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SME Office NEWSLETTER

Information for SMEs on the EU regulatory environment for medicines.
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IN THIS ISSUE

15-year anniversary of the SME Regulation

To mark the 15th anniversary of the implementation of the European Medicine Agency's (EMA's) SME regulation (Commission Regulation (EC) No 2049/2005), EMA held a virtual roundtable meeting with industry organisations, the European Commission (EC), the EU Agencies network and the European Investment Bank on 27 November 2020. Key achievements of the SME programme were discussed, as well as challenges and future opportunities to support SMEs and innovation in the pharmaceutical sector (Link to the event webpage, Link to the meeting report). The results of an SME survey launched by the Agency in 2020 were also presented. The report of the survey (Link) includes feedback on the implementation of the SME regulation, highlights challenges experienced by SMEs, and provides suggestions on how to expand services and incentives to SMEs.

UK withdrawal from the EU

The Withdrawal Agreement between the United Kingdom and the European Union (EU) which provided for a transition period ended on 31 December 2020. The protocol on Ireland/Northern Ireland forms an integral part of the withdrawal agreement and became applicable at the end of the transition period.

A revised question and answers document on the implementation of the Protocol was published (EMA/520875/2020). This document gives practical guidance on the applicable rules in Northern Ireland with respect to EMA activities and medicinal products for human and veterinary use within the framework of the centralised procedure.

A meeting with industry stakeholders was held virtually on 30 November 2020 to discuss the end of the transition period and to provide updates on the practical implementation of the Ireland / Northern Ireland Protocol (Link).

The EC has also published on 22 December 2020 a Commission notice on the application of the Union's pharmaceutical acquis in markets historically dependent on medicines supply from or through Great Britain after the end of the transition period (Commission notice C (2020)9264).

COVID-19

The first COVID-19 vaccines have been authorised by the EC: Comirnaty (news item ; press briefing) and Moderna Covid-19 vaccine (news item) .

On 11 December 2020, EMA organised a public meeting to inform European citizens about the EU regulatory processes for the approval of COVID-19 vaccines and the Agency's role in their development, evaluation, approval and safety monitoring (Link). EMA organised a second public meeting on 8 January 2021 to inform European citizens about the assessment, approval and roll-out of new COVID-19 vaccines (Link).

Latest news, guidance for companies (e.g. on research and development, assessment, marketing authorisation, pharmacovigilance), information on treatments and vaccines, medicines availability, public-health advice and transparency are regularly updated on EMA's dedicated webpage (Link).

Pharmaceutical strategy for Europe

On 25 November 2020, the EC adopted a 'Pharmaceutical strategy for Europe' (Link).The strategy is a key component of strengthening Europe's new Health Union (Link). It aims to improve and accelerate patients' access to safe and affordable medicines and support competitiveness, innovation and sustainability of the EU pharmaceutical industry. It will allow Europe to cover its pharmaceutical needs, including in times of crisis, through robust supply chains. Its implementation includes an agenda of legislative and non-legislative actions covering the full lifecycle of a medicine and will be launched over the coming years. More information on the strategy can be found in the dedicated press release (Link).

European Medicines Agencies Network strategy to 2025

The 'European medicines agencies network strategy to 2025' was published on 8 December 2020 and provides a roadmap for EMA and National Competent Authorities in developing their workplans for the next five years (Link). It was developed by EMA and the Heads of Medicines Agencies (HMA) and a stakeholder consultation was launched in July 2020 (analysis and summaries of the consultation can be found here). The strategy focuses on six key areas: availability and accessibility of medicines; data analytics, digital tools and digital transformation; innovation; antimicrobial resistance and other emerging health threats; supply chain challenges and sustainability of the network and operational excellence. It aligns with the broader Pharmaceutical Strategy for the EU developed by the EC (see above and Link). More information can be found in the dedicated press release (Link).

Big Data

The joint HMA/EMA Big Data Steering Group advises the EMA Management Board and HMA on prioritisation and planning of actions to implement the ten priority recommendations (Link) outlined in the Big data task force final report (Link). In September 2020, the group published its workplan which sets out actions to be delivered in 2020-21 (Link). The workplan aims to progress the evolution to data-driven regulation through actions including business case for DARWIN EU, study to analyse existing data quality initiatives, workshop on metadata, data discoverability roadmap, training curricula, transparency of observational research, rapid analytics of real-world data pilot, learnings and guidance development, analysis of patient level data pilots, methods expert advice, guidance on ethics/secondary use of healthcare data and data protection, standardisation roadmap and stakeholder fora. The work carried out by the Big Data Steering Group builds on the Regulatory Science Strategy to 2025 (Link) and supports the European Medicines Agencies Network Strategy to 2025 (see above and Link). More information can be found in a dedicated press release (Link).

