that currently detected levels of these toxic elements were orders of magnitude below those defined in the EU specifications and therefore the current limits could be lowered.
- to harmonise the microbiological specifications in the EU Regulation for polysaccharidic thickening agents, such as gums, and to include criteria for the absence of Salmonella spp. and E. coli, for TAMC and for TYMC into the EU specifications of guar gum (E 412).
- to give separate specifications in the EU regulation for guar gum and clarified guar gum differing significantly in the protein content.
- The Panel considered that no threshold dose can be established for allergic reactions. Therefore, it is advisable that exposure to eliciting allergens, such as proteinaceous compounds, is avoided as much as possible, and therefore, the Panel recommended that their content should be reduced as much as possible, which can be achieved for example by clarification of guar gum.
- additional data should be generated to assess the potential health effects of guar gum (E 412) when used in 'dietary foods for infants for special medical purposes and special formulae for infants' (Food category 13.1.5.1) and in 'dietary foods for babies and young children for special medical purposes' as defined in Directive 1999/21/EC (Food category 13.1.5.2).

■ Amendment to specifications for Basic methacrylate copolymer (E 1205) published

Commission Regulation (EU) 2017/324 of 24 February 2017 amending the Annex to Regulation (EU) No 231/2012 laying down specifications for food additives listed in Annexes II and III to Regulation (EC) No 1333/2008 of the European Parliament and of the Council as regards specifications for Basic methacrylate copolymer (E 1205) has recently been published.

The entries for the definition and particle size for food additive Basic methacrylate copolymer (E1205) in the Annex to Regulation (EU) No 231/2012 are amended so as to reflect the requested changes.

i

E 1205 is authorised for use as a glazing agent/coating agent in solid food supplements (category 17.1) up to maximum 100000 mg/kg per the Food Additives Regulation.
The applicant has requested the definition of the food additive to be amended with regard to the short description of the manufacturing process due to a modernization of the manufacturing process. Following a thorough review of the particle size in the current specification, the applicant has requested a change in the particle size of the powder. Based on the data provided by the applicant and taking into account the original evaluation of the substance in 2010, EFSA concluded in its opinion that the proposed amendments to the specifications of the food additive Basic methacrylate copolymer (E 1205) are not of a safety concern.

■ Titanium dioxide re-evaluation - List of interested business operators

The European Commission has published the List of interested business operators who responded to the call for scientific and technical data.

Importantly, two operators including the Titanium Dioxide Manufacturers Association expressed their interest in submitting the requested toxicological data and the data related to the specifications.

This list is only intended to facilitate interactions among the operators interested to submit data and possible coordination in the data submission. AESGP will keep monitoring the follow-up process for this additive.

Next step: The operators listed are now to confirm the submission of the required data and to determine deadlines and milestones for such submission by 30 July 2017.

■ EFSA opinion on the re-evaluation of soybean hemicellulose (E 426)

The Panel concluded that it is very unlikely that there is a safety concern from the current use of soybean hemicellulose (E 426) as a food additive for the general population, and that there is no need for a numerical ADI.

i

Soybean hemicellulose (E 426) is authorised according to Annex II of the Food Additives Regulation 1333/2008 in Food Supplements (Category 17) in all forms up to 1500 mg/kg or mg/l as appropriate.

Following the conceptual framework (EFSA ANS Panel, 2014) for the risk assessment of certain food additives re-evaluated under Commission Regulation (EU) No 257/2010, and given that:

- soybean hemicellulose is not absorbed intact, but is extensively fermented by the intestinal microflora in animals and humans to SCFA;
- no adverse effects were reported in an adequate dietary 90-day study in rats at the highest dose tested of 2,430 mg/kg bw per day for males and 2,910 mg/kg bw per day for females;
- soybean hemicellulose is not of genotoxic concern;
- the highest exposure estimates, calculated based on the MPLs to be up to 191 mg/kg bw per day for children (95th percentile), are very conservative;
- no uses were reported by industry and only one food product containing soybean hemicellulose (E 426) was found in the Mintel GNPD

The Panel recommended that:

- Due to the absence of information provided by the industry on the usage of E 426 and only a single food product containing soybean hemicellulose (E 426) reported in the Mintel GNPD database, the collection of data on usage and use levels of soybean hemicellulose(E 426) in order to perform a more realistic exposure assessment.
- the maximum limits for the impurities of toxic elements (arsenic, lead, mercury and cadmium) in the EU specifications for soybean hemicellulose (E 426) should be revised in order to ensure that soybean hemicellulose (E 426) as a food additive will not be a significant source of exposure to those toxic elements in food.
- that the amount of residual proteins in soybean hemicellulose (E 426) should be reduced as much as possible, and that the consumers should be informed of the presence of allergenic proteins in the food additive E 426.

