ISSUE. 15 NEWSLETTER 1Q 2023

SMT@ESPL-REGULATORY.COM



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, Q1 2023 has been a very busy time for new emerging guidelines from the regulatory agencies of the world.
Feel free to contact us on smt@espl-regulatory.com if you have any questions on the information provided.

# EUROPEAN NEWS

## CONSIGLIO EUROPEO

### UPDATE REGARDING THE STATE OF PLAY ON THE IMPLEMENTATION OF THE MEDICAL DEVICE REGULATIONS

This update provides further proposals for solutions to address to the challenges related to the implementation of the MDR Regulation 2017/745, in particular, the threat to the continued availability of certain medical devices.
See: https://data.consilium.europa.eu/doc/document/ST-15520-2022-INIT/en/pdf

## EUROPEAN MEDICINES AGENCY

### ICH GUIDELINE M10 ON BIOANALYTICAL METHOD VALIDATION AND STUDY SAMPLE ANALYSIS – FREQUENTLY ASKED QUESTIONS (FAQ) (UPDATED)

In response to questions posted to ICH M10 comment period, a number of Q&As have been devised to provide clarity around some of the bioanalytical issues covered in the Guideline.
This Q&A document is intended to provide additional clarification and to promote convergence and improve harmonization of the bioanalytical method validation and study sample analysis.
See: https://www.ema.europa.eu/documents/scientific-guideline/ich-guideline-m10-bioanalytical-method-validation-study-sample-analysis-frequently-asked-questions_en.pdf

### TEMPLATE FOR REGISTERING NEW ACTIVE SUBSTANCE ON EUTCT

The template for registering a new active substance on the European Union Telematics Controlled Terms repository (EUTCT) has been updated. See: https://www.ema.europa.eu/documents/template-form/template-registering-new-active-

### ICH GUIDELINE Q13 ON CONTINUOUS MANUFACTURING OF DRUG SUBSTANCES AND DRUG PRODUCTS - STEP 5

Building on existing ICH Quality guidelines, this guideline provides clarification on CM concepts and describes scientific approaches and regulatory considerations specific to continuous manufacturing (CM) of drug substances and drug products. See: https://www.ema.europa.eu/documents/scientific-guideline/ich-guideline-q13-continuous-manufacturing-drug-substances-drug-products-step-5_en.pdf

### MEDICAL DEVICES – 'HIGH-RISK MEDICAL DEVICES' (UPDATED)

The EMA runs a pilot that enables the expert panels to provide scientific advice for manufacturers of high-risk medical devices. Starting with 27 February 2023, manufacturers in the EU can apply to take part in the pilot via EMA's ServiceNow portal. See: https://www.ema.europa.eu/en/human-regulatory/overview/medical-devices#high-risk-medical-devices-(updated)-section

### CENTRALISED PROCEDURE GUIDANCE UPDATES

Three guidance documents addressing questions MAHs may have on centralised procedures, relating to extensions, pre-authorisation guidance and notifying a change of MA status in post-authorisation procedures have recently been updated. See:

- https://www.ema.europa.eu/en/human-regulatory/post-authorisation/variations/extensions-marketing-authorisations-questions-answers
- https://www.ema.europa.eu/en/human-regulatory/marketing-authorisation/pre-authorisation-guidance
- https://www.ema.europa.eu/en/human-regulatory/post-authorisation/notifying-change-marketing-status

## VALIDATION CHECKLIST FOR TYPE II (NON) CLINICAL VARIATIONS

The validation checklists which "enable applicants to submit high quality applications that avoid frequent mistakes and comply with the legal and regulatory requirements, ensuring submissions can be validated speedily" have recently been updated. See: https://www.ema.europa.eu/documents/regulatory-procedural-guideline/validation-checklist-type-ii-non-clinical-variations_en.docx

## GUIDANCE ON GOOD DISTRIBUTION PRACTICE Q&A UPDATED

https://www.ema.europa.eu/en/human-regulatory/research-development/compliance/good-manufacturing-practice/guidance-good-manufacturing-practice-good-distribution-practice-questions-answers

