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HEADLINES

Welcome to our regular newsletter, which provides a digest of some of the latest EU/UK and some of the worldwide regulatory news. As ever, spring is always a busy time for new emerging guidelines from the EU regulatory agencies.
Feel free to contact us on smt@espl-regulatory.com if you have any questions on the information provided.

EUROPEAN NEWS

EUROPEAN MEDICINES AGENCY (EMA)

CENTRALISED PROCEDURE: UPDATED PRE- AND POST-AUTHORISATION PROCEDURAL ADVICE - IRELAND

The Irish (Gaelic) language has become the official language of Commission decisions on MAs addressed to MA holders in Ireland, unless a language waiver is requested.
See: https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/european-medicines-agency-pre-authorisation-procedural-advice-users-centralised-procedure_en-0.pdf
https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/european-medicines-agency-post-authorisation-procedural-advice-users-centralised-procedure_en.pdf

NEW INITIATIVE -REGULATORY SCIENCE RESEARCH NEEDS

The EMA has published a list of ~ 100 topics which should be addressed to improve medicine development and evaluation, to enable access to innovative medicines that address patients' needs. The agency hopes this will stimulate researchers and funding organisations to consider addressing these needs in their work and programmes.
See: https://www.ema.europa.eu/en/documents/other/regulatory-science-research-needs_en.pdf

ADOPTED GUIDELINE: NOTIFICATION OF SERIOUS BREACHES OF REGULATION (EU) No 536/2014 OR THE CLINICAL TRIAL PROTOCOL

This guideline has now been adopted by the GCP Inspectors Working Group (GCP IWG) and the Clinical Trial Facilitation Group (CTFG) and came into effect at the end of January. It outlines the practical arrangements for notification of serious breaches of the CT regulation or the clinical trial protocol.
See: https://www.ema.europa.eu/en/documents/scientific-guideline/guideline-notification-serious-breaches-regulation-eu-no-536/2014-clinical-trial-protocol_en.pdf

ACCELERATING CLINICAL TRIALS IN THE EU

This paper sets out proposals, objectives, and priority actions in the initial set up of an EU clinical trials transformation initiative: "Accelerating Clinical Trials in the EU (ACT EU)". The implementation of which will transform how clinical trials are initiated, designed, and run. It aims to further develop the EU as a focal point for clinical research, promote the development of high quality, safe and effective medicines, and to better integrate clinical research in the European health system.
https://www.ema.europa.eu/en/news/accelerating-clinical-trials-eu-act-eu-better-clinical-trials-address-patients-needs

UPDATE TO THE SCIENTIFIC ADVICE AND PROTOCOL ASSISTANCE GUIDELINE

Guidance on how to seek Scientific Advice and Protocol Assistance was updated in January. This provides an overview of the revised process and gives guidance to Applicants on preparing their request.
https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/european-medicines-agency-guidance-applicants-seeking-scientific-advice-protocol-assistance_en.pdf

EUDRAVIGILANCE TRAINING AND SUPPORT

EudraVigilance is the system for managing and analysing information on suspected adverse reactions to medicines which have been authorized or being studied in clinical trials within the European Economic Area (EEA).
New training dates on the use of this system have been made available throughout 2022: https://www.ema.europa.eu/en/human-regulatory/research-development/pharmacovigilance/eudravigilance/eudravigilance-training-support

Updated guidance on the electronic submission of information on investigational medicinal products for human use in the extended EudraVigilance medicinal product dictionary (XEVMPD) is also available
https://www.ema.europa.eu/en/documents/other/guidance-electronic-submission-information-investigational-medicinal-products-human-use-extended_en.pdf

RECENT REFLECTION PAPER ON GMP-RELATED RESPONSIBILITIES FOR MA HOLDERS

This recent paper seeks to clarify the various responsibilities of MA Holders with regard to GMP – and what they mean for MA Holders at a practical level.
https://www.ema.europa.eu/en/documents/scientific-guideline/reflection-paper-good-manufacturing-practice-marketing-authorisation-holders_en.pdf

PROCEDURAL GUIDANCE FOR NOTIFIED BODIES SEEKING A SCIENTIFIC OPINION FROM THE EMA Plus related Q&A DOCUMENT

The consultation period for procedural guidance for NBs seeking a scientific opinion from the EMA has now expired. This aimed to provide interested parties with information on the procedural aspects of the process, to facilitate the consultation procedure on companion diagnostics. A Q&A document was also provided on the practical arrangements of this consultation.
See: https://www.ema.europa.eu/en/human-regulatory/overview/medical-devices