■ Food Additives re-evaluation - E 200, E 202 and E 203 - Removal of calcium sorbate (E 203)

A Draft Commission Regulation amending Annexes II and III to Regulation (EC) No 1333/2008 of the European Parliament and of the Council and the Annex to Commission Regulation (EU) No 231/2012 as regards the removal of calcium sorbate (E 203) has been notified to other WTO members on 6 March 2017 under the Agreement on Technical Barriers to Trade (the TBT Agreement).

As anticipated, the proposed measure removes calcium sorbate (E 203) from the Union list of authorised food additives in Regulation (EC) No 1333/2008, since no business operator has committed to generating the requested genotoxicity data it is not possible to assess the risk posed by the use of this substance as a food additive to human health. Annexes II and III to Regulation (EC) No 1333/2008 (authorised uses and use levels for food additive) and the Annex to Regulation (EU) No 231/2012 (specifications for food additives) are amended accordingly.

The draft regulation is expected to be put to the vote of the Standing Committee on Plants, Animals, Food and Feed - Section Novel Food and Toxicological Safety of the Food Chain – in June 2017 and formally adopted (after the scrutiny period) in September 2017.

i

On 30 June 2015 EFSA delivered a Scientific Opinion on the reevaluation of sorbic acid (E 200), potassium sorbate (E 202) and calcium sorbate (E 203) as food additives. The opinion stated that there was a lack of genotoxicity data on calcium sorbate. Consequently EFSA was not able to confirm the safety of calcium sorbate as a food additive and concluded that this substance should be excluded from the group Acceptable Daily Intake (ADI) defined for sorbic acid (E 200) and potassium sorbate (E 202). On 10 June 2016 the European Commission launched a public call for genotoxicity data on calcium sorbate (E 203). However, by the closure date of the call (25 November 2016) no business operator committed to providing the requested data. Without those data EFSA cannot complete the re-evaluation of the safety of calcium sorbate as a food additive and consequently it cannot be determined whether this substance still fulfils the conditions pursuant to Article 6(1) of Regulation (EC) No 1333/2008 for inclusion in the Union list of approved food additives. It is therefore appropriate to remove calcium sorbate (E 203) from the Union list of approved food additives.

■ EFSA opinion on re-evaluation of glycerol (E 422) as a food additive

EFSA has just published its scientific opinion on the re-evaluation of glycerol (E 422) as a food additive.

The Panel concluded that:

- there is no need for a numerical ADI for glycerol (E 422).
- there is no safety concern regarding the use of glycerol (E 422) as a food additive according to Annex II and III (Part 1, 2, 3, 4 and 5) for the general population at the refined exposure assessment for the reported uses of glycerol as food additive.
- The Panel identified that there remain uncertainties over the lack of identification and quantification of residuals especially those that are genotoxic and carcinogenic. The Panel noted that these residuals are mostly present when chemical synthesis is used to produce glycerol.
  - the manufacturing process for glycerol should not allow the production of a food additive, which contains these residuals at a level which would result in a MOE below 10,000.
  - if 3-MCPD is present at its maximum authorised level of 0.1 mg 3-MCPD/kg glycerol, the maximum exposure to 3-MCPD was below the TDI of 0.8 lg/kg bw per day, and therefore exposure via glycerol (E 422) alone was of no concern.
  - The Panel could not calculate exposures to other genotoxic impurities or contaminants that may be present in glycerol (E 422) as a result of the manufacturing process, e.g. glycidol, due to the lack of data on their concentrations in the food additive.
- infants and toddlers could be exposed to more than 125 mg/kg bw perhour by drinking less than the volume of one can (330 mL) of a flavoured drink.
- the acute bolus exposure to glycerol (E 422) by its use as a food additive should stay below doses at which pharmacological or side effects could occur.

AESGP reported use levels submitted to EFSA on 29 November 2013 in response to the EFSA call for food additives usage level and/or concentration data in food and beverages (Batch 2) have been taken into account in EFSA exposure assessment.

i

Glycerol (E 422) is authorised according to Annex II of the Food Additives Regulation 1333/2008 as part of Group I in Food Supplements (Category 17) in all forms at *quantum satis* level.