IRIS

IRIS for scientific advice

Since 19 October 2020, EMA requires scientific advice (SA) applicants for human and veterinary medicines to use EMA's secure online regulatory and scientific information management platform, IRIS (Link). With the addition of SA, there are now four business processes on the IRIS platform (Orphan Designation, Parallel Distribution, Innovation Task Force, SA). IRIS provides a single space for applicants to submit and manage information and documents related to their applications. In September and October 2020, EMA delivered several online training sessions on IRIS that have been recorded and are available on the EMA website:

- session on IRIS registration and request of Research Product Identifier (Link);
- session on how to submit SA using IRIS for human products (Link);
- session on how to submit SA using IRIS for veterinary products (Link).

IRIS guidance (Link) and SA guidance (Human, veterinary, qualification of novel methodologies) have also been updated. More information on the launch of IRIS for SA can be found in the dedicated press release (Link).

IRIS stakeholder forum

EMA launched the IRIS stakeholder forum (Link), a public platform where users can stay up-to-date on the latest IRIS news, ask questions, provide suggestions, and discuss best practices related to working in IRIS.

Paediatric medicines

In December 2020, the EC and EMA published a progress report of the 2018 EMA/EC joint action plan on paediatrics to support the development of medicines for children in Europe (Link). It provides an update on the achievements in five key areas outlined in the 2018 action plan with the objective to increase the efficiency of paediatric regulatory processes in the current legal framework and to boost the availability of medicines for children.

Clinical Trial Regulation

The Clinical Trial Regulation (Regulation (EU) No 536/2014) harmonises the assessment and supervision processes for clinical trials throughout the EU, via a Clinical Trials Information System (CTIS). CTIS will contain the centralised EU portal and database for clinical trials foreseen by the Regulation and is being set up by EMA in collaboration with the Member States and the EC. The implementation of the Clinical Trial Regulation depends on the full functionality of CTIS that is now planned to go live in December 2021. More information can be found here and in the CTIS highlights which provides updates on the status of the project (Link). A training event on CTIS dedicated to SMEs and non-commercial sponsors will be organised in two parts on 22 February and on 4 March 2021. More information will be available on the events page shortly (Link).

European Medicines Regulatory Network's report on nitrosamines

The European Medicines Regulatory Network (Link) published a report in June 2020 on the lessons learnt from the presence of *N*-nitrosamines in sartan medicines (Link). It sets out a number of recommendations for strengthening the regulatory framework to reduce the potential of *N*-nitrosamines and other impurities in human medicines and to prepare the network in case similar cases occur in the future. An implementation plan giving a summary of the recommendations, responsibilities and implementation timelines has been published in October 2020 (EMA/503522/2020).

Veterinary products

Antimicrobials

The annual report from the European Surveillance of Veterinary Antimicrobial Consumption project (ESVAC) published by EMA shows that European countries continue to reduce the use of antibiotics in animals (Link). The overall sales of veterinary antibiotics in European countries dropped by more than 34% between 2011 and 2018. More information on the ESVAC project and its key achievements can be found here.

A draft concept paper on the reporting of antimicrobial sales and use in animals at EU level has been released for public consultation until 31 January 2021 (EMA/222040/2020). It aims to further develop standards for the reporting of veterinary antimicrobial sales and use data.

New Veterinary Medicines Regulation

The second issue of the Veterinary Medicines Regulation highlights (VMR) was published (Link). This new edition provides an update on the progress of the VMR implementation and other ongoing projects including the Union Product Database and the Union Pharmacovigilance database. More information can be found here.

Scientific guidelines

A VICH guideline on the stability data package for a new veterinary substance and medicinal product to be included in a registration application submitted within climatic zones III and IV regions came into effect on 1 November 2020 (EMA/CVMP/VICH/335918/2016). The document should be read in conjunction with the VICH parent stability guideline (VICH GL3 (R)).