EMA NEWSLETTERS

The EMA publishes monthly newsletters to provide updates on various topics to patients, healthcare professionals and the pharmaceutical industry.
https://www.ema.europa.eu/en/news-events/publications/newsletters

The latest newsletters are:

- **Human medicines highlights**

This contains key information on human medicines and changes to regulatory processes in the past month and can be found via:
https://www.ema.europa.eu/documents/newsletter/human-medicines-highlights-january-2022_en.pdf

- **SME newsletter**

This provides information for small-medium enterprises on the EU regulatory environment for medicines, typically published four times a year.
https://www.ema.europa.eu/documents/newsletter/news-bulletin-small-medium-sized-enterprises-issue-54_en.pdf

- **Veterinary medicines highlights**

This provides an update on progress towards implementing the new veterinary medicinal products regulation which took effect in January 2022.
https://www.ema.europa.eu/documents/newsletter/veterinary-medicines-regulation-highlights-issue-9_en.pdf

NEW REGULATION: MONITORING MEDICINES SUPPLY

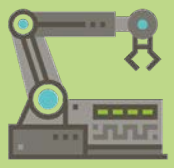
This new regulation gives the EMA a tool for monitoring medicines supply and preventing shortages in the event of a major public health crisis such as a future pandemic.
It became applicable on the 1st March [excluding the provisions on shortages of critical medical devices which will apply as of the 2nd February 2023].
The EMA have set up a new "European Shortages Monitoring Platform" to facilitate the gathering of information on drug shortages, supply, and demand. This electronic platform will need to be able to determine the volume of stocks available at any given moment and to detect and predict shortages.
A public webpage will also be maintained. The platform is expected to be fully operational by early 2025. https://www.ema.europa.eu/en/news/stronger-role-ema

EUR-LEX

ELECTRONIC INSTRUCTIONS FOR USE OF MEDICAL DEVICES

The European Commission has committed to implement regulation (EU) 2021/2226 of 14th of December 2021 laying down rules for the application of regulation (EU) 2017/745 of the European parliament and of the council regarding electronic instructions for use of medical devices;
https://eur-lex.europa.eu/legal-content/IT/TXT/PDF/?uri=CELEX:32021R2226&from=EN

SCIENTIFIC ADVICE, STRATEGY & SPECIALIST APPLICATION



MEDICAL DEVICE SUBMISSIONS

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EUROPEAN COMMISSION

QUESTIONS AND ANSWERS ON COMMISSION PROPOSAL TO ENSURE CONTINUED SUPPLY OF MEDICINES TO NORTHERN IRELAND, AS WELL AS CYPRUS, IRELAND, AND MALTA

Following extensive talks between the European Commission and the UK government, a package of measures has been put forward by the Commission to ensure the continued long-term supply of medicines from Great Britain to Northern Ireland. Outstanding supply concerns in Cyprus and Malta have also been addressed as they represent additional markets historically supplied through or by Great Britain. The Commission has proposed to change EU rules to ensure that the same medicines are available in Northern Ireland at the same time as they are in the rest of the United Kingdom. For more details see: https://ec.europa.eu/commission/presscorner/detail/en/qanda_21_6912

MEDICAL DEVICE GUIDANCE: MDCG 2022-1 NOTICE TO THIRD COUNTRY MANUFACTURERS OF SARS-COV-2 IN VITRO DIAGNOSTIC MEDICAL DEVICE

This notice is addressed to manufacturers of *in-vitro* diagnostic medical devices (IVDs) with the intended purpose to detect and/or quantify markers of SARS-CoV-2 infection who are based in countries outside the EU or the EEA and who place or intend to place the abovementioned devices on the EU market. The aim is to highlight a number of common issues that EU national competent authorities have had regarding compliance of these IVDs with the requirements of Directive 98/79/EC on *in-vitro* diagnostic medical devices.
https://ec.europa.eu/health/latest-updates/mdcg-2022-1-notice-3rd-country-manufacturers-sars-cov-2-vitro-diagnostic-medical-devices-2022-01-12_en

PROGRESSIVE ROLL-OUT OF THE IN VITRO DIAGNOSTIC MEDICAL DEVICES REGULATION

The in vitro diagnostic medical devices regulation that will apply from the 26th May 2022 has now been adopted by the European Parliament and the Council meaning that it can now be **progressively** rolled out. See the following press release for more information: https://ec.europa.eu/commission/presscorner/detail/en/ip_21_6965

QUESTIONS AND ANSWERS (VERSION 19)- SAFETY FEATURES FOR MEDICINAL PRODUCTS FOR HUMAN USE

This document published in December 2021 sets out frequently-asked 'questions and answers' regarding the implementation of the rules on the safety features for medicinal products for human use.
https://ec.europa.eu/health/sites/default/files/files/falsified_medicines/qa_safetyfeature_en.pdf