According to the conceptual framework for the risk assessment of certain food additives re-evaluated under Commission Regulation (EU) No 257/2010 (EFSA ANS Panel, 2014) and given that:

- the safety assessment carried out by the Panel is limited to the use and use levels received from industry and Member States in 28 food categories out of 68 food categories in which glycerol (E 422) is authorised;
- the highest 95th percentile of exposure of glycerol (E 422) according to Annex II, carry-over (Annex III) and natural sources was estimated at 460 mg/kg bw per day in children in the refined non-brand-loyal exposure scenario;
- glycerol (E 422) as a food additive is identical to a compound which is a normal constituent in the body (an endogenous compound) and is a regular component of the diet;
- sufficient toxicity data were available;
- the toxicological studies in animals did not provide any indication for adverse effects, including at the highest dose tested in a chronic toxicity study (10,000 mg/kg bw per day);

The Panel recommended that:

- given that during the manufacturing processes of glycerol, genotoxic impurities – e.g. glycidol, epichlorohydrin – could be formed, limits for such impurities should be included in the EU specifications for glycerol (E 422);
- given that during the manufacturing processes of glycerol, other potential impurities of toxicological concern (e.g. dichlorohydrin) could be formed, limits for such impurities should be included in the EU specifications for glycerol (E 422);
- more data should be generated to decrease uncertainty arising from the presence in the food additive (E 422) of compounds of toxicological concern (e.g. acrolein, 3-MCPD or 3-MCPD ester), which can be produced under some food processing conditions (e.g. use of glycerol(E 422) in parallel with lactic acid bacteria; use of glycerol (E 422) in food containing significant amounts of sodium chloride (more than 5%) and treated at temperatures above160°C, etc.).
- a numerical limit for acrolein should be included in the EU specifications for glycerol (E 422);
- the maximum limits for the impurities of toxic elements (arsenic, lead, mercury and cadmium)in the EC specification for glycerol (E 422) should be revised in order to ensure that glycerol(E 422) as a food additive will not be a significant source of exposure to those toxic elements in food;
- more information on uses and use levels and analytical data should be made available to the Panel in order to perform an adequate exposure assessment, in particular in the case of estimate acute exposure, more data on flavoured drinks is needed.

■ AESGP to submit usage levels data to EFSA on Batch 6 – Update of the list of additives covered

The Batch 6 call for data has been updated to include the following food additives:

E 1200	Polydextrose
E 1201	Polyvinylpyrrolidone
E 1202	Polyvinylpolypyrrolidone

AESGP members interested in submission of data on the additives usage levels in food supplements are requested to fill in the EFSA template and send it to AESGP at the earliest convenience by 27 October 2017 in order to provide a timely submission to EFSA.

Novel Food

■ EFSA opinion on hydroxytyrosol

EFSA has just published its Scientific Opinion on the safety of hydroxytyrosol as a novel food (NF) pursuant to Regulation (EC) No 258/97.

The panel concludes that the novel food, hydroxytyrosol, is safe under the proposed uses and use levels.

The NF that is subject of this application is hydroxytyrosol, which is chemically synthesised. The information provided on the composition, specifications, batch-to-batch variability, stability and production process of the NF is sufficient and does not raise concerns about the safety of the NF.

The applicant intends to add hydroxytyrosol to fish and vegetable oils up to 215 mg/kg and to margarines up to 175 mg/kg.

The target group is the general population which excludes children under 36 months of age, pregnant women and breastfeeding women.

■ Authorisation of lactitol published

Commission Implementing Decision (EU) 2017/450 of 13 March 2017 authorising the placing on the market of lactitol as a novel food ingredient was published in the EU Official Journal on 15 March 2017.

Per this decision, lactitol as specified in the Annex to this Decision may be placed on the market in the Union as a novel food ingredient to be used in food supplements in capsule or tablet form intended for the adult population with a maximum dose of 20 g lactitol per day as recommended by the manufacturer.

This Decision is addressed to the applicant.

Medical devices

Medical Devices Regulation

■ ENVI Committee endorses Council's Position

On 21 March 2017, the ENVI Committee of the European Parliament (EP) has adopted a draft recommendation for second reading on the adoption of the Medical Devices Regulation.

As expected, the ENVI Committee has endorsed the Council's 1st reading position without amendment.

The Council's 1st reading position and ENVI committee's 2nd reading recommendation are now tabled for the next EP Plenary session scheduled on 4 April 2017. The expected next steps are:

- 4 April 2017: Early 2nd reading agreement by EP Plenary
- By end of April/early May 2017: Publication in EU Official Journal

■ AESGP participates in the European Commission/ CAMD meeting on the new Regulations

On 9 March 2017, AESGP participated in the meeting of the European Commission/Competent Authorities for Medical Devices (CAMD) meeting on the new Regulations on medical devices (MDR) and in-vitro diagnostic medical devices (IVDR).