## EMA NEWSLETTERS

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

The latest newsletters are:

- **Human medicines highlights**

Key information on human medicines and changes to regulatory processes in the past month. See: https://www.ema.europa.eu/documents/newsletter/human-medicines-highlights-april-2023_en.pdf

- **SME newsletter**

Information for SMEs on the EU regulatory environment for medicines. See: https://www.ema.europa.eu/documents/newsletter/news-bulletin-small-medium-sized-enterprises-issue-57_en.pdf

- **Veterinary medicines highlights**

An update on progress towards implementing the new veterinary medicinal products regulation which took effect in January 2022. See: https://www.ema.europa.eu/documents/newsletter/veterinary-medicinal-products-regulation-highlights-issue-11_en.pdf

- **eAF (DADI) newsletter**

The EMA provides a newsletter containing news, views and interviews relating to the web-based Human Variations electronic application form (eAF) for Centrally Authorised Products, often referred to by its former project name (DADI). See: https://www.ema.europa.eu/documents/newsletter/dadi-newsletter-issue-2_en.pdf

# HEADS OF MEDICINES AGENCY (HMA)

## UPDATE - ADDITIONAL YEAR OF MARKET PROTECTION FOR NEW THERAPEUTIC INDICATION AGREED BY CMDh

Several products have recently been granted an additional year of market protection/data exclusivity. The decision for three of the products was related to new proposed indications, Oxynal/Targin for restless leg syndrome, Somatuline solution for injection used in the treatment of gastroenteropancreatic neuroendocrine tumours, and Concerta XL tablets for the de novo treatment of ADHD in adults. One further extension was granted for Palexia/Yantil oral solution on the basis of extending the indication to children from 2 years and older. See: https://www.hma.eu/fileadmin/dateien/Human_Medicines/CMD_h_/Advice_from_CMDh/CMDh_341_2015_Rev1_2022_12_Decisions_on_additional_year_of_market_protectiondata_exclusivity_for_new_therapeutic_indication_agreed_-_NEW.pdf

## UPDATE - APPLICANT'S RESPONSE TEMPLATE

The applicants' response template for decentralised procedures has recently been updated. See: https://www.hma.eu/fileadmin/dateien/Human_Medicines/CMD_h_/Templates/AR/DCP_AR_Comments/CMDh_436_2022_Rev.1_2022_12_clean_-_Joint_response_template_for_the_applicant.docx

# EUROPEAN COMMISSION

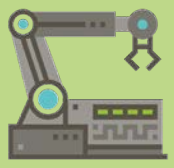
## GUIDANCE ON PERIODIC SAFETY UPDATE REPORT (PSUR) ACCORDING TO REGULATION (EU) 2017/745 (MDR)

The main objective of this recent guidance document is to assist manufacturers to implement the legal requirements laid down in Article 86 MDR.
See: https://health.ec.europa.eu/latest-updates/mdcg-2022-21-guidance-periodic-safety-update-report-psur-according-regulation-eu-2017745-december-2022-12-16_en

## MANUAL ON BORDERLINE AND CLASSIFICATION UNDER REGULATIONS (EU) 2017/745 AND 2017/746

This document records the agreements reached by the Member State Members of the Borderline and Classification Working Group concerning the borderline between medical devices and other types of product. See: https://health.ec.europa.eu/latest-updates/manual-borderline-and-classification-under-regulations-eu-2017745-and-2017746-version2-december-2022-2022-12-15_en

**SCIENTIFIC ADVICE, STRATEGY & SPECIALIST APPLICATION**



**MEDICAL DEVICE SUBMISSIONS**

**PUBLISHING**

**https://www.espl-regulatory.com/**

**https://www.linkedin.com/company/espl-regulatory-consulting/**

**tel:+441806242852**

**smt@espl-regulatory.com**

## FACTSHEET- SUPPORTING THE TRANSITION TO THE NEW MEDICAL DEVICE FRAMEWORK

The European Commission have provided a factsheet for stakeholders involved in the transition to the enw medical device framework. See: https://health.ec.europa.eu/system/files/2023-01/mdr_proposal_factsheet_0.pdf