HTA: COMMISSION WELCOMES THE ADOPTION OF NEW RULES TO IMPROVE ACCESS TO INNOVATIVE TECHNOLOGIES

The Regulation on **Health Technology Assessment (HTA)** was adopted in December 2021. The new rules allow vital and innovative health technologies such as innovative medicines, certain medical devices, medical equipment and prevention and treatment methods to be more widely available. It will ensure the efficient use of resources and save national bodies and industry from duplicating their efforts.
https://ec.europa.eu/commission/presscorner/detail/en/ip_21_6771

PHARMEUROPA 34.1

All new Ph Eur texts and those which have undergone technical revisions are published in Pharmeuropa for public consultation. The deadline for comments on Pharmeuropa 34.1 is 31st of March 2022. https://www.edqm.eu/en/news/pharmeuropa-341-just-released

EUROPEAN DIRECTORATE FOR THE QUALITY OF MEDICINES (EDQM)

JOURNAL OF PHARMACEUTICAL AND BIOMEDICAL ANALYSIS PUBLISHES RESULTS OF THE OMCL FINGERPRINT STUDY ON OMEPRAZOLE API SAMPLES

An API fingerprint is a specific analytical profile that includes information on the physio-chemical properties of the substance. API fingerprint studies are performed in order to identify substandard or falsified APIs, which represent a threat to patient health. The results of one such study on omeprazole, a medicine used in the treatment of heartburn and indigestion, have recently been published in the journal of pharmaceutical and biomedical analysis, Vol. 208 (2021). See:
https://www.edqm.eu/en/news/journal-pharmaceutical-and-biomedical-analysis-publishes-results-omcl-fingerprint-study

EUROPEAN PAEDIATRIC FORMULARY: TWO DRAFT TEXTS RELEASED FOR PUBLIC CONSULTATION

Issue 4 of Pharmeuropa PaedForm contains two texts for public consultation, ***Simple syrup (preservative free)*** and ***Phosphate 60 mg/ml Oral solution*****,** prior to their inclusion in the European Paediatric Formulary. The mission of this initiative is to provide a platform to make freely available a formulary for extemporaneous formulations for paediatric medicines, in Europe. The formulary comprises a compilation of monographs for the preparation of such formulations. See: https://www.edqm.eu/en/news/european-paediatric-formulary-two-draft-texts-released-public-consultation

HPRA - IRELAND

NOTIFICATION OF CHANGES TO THE HEALTH PRODUCTS REGULATORY AUTHORITY FEES

Details on the new fees applicable in Ireland since January are available at: https://www.hpra.ie/homepage/medicines/regulatory-information/medicines-fees

UK MHRA

GUIDANCE ON HANDLING OF DECENTRALISED AND MUTUAL RECOGNITION PROCEDURES WHICH ARE APPROVED OR PENDING

Updates to post-Brexit protocols were made on the 22nd December 2021 relating to the handling of Decentralised and Mutual Recognition Procedures which are approved or pending. They can be found via: https://www.gov.uk/guidance/guidance-on-handling-of-decentralised-and-mutual-recognition-procedures-which-are-approved-or-pending#history

NEW CLINICAL TRIAL LEGISLATION

- **Medicines**

The UK is following a similar initiative to the EU's new clinical trial legislation. As of the 1st January 2022, the combined review service became the way that all new clinical trials of investigational medicinal products (CTIMPs) are prepared, submitted and reviewed. See: https://www.gov.uk/guidance/clinical-trials-for-medicines-apply-for-authorisation-in-the-uk#full-publication-update-history

- **Medical Devices**

In addition, updated guidance has been released which outlines how an Applicant should notify the MHRA about a clinical investigation for a medical device.
The MHRA is working with the Health Research Authority (HRA) to develop a new coordinated assessment pathway which will streamline the review of clinical investigations involving medical devices.
https://www.gov.uk/guidance/notify-mhra-about-a-clinical-investigation-for-a-medical-device

GUIDANCE ON THE USE OF REAL-WORLD DATA IN CLINICAL STUDIES TO SUPPORT REGULATORY DECISIONS

New guidance has been published by the MHRA that outlines how greater use of real-world data (e.g electronic health records and patient reported outcomes) for clinical trials could help expedite the availability of cost-effective treatments.
With fewer logistical hurdles related to conducting clinical trials outside a clinical study setting such as through wearable devices, specialized/secure websites or tablets, real world data could make it more feasible for trial sponsors to repurpose existing medicines for new conditions. See :
https://www.gov.uk/government/news/mhras-new-guidance-on-using-real-world-data-to-support-clinical-trials-could-get-medicines-to-patients-sooner