CVMP guidance on the safe and efficient oral administration of veterinary medicinal products via routes other than medicated feed was published on 28 August 2020 (EMA/CVMP/508559/2019). It aims to ensure that consistent rules are applied for veterinary medicinal products administered orally, whether via medicated feed (i.e. under Regulation 2019/4) or via other oral routes of administration (i.e. under Regulation (EU) 2019/6).

Regulatory guidance

A revised list of biological substances considered as not requiring a maximum residue limits (MRL) evaluation as per Regulation (EU) No. 2018/782, with regard to residues of veterinary medicinal products in foodstuffs of animal origin was published on 10 December 2020 (EMA/CVMP/572629/2019–Rev.1). Additional information can be found in the dedicated section 'Biological substances not requiring an MRL evaluation' in the MRL webpage.

A revised list of substances considered as not falling within the scope of Regulation (EC) No. 470/2009 ('MRL regulation'), with regards to residues of veterinary medicinal products in foodstuffs of animal origin was published on 5 November 2020 (EMA/CVMP/519714/2009–Rev.47).

Procedural advice to applicants/marketing authorisation holders (MAHs) on re-examination of CVMP opinions was updated to clarify that a positive opinion may also be subject to re-examination (EMA/CVMP/321528/2017 – Rev.1).

Pre- and post-authorisation procedural Q&As have been updated on topics including submission of active substance master file (ASMF) and centralised procedure timetables (Q&A: 21-40).

The following Q&A have also been updated:

- Q&As on extension applications (timetables) (Link);
- Q&As on type II variations (timing of post-opinion changes implementation) (Link).

Scientific guidelines for human medicines

Preclinical and clinical guidelines

A reflection paper on the pharmaceutical development of medicines for use in older populations will come into effect on 1 May 2021 (EMA/CHMP/QWP/292439/2017). It applies to any new application for a marketing authorisation or variation thereof, and for all application types (full and abridged).

A revised draft guideline on the clinical evaluation of anticancer medicinal products has been released for consultation until 15 February 2021 (EMA/CHMP/205/95 Rev.6). The revision addresses the most recent designs in oncology (such as umbrella and basket trials, so-called master protocols) and the emergence of indications defined by a biomarker selective for a disease sensitive to the treatment. A new appendix providing an example of mock-up for section 4.8 of the summary of product characteristics for anticancer medicinal products has also been released for consultation (EMA/593364/2020).

A CHMP Q&A document on the role and need for a Data Monitoring Committee (DMC) in the different phases of drug development and the product lifecycle was adopted in September 2020 (EMA/CHMP/470185/2020). It supplements the CHMP Guideline on DMC (EMEA/CHMP/EWP/5872/03 Corr).

Patient Focused Drug Development

A reflection paper on a proposed ICH guideline to advance patient focused drug development has been released for public consultation until 7 March 2021 (Link). The paper identifies key areas where considering the patient's perspective could improve the quality, relevance, safety and efficiency of drug development and inform regulatory decision making. It also presents opportunities for new guidelines development to include patient's perspectives that are methodologically sound for industry and regulators.

Multi-disciplinary guideline

A revised guideline on quality, non-clinical and clinical aspects of medicinal products containing genetically modified cells will come into effect on 1 June 2021 (EMA/CAT/GTWP/671639/2008 Rev. 1). The revision reflects the experience gained with the approval of such products and incorporates guidance on genetically modified cells developed using novel technologies (e.g. CAR-T cells, induced pluripotent stem cells and genome editing). The clinical part has also been updated to clarify that controlled clinical trials should be the standard and that compelling clinical results should be presented to justify single arm trials.

The following Q&As have also been updated:

- Good manufacturing practice Q&As on topics including production and batch numbers (Link)
- Good clinical practices Q&As on Investigational Medicinal Product (IMP) manufacturer audit (Link).

Regulatory guidance

Article 58 procedure are now called EU-Medicines for all (EU-M4all). EMA has published a draft public guidance on parallel application for EU-M4all opinion and Centralised Marketing Authorisation procedure for public consultation until 15 February 2021 (EMA/589001/2020). The draft guidance describes the possibility to run the evaluation of centralised and EU-M4all applications in parallel and to obtain an EU-M4all Scientific Opinion and a Centralised Marketing Authorisation at about the same time. Stakeholders are invited to send their comments via an online form (Link). More information can be found in a dedicated infographic (Link) and in the EMA webpage (Link).