## ANNUAL OVERVIEW OF DEVICES SUBJECT TO THE CLINICAL EVALUATION CONSULTATION PROCEDURE (CECP)

The European Commission have recently published their annual overview of devices subject to the clinical evaluation consultation procedure. See: https://health.ec.europa.eu/latest-updates/annual-overview-devices-subject-clinical-evaluation-consultation-procedure-cecp-april-2021-june-2022-2023-01-23_en

## COVERAGE OF DESIGNATION CODES BY MDR/IVDR NOTIFIED BODIES

The European Commission have provided a powerpoint which details the distribution of medical devices approved across the different codes of the MDA. See: https://health.ec.europa.eu/latest-updates/update-coverage-designation-codes-mdrivdr-notified-bodies-january-2023-2023-01-13_en

## PERFORMANCE STUDY APPLICATION/NOTIFICATION DOCUMENTS UNDER REGULATION (EU) 2017/746

In the absence of the European database on medical devices (EUDAMED), a series of performance study application/notification documents have been created to support performance study procedures with respect to the IVDR. See: https://health.ec.europa.eu/latest-updates/mdcg-2022-19-performance-study-applicationnotification-documents-under-regulation-eu-2017746-2022-12-12_en

## MDCG POSITION PAPER ON 'HYBRID AUDITS'

This paper outlines the Medical Device Coordination Group (MDCG) position on the possible use of hybrid audits by notified bodies under the MDR and IVDR. It aims to provide a definition for hybrid audits and clarifications with respect to how hybrid audits can be used under MDR and IVDR as advised following the publication of MDCG 2022-14.
See: https://health.ec.europa.eu/latest-updates/mdcg-2022-17-mdcg-position-paper-hybrid-audits-december-2022-2022-12-06_en

## IMPLEMENTATION ROLLING PLAN: REGULATION (EU) 2017/745 AND REGULATION (EU) 2017/746

This rolling plan contains a list of identified essential implementing acts and other relevant initiatives that the Commission has adopted or intends to adopt in the future. This plan is divided into two sections: implementing acts, and other actions/initiatives. See: https://health.ec.europa.eu/system/files/2022-12/md_rolling-plan_en.pdf

## IMPLEMENTATION OF THE MEDICAL DEVICE REGULATION (MDR): EU MDR TRANSITION PERIOD EXTENSION PROPOSAL BY THE EUROPEAN COMMISSION

A recording of the discussion of the Employment, Social Policy, Health and Consumer Affairs Council on the implementation of the medical device regulation and their proposal to extend the transition period is available online.
See: https://video.consilium.europa.eu/event/en/26353

# EDQM

## REDESIGN OF CEP FORMAT (CEP 2.0)

A CEP is a certificate of compliance with the European Pharmacopoeia granted to manufactures of drug products who conform to legally binding Ph Eur quality standards. The CEP 2.0 aims to enhance user-friendliness and create greater transparency of the information conveyed without increasing the regulatory burden related to revisions. The changes linked to the implementation of the new CEP format will be further detailed within the next months.
See: https://www.edqm.eu/en/what-is-the-cep-2.0

# ICH

## (DRAFT) ICH M13A – BIOEQUIVALENCE FOR IMMEDIATE RELEASE SOLID ORAL DOSAGE FORMS

This draft guideline is intended to provide recommendations on conducting bioequivalence (BE) studies by describing the scientific and technical aspects of study design and data analysis to support BE assessment. See: https://www.hma.eu/fileadmin/dateien/Human_Medicines/CMD_h_/Advice_from_CMDh/CMDh_341_2015_Rev1_2022_12_Decisions_on_additional_year_of_market_protectiondata_exclusivity_for_new_therapeutic_indication_agreed_-_NEW.pdf

# UK MHRA

## ACCESS GENERIC MEDICINES WORK SHARING INITIATIVE – NEW DOCUMENTS ADDED

Two new documents have been added which applicants should review: the "Operational procedures for the generic medicines work-sharing initiative (GMWSI) for planning and filing of the application and the "GMWSI Expression of Interest (EOI)" form which should be completed 3-6 months before the target submission date. See: https://www.gov.uk/guidance/access-generic-medicines-work-sharing-initiative#assessment-procedure