UK: UPDATES TO GUIDANCES ON HOW TO PLACE MEDICAL DEVICES ON THE MARKET

These guidances have been updated to reflect changes in medical device registration and other regulatory requirements, which took effect on the 1st January 2022:

- https://www.gov.uk/guidance/register-medical-devices-to-place-on-the-market?utm_medium=email&utm_campaign=govuk-notifications&utm_source=6d97427b-259b-48e2-9ad0-86e6a02f533c&utm_content=immediately#history
- https://www.gov.uk/guidance/regulating-medical-devices-in-the-uk?utm_medium=email&utm_campaign=govuk-notifications&utm_source=6864cd5d-7c05-44e5-ba7b-5e4c721ab382&utm_content=immediately

IMPORTING MEDICINES INTO NORTHERN IRELAND

The guidance on 'Importing medicines into Northern Ireland' has been updated to provide a revision to the description of the derogation mentioned and to remove all references to "before 31st December 2021": https://www.gov.uk/guidance/importing-medicines-into-northern-ireland#history

MHRA CONSULTATION: THE FUTURE OF UK CLINICAL TRIALS LEGISLATION

The MHRA 8-week consultation period on proposals for legislative changes for clinical trials, is due to end on the 14th March 2022. The aim is to update and strengthen the current legislation to promote public health, remove obstacles to innovation whilst maintaining trial safety, streamline the regulation process and ensure that international interoperability is maintained so that the UK remains a preferred site to conduct multi-national trials. The proposals being consulted on involve patient and public involvement, research transparency, the clinical trial approval processes, proposals for research ethics reviews, informed consent in cluster trials and safety reporting amongst others. See: https://www.gov.uk/government/consultations/consultation-on-proposals-for-legislative-changes-for-clinical-trials

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ICH GUIDELINE Q9 (R1) ON QUALITY RISK MANAGEMENT

This guideline was released for public consultation on the 18th of November 2021 and provides principles and examples of tools for quality risk management that can be applied to different aspects of pharmaceutical quality. The deadline for comment is the 15th of March 2022. See: https://www.ema.europa.eu/en/documents/scientific-guideline/draft-international-conference-harmonisation-technical-requirements-registration-pharmaceuticals_en-1.pdf

ICMRA: INTERNATIONAL COALITION OF MEDICINES REGULATORY AUTHORITIES

PAPER ON REMOTE INSPECTIONS

A paper entitled "Reflections on the regulatory experience of remote approaches to GCP and GMP regulatory oversight during the COVID-19 Pandemic" has been published by the ICMRA. It concludes that "the use of digital technologies in the remote conduct of inspections, evaluations, and assessments was a key business continuity tool for regulatory oversight of certain activities and sites during the COVID-19 pandemic".

Several regulators have expressed an interest in continuing to carry out inspections in this manner and for many authorities (including the UK MHRA and the US FDA) 'hybrid' inspections are likely to become the norm going forward.

https://www.ema.europa.eu/en/news/international-regulators-reflections-remote-approaches-gcp-gmp-regulatory-oversight-during-covid-19

ANVISA - BRASIL:

NEW REGULATION ON IMPORT, MARKETING AND DONATION OF USED AND RECONDITIONED MEDICAL DEVICES

A video has been released with clarifications on the Resolution of the Collegiate Board (RDC) 579/2021, which took effect on the 1st January 2022 and is relevant to the import, sale, and donation of used and refurbished medical devices.

https://www.gov.br/anvisa/pt-br/assuntos/noticias-anvisa/2021/anvisa-divulga-gravacao-sobre-a-rdc-579-2021

SWISSMEDIC

NEW ORDINANCE: THE ROLES AND OBIGATIONS OF THE ECONOMIC OPERATORS IN THE MEDICAL DEVICE SUPPLY CHAIN

The Medical Device Ordinance (MedDO; SR 812.213) published in December 2021, sets out requirements and responsibilities for operators in the medical devices supply chain such as the Swiss authorized representative, the importer, and the distributer.

https://www.swissmedic.ch/dam/swissmedic/en/dokumente/medizinprodukte/mep_urr/mu600_00_016d_mb_pflichten_wirtschaftsakteure_ch.pdf.download.pdf/MU600_00_016e_MB_Obligations_Economic_Operators_CH.pdf

US FDA

DIGITAL HEALTH TECH IN CLINICAL INVESTIGATIONS: DRAFT GUIDANCE

These draft recommendations published in December 2021 address digital health tech suitable for the use in clinical investigations and their associated risks, for example in data collection for trial endpoints. https://www.fda.gov/media/155022/download