The following documents have been updated:

- Pre-authorisation guidance (EMA/821278/2015) on topics including applicant's EEA establishment, eligibility request, rapporteurs/co-rapporteurs appointment, marketing authorisation application submission, accelerated assessment eligibility, pre-submission meeting, ASMF submission and fees.

- Post-authorisation guidance (EMEA-H-19984/03 Rev. 87) on topics including submission of type IA and type IB variations, grouping and work-sharing of variations, post authorisation safety studies and post authorisation measures.

The following documents have also been updated:

- Q&As on labelling flexibilities for COVID-19 vaccines (EMA/689080/2020 rev.1);
- Procedural timetables (Link);
- Updated eAF (v1.24.0.1) (Link).

Pharmacovigilance

Pharmacovigilance fees payable to EMA by Marketing Authorisations Holders (MAHs) increased 1 November 2020 to account for inflation in 2018 (1.7%) and 2019 (1.6%). Full details of the new fee levels are available in the explanatory note on pharmacovigilance fees payable to the EMA (Link) and in the updated Q&As on pharmacovigilance fees (Link).

A revised guideline on remote pharmacovigilance inspections of MAHs during a crisis situation was adopted in September 2020 (EMA/509041/2020, Rev 1*). The document outlines specificities of remote pharmacovigilance inspections and points to consider during the preparation, conduct and reporting of inspections of MAHs of centrally and nationally authorised products.

The Important Medical Event Terms (IME) list aims to facilitate the classification of suspected adverse reactions, aggregated data analysis and case assessment in EU pharmacovigilance activities. Inclusion/exclusion criteria for the list were developed and updated to the current version of MedDRA (EMA/454024/2020).

Events of interest

Presentations, reports and/or videos of the following events have been published:

- 22/09/2020: Workshop on benefit-risk of medicines used during pregnancy and breastfeeding (Link)
- 28/09/2020: 2020 Annual meeting of the Coordinating Group of the European network of paediatric research at the EMA (Enpr-EMA) (Link)
- 19/10/2020 : Workshop on the draft guideline on registry-based studies (Link)
- 22/10/2020: 25 Years of EMA: building, learning and adapting to new challenges (Link)
- 29/10/2020: EMA 25th anniversary symposium: new approaches in patient-focused cancer drug development (Link)
- 27/11/2020: Multi-stakeholder webinar to support implementation of the Medical Devices Regulation on drug-device combinations (Link)
- 30/11/2020 : Workshop on support for orphan medicines development (Link)
- 15/12/2020 : EU big data stakeholder virtual forum (Link)

Upcoming event:

- 25/03/2021 : 2021 EMA/AnimalhealthEurope Info day (Link)

Other news

- Highlights of academia interaction 2017-2019 (Link)
- Ten year analysis of the EU incident management plan (EU-IMP) (Link)

- ADVANCE Online Course on ATMPs (Link, registration needed):
  - "How to apply for ATMP classification from EMA/CAT?"
  - "Environmental Risk Assessment for ATMPs containing a GMO"

- Scientific articles :
  - "*Advancing development of medicines by academia and non-profit research organizations in the European Union*", Nat Rev Drug Discov. 2020 Nov 23 (Link)
  - "*Towards a better use of Scientific Advice for developers of advanced therapies*", British Journal of Clinical Pharmacology, 2020 Nov 25 (Link).

Registered SMEs

At year end 2020, 1912 companies had SME status assigned by the Agency.

The names and profiles of these companies are published in the Agency's public SME Register.

If you would like to have your company details included in the SME Register, you must first apply for SME status at the Agency.

See the Applying for SME status section of the SME Office pages on the Agency's website for information on how to do this.

About the SME Office

The SME Office was set up within the European Medicines Agency to address the particular needs of smaller companies.

The Office has dedicated personnel who can help SMEs by:

- responding to practical or procedural enquiries;
- setting up briefing meetings to discuss their regulatory strategy;
- organising info days and training sessions.

Need more information?

Visit the European Medicines Agency website:

http://www.ema.europa.eu

In particular, these sections may interest you:

SME Office
Pre-authorisation (human medicines)
Pre-authorisation (veterinary medicines)

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