## LIFE SCIENCES COUNCIL JOINT STATEMENT ON MEDICAL DEVICES REGULATORY REFORM

This article describes a new agreement by the life sciences council to accelerate the delivery of the future UK HealthTech regulatory system. See: https://www.gov.uk/government/news/life-sciences-council-joint-statement-on-medical-devices-regulatory-reform

## MHRA TO RECEIVE £10M FROM HM TREASURY TO FAST-TRACK PATIENT ACCESS TO CUTTING-EDGE MEDICAL PRODUCTS

The funding will be used to accelerate routes for bringing innovative medical products developed in the UK onto the market, as well as those made and approved by other trusted regulatory partners globally. See: https://www.gov.uk/government/news/mhra-to-receive-10m-from-hm-treasury-to-fast-track-patient-access-to-cutting-edge-medical-products

## MHRA TO RECEIVE NEARLY £1M BEIS FUNDING TO UNLOCK DIGITAL, DATA AND SCIENTIFIC REGULATORY INNOVATION

The MHRA has receive funding for three projects which aim to improve how patients can access life-changing treatments in clinical trials, find a way to introduce complex AI safely into front line clinical settings and make the UK the place to launch advanced microbiome products that can support the development of personalized medicine. See: https://www.gov.uk/government/news/mhra-to-receive-nearly-1m-beis-funding-to-unlock-digital-data-and-scientific-regulatory-innovation

# CANADA (HC)

## CONSULTATION ON PROPOSED AGILE REGULATIONS AND GUIDANCE FOR LICENSING DRUGS AND MEDICAL DEVICES

Health Canada is proposing new targeted provisions and regulatory amendments to the Food and Drug Regulations and Medical Devices Regulations and is inviting participants to provide feedback on their proposal. See: https://www.canada.ca/en/health-canada/programs/consultation-proposed-agile-regulations-guidance-licensing-drugs-medical-devices.html

# MALAYSIA (MDA)

## PUBLIC COMMENT DRAFT GUIDANCE DOCUMENT REQUIREMENTS FOR APPLICATION OF CFS, MC AND CFS EO MEDICAL DEVICES (MDA/GD/0045)

This guidance document is developed to assist applicants in their application for Certificate of Free Sale (CFS), Manufacturing Certificate (MC) and Certificate of Free Sale for Export Only (CFS EO) medical devices. See: https://portal.mda.gov.my/doclink/gd-public-comment-cfs-mc-and-cfs-eo-pdf/eyJ0eXAiOiJKV1QiLCJhbGciOiJIUzI1NiJ9.eyJzdWIiOiJnZC1wdWJsaWMtY29tbWVudC1jZnMtbWMtYW5kLWNmcy1lby1wZGYiLCJpYXQiOjE2NzE3Njk2ODEsImV4cCI6MTY3MTg1NjA4MX0._4cu7SpcvSkUvWW9q43OIV7cXW2gdTzC7MKFD_m9_00

# IRELAND (HPRA)

## GUIDE TO APPLICATIONS FOR CERTIFICATES OF FREE SALE FOR MEDICAL DEVICES

Certificates of free sale are documents used in the registration of devices in third countries (i.e. countries outside the European Economic Area). They indicate that the devices listed are eligible for sale in the EU market. This guidance provides advice to applicants See: http://www.hpra.ie/docs/default-source/publications-forms/guidance-documents/aut-g0026-guide-to-applications-for-certificates-of-free-sale-for-medical-devices-v8.pdf?sfvrsn=45

## NOTIFICATION OF CHANGES TO THE HEALTH PRODUCTS REGULATORY AUTHORITY FEES (HUMAN)

The HPRA wishes to advise all MA and WDA holders that approval has been given for a general increase in fees by 9%, effective from 1 January 2023.
See: https://www.hpra.ie/docs/default-source/publications-forms/guidance-documents/fin-g0002-guide-to-fees-for-human-products-v27.pdf?sfvrsn=69