As an introduction to the discussion, the Commission highlighted that every draft implementing/delegated acts called for by the MDR and IVDR will be subject to the 4-week public feedback procedure* and that, where an impact assessment is required, a 12 week public consultation will run. The Committee on Medical Devices will be the Committee responsible for the adoption of the implementing acts. The new Medical Devices Coordination Group (MDCG) in performing its various missions will consult stakeholders through its subgroups in similar format than the existing ones.

At this stage, the highest priorities identified by the Commission and where the work has already started for some time are the followings:

- NB designation and application
- Governance MDCG including subgroups
- Common specification on aesthetic devices and reprocessing devices
- EUDAMED and UDI system
- 12 months deadline to mandate SCHEER for guidelines on phthalates

In the first part of the discussion setting the scene from an industry standpoint, AESGP presented the key priorities & challenges specific to substance-based medical devices. Overall, the priorities and challenges identified by the industry representatives (MedTech Europe, COCIR and AESGP) presented many similarities showing common concerns.

In the second part of the meeting, the participants discussed the implementation priorities on the basis of a draft initial list of priorities. Importantly, the meeting was not intended to reach any agreement on the list of priorities for the smooth implementation of the new Regulations but rather to collect the comments from the stakeholders and make sure that the planning will reflect the needs of all stakeholders engaging in the new framework. The CAMD is expected to put out a roadmap to allow better identifying their priorities and creating an email box to collect further comments in the coming weeks.

■ Council adopts the Medical Devices Regulation

On 7 March 2017, the Council has adopted at unanimity the final version of the Medical Devices Regulation as its position at first reading.

While supporting the adoption of the text, the French authorities made a statement on three points: the transitional provisions, class IIb active MDs and the terms 'seriousness' and 'severity'. Regarding the transitional provisions, the French statement reads as follows:

We regret that the amendments made to the transitional provisions of the proposal for a Regulation on medical devices (Article 120) stop short of ruling out the possibility of extending the placing on the market of MDs covered by a certificate of conformity issued under the current Directives when their classification has changed under the Regulation. This had been proposed by some Member States during the discussions and would have meant that as soon as the risk classification of an MD changed, it would be required to undergo a new conformity assessment procedure before it could be placed on the market. We regret that the amendments made to the transitional provisions of the proposal for a Regulation on medical devices (Article 120) stop short of ruling out the possibility of extending the placing on the market of MDs covered by a certificate of conformity issued under the current Directives when their classification has changed under the Regulation. This had been proposed by some Member States during the discussions and would have meant that as soon as the risk classification of an MD changed, it would be required to undergo a new conformity assessment procedure before it could be placed on the market.

Cranberry products

■ AESGP submits comments on the draft Commission Implementing Decision

The Commission launched the 4-week 'feedback procedure'* on the Draft Commission Implementing Decision on the group of products whose principal intended action, depending on proanthocyanidins (PAC) present in cranberry (Vaccinium Macrocarpon), is to prevent or treat cystitis on 28 February 2017.

AESGP submitted detailed comments on this draft decision and urged the Commission together with Member States not to proceed with its adoption.

These comments being based on the arguments developed earlier by the AESGP Medical Devices Committee, they were submitted together with the following enclosures:

- AESGP comments related to the *CHMP scientific opinion on the principal mode of action of proanthocyanidins intended to be used for prevention and treatment of urinary tract infections* and
- the revised paper on the mechanism of action of cranberry-like products whose mode of action depends on PACs in preventing UTIs which have been sent to the Commission this morning.

All the feedback received (including AESGP's comments) is published on the Commission's dedicated webpage.

*Background on the feedback procedure: As part of its better regulation agenda, the Commission wants to listen more closely to the views of citizens and stakeholders. To do so, the Commission created a space where they can share their views on:

- roadmaps and inception impact assessments, which set out ideas for new laws and policies, or for evaluations of existing ones
- legislative proposals and accompanying impact assessments, once they have been agreed on by the Commission and put forward to the EU Parliament and Council

draft delegated and implementing acts, which either amend or supplement existing laws or, set the conditions for existing laws to be implemented in the same way across the EU

