Newsletter

ClinChoice
The Standard of Excellence

REGULATORY NEWSLETTER

January - March 2024

Contents

MEDICINAL PRODUCTS/ DRUGS

News from the European Commission

EMA Updates SME Guide to Incorporate Significant Updates to Reflect Major Changes in the EU

On 23 January 2024, the European Medicines Agency (EMA) released a major revision of its user guide for micro, small, and medium-sized enterprises (SMEs) in the pharmaceutical sector. The revised user guide offers comprehensive information on the EU legislative framework for medicines, outlining requirements for the development and authorisation of medicines for human and veterinary use.

New Regulation on Blood, Blood Products and Plasma

On 30 January 2024, the Council of the European Union released the proposal for a Regulation on standards of quality and safety for substances of human origin intended for human application and repealing Directives 2002/98/EC and 2004/23/EC. This Regulation aims at setting high quality and safety standards by ensuring, amongst others, the protection of safety for organs and substances of human origin (SoHO) donors, taking into consideration their fundamental role in the provision of SoHOs and for recipients, as well as measures to monitor and support the sufficiency of the supply of SoHOs that are critical for the health of patients.

News from the European Medicines Agency (EMA)

New Transparency Rules: CTIS Public Portal Update Effective 18 June 2024

The revised transparency rules for the Clinical Trials Information System (CTIS) will become applicable on 18 June 2024, with the launch of a new version of the CTIS public portal. The updated rules strike a balance between transparency of information and protection of Commercially Confidential Information (CCI).

EMA Reminds Industry on Transition of Clinical Trials from Directive to Regulation

The Clinical Trials Information System (CTIS) supports the business processes of clinical trial sponsors and national regulators throughout the lifecycle of a clinical trial, via secure workspaces. On this page you will find some basic questions about the use of CTIS and transitioning of clinical trials.

https://euclinicaltrials.eu/guidance-and-q-as/#qas-transitioning

CTCG Updated the Best Practice Guide and Cover Letter Template for Sponsors Transitioning Trials to the EU Clinical Trials Regulation (EU CTR)

The updated Best Practice Guide and Cover Letter Template, vs. 4.0 was adopted at Clinical Trials Facilitation and Coordination Group (CTCG) plenary on 7 March 2024. "Sponsor should propose trial category but not apply for low-intervention clinical at time of transition from CTD to CTR. Details on CTIS submission for specific situations and description of the changes include 1) sponsor is not product owner of an IMP; 2) recommendations for IMPs and AxMPs; and 3) when, under CTD, a study was regarded as an interventional clinical trial in some Member States and as a non-interventional clinical study in other Member States. Archiving rules and end of trial for CTD trials when some but not all Member States included in transition".

The Annex Cover Letter Template vs. 4.0 was adopted at CTCG plenary on 6 March 2024.

The Clinical Trial Advisory Group's Guidance for the Transition of Clinical Trials Updated

This Guidance was released in March 2024 under Version 3 and again in May 2024 under version 4. It reflects the agreement reached by the National Contact Points and supersedes the chapter 11 of the Q&A on the application of the CTR (version 6.4).

CTCG Published a Recommendation Paper on Principles of Good Laboratory Practices (GLP) for Clinical Trial Applications under the CTR

Recommendation paper on principles of Good Laboratory Practices (GLP) for clinical trial applications under the EU Clinical Trials Regulation (Regulation (EU) No 536/2014), Version 01 was endorsed on 1 March 2024. The scope of this recommendation paper is to share the common approach agreed on the requirements regarding Organisation for Economic Co-operation and Development (OECD) GLP compliance of pivotal non-clinical data submitted to support a clinical trial application (CTA); and provide transparency on regulatory acceptability for sponsors and test facilities, and other interested parties. GLP Template table is provided.

Template-GLP-table.docx (live.com)

Clinical Trials Regulation (EU) No 536/2014 (CTR) Questions & Answers (Q&A) Update

The document was released in March 2024 and addresses the rules governing medicinal products in the European Union Volume 10 - Guidance documents applying to clinical trials Clinical Trials Regulation (EU) No 536/2014 Questions & Answers, Version 6.8.

https://health.ec.europa.eu/document/download/bd165522-8acf-433a-9ab1-d7dceae58112_en

Update of the Q&A on Protection of Confidential Information and Personal Data in CTIS

This Q&A document was released on 31 January 2024 as version 1.4 and to provide preliminary guidance to CTIS users on how to protect personal data and commercially confidential information (CCI) in CTIS, the EU database established in accordance with the requirements of Regulation (EU) No 536/2014 (CTR). The Q&A document was produced to address a number of questions related to the transparency aspects of CTIS.