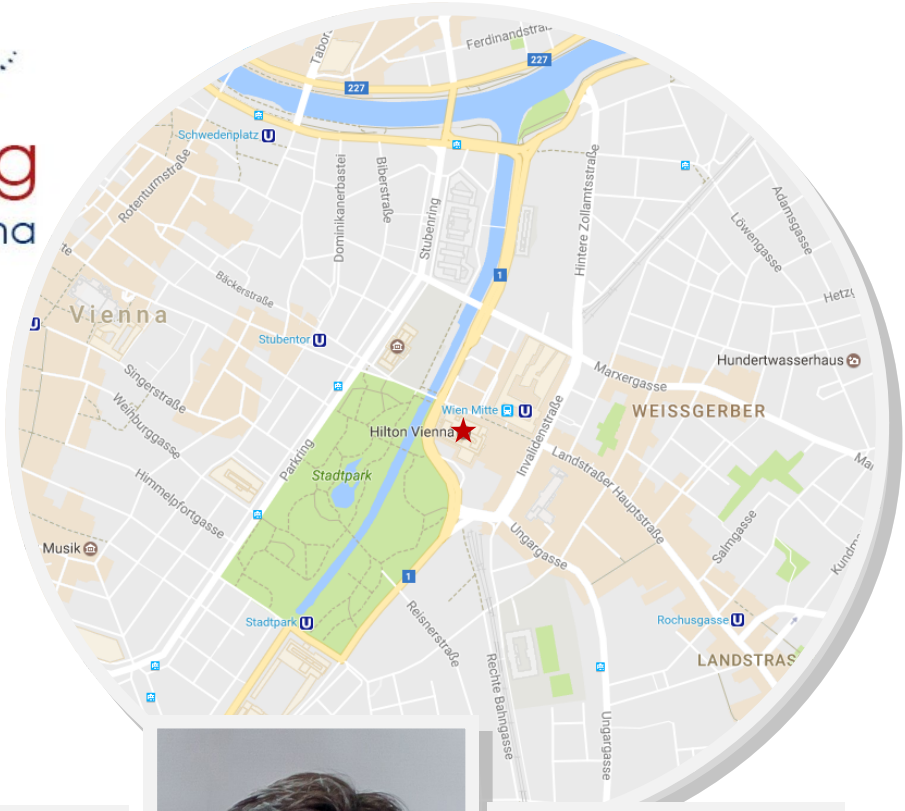
While the Commission will not provide an individual response, the feedback is expected to be taken into account by the Commission when further developing the act. An overview of the feedback gathered will be presented to the committee dealing with this act. A summary of the discussion will be included in the summary record, which is published in the comitology register.

53rd AESGP Annual Meeting

30 May – 1 June 2017, Vienna

Self-care in a changing world

Hilton Vienna Stadtpark



Speakers include:

Karl Broich

Nenad Pacek

Olaf Schwabe

Thomas Senderovitz

Max Wellan

Alexandra Nikolakopoulou

Max Orgeldinger

Lilian Azzopardi

Brian Ager

Andy Tisman

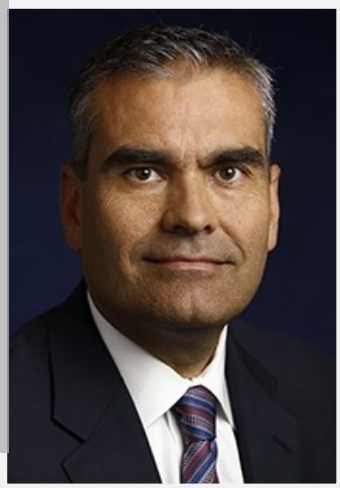
Bernhard Url

Ralph Ahrbeck

Birgit Schuhbauer

Briain de Buitleir

Laurent Faracci



Brian McNamara

Karl Pall

Chris Slager

Christa Wirthumer-Hoche

Dirk Ossenberg-Engels

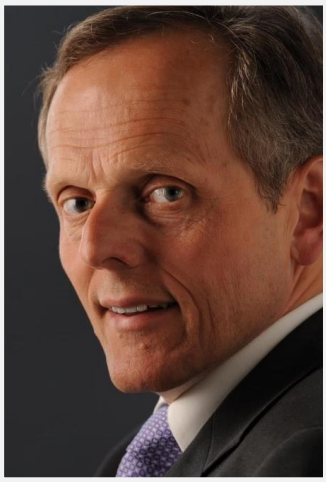
Fuad Sawaya

Gerhard Lötsch

Gesine Meissner

Guido Rasi

Helena Dalli



Hubertus Cranz

Ilaria Passarani

Jacques de Haller

Jaume Pey

Jurate Svarcaite

Karin Kadenbach

For detailed information on the meeting and registration:

aesgp.eu/53