Q&A on Protection of Confidential Information and Personal Data in CTIS

EMA Proposes New Concept Paper on Non-Inferiority and Equivalence Comparisons in Clinical Trials

On 12 February 2024, EMA released a proposed guideline that will replace CPMP/EWP/482/99: "Points to consider on Switching between Superiority and Non-Inferiority" and CPMP/EWP/2158/99 "Guideline on the Choice of Non-Inferiority Margin".

Concept Paper for the Development of a Reflection Paper on a Tailored Clinical Approach in Biosimilar Development

On 24 November 2023, EMA released the concept paper for the development of a Reflection Paper on a tailored clinical approach in Biosimilar development. The concept paper was adopted by Committee for Medicinal Products for Human Use (CHMP) for release for consultation on 25 January 2024 and end of consultation (deadline for comments) was 30 April 2024. A biosimilar is a biological medicinal product that contains a version of the active substance of an already authorised original biological medicinal product (Reference Medicinal Product, RMP), where similarity to the reference medicinal product based on a comprehensive comparability exercise has been established. Biosimilars have become important therapeutic options, improving patient access to essential treatments. Therefore, CHMP (EMA) acknowledges the significance of biosimilars.

Other Initiatives

Revision of Declaration of Helsinki

The Declaration of Helsinki, established by the World Medical Association (WMA) in 1964, outlines ethical guidelines for medical research involving humans, including identifiable human material and data. Regarded as a cornerstone in research ethics, it is undergoing current revisions through a recent consultation by the WMA. These revisions aim to ensure the Declaration remains relevant in addressing emerging ethical challenges worldwide. The current (2013) version is the only official one; all previous versions have been replaced and should not be used or cited except for historical purposes.

https://www.wma.net/what-we-do/medical-ethics/declaration-of-helsinki/

News from Individual Countries

Germany

New Guideline on the Collection of Blood and Blood Components and on the Use of Blood Products

The "Guideline on the collection of blood and blood components and on the use of blood products" was revised by the German Medical Association (Bundesärztekammer – BÄK) in cooperation with the Paul-Ehrlich-Institut (PEI – the German Federal Institute for Vaccines and Biomedicines).

Richtlinie Hämotherapie 2023 (bundesaerztekammer.de)

Netherlands

Template Research Protocol (WMO): Explanation 'Safety' Extended

The template research protocol was modified on 9 April 2024 on two minor points. The changes only serve to clarify the submission process. The previous version (modified in September 2018) therefore remains valid.

The United Kingdom

HRA Policy regarding Registration of Clinical Trials of Investigational Medicinal Products (CTIMPs) with the EU Clinical Trials Information System (CTIS)

The Health Research Authority (HRA) has updated its standard approval conditions, emphasizing that CTIMPs registered only with the EU CTIS must also be registered on a public registry within six weeks of enrolling the first participant in the UK. This ensures compliance with the HRA transparency standards and REC approval conditions.

For CTIMPs conducted in the UK, researchers are now required to register their trials on a public registry such as ISRCTN and ClinicalTrials.gov within six weeks of enrolling the first participant, aligning with similar requirements for CTIMPs conducted in the European Union (EU) or European Economic Area (EEA). Updates and revisions are effective from 29 January 2024.

https://content.govdelivery.com/accounts/UKNHSHRA/bulletins/3871436

North America

United States of America

FDA Issues Final Guidance on Assessing COVID-19-Related Symptoms in Outpatient Adult and Adolescent Subjects in Clinical Trials of Drugs and Biological Products

On 21 February 2024, the FDA issued the final guidance Assessing COVID-19-Related Symptoms in Outpatient Adult and Adolescent Subjects in Clinical Trials of Drugs and Biological Products for COVID-19 Prevention or Treatment. This supersedes the guidance of the same name initially published in September 2020.

This guidance provides sponsors and investigators with considerations for approaches on how common COVID-19-related symptoms can be measured and analyzed in clinical trials evaluating drugs or biological products for the prevention or treatment of COVID-19 in outpatient adults and adolescents. The guidance provides considerations for outpatient clinical trial endpoint selection, handling data and additional assessments.

Canada

Health Canada Implements ICH E19: A Selective Approach to Safety Data Collection in Specific Late-Stage Pre-approval or Post-approval Clinical Trials

Health Canada, as an official member to the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH), is committed to the adoption and implementation of ICH guidelines. Health Canada announced with a notification revision on 27 February 2024 the implementation of the ICH E19 guideline: ICH E19 guideline: "A Selective Approach to Safety Data Collection in Specific Late Stage Pre-approval or Post-approval Clinical Trials." Selective Safety Data Collection refers to the recording of certain data by investigators in case report forms. It does not affect the monitoring and clinical care of individual trial participants or documentation of their adverse events in medical records. It also does not affect regulatory reporting requirements.

Therefore, all safety reporting requirements outlined in the regulations must still be met. In the interest of continuing to attract clinical trials that offer access to new therapies to Canadians, Health Canada will not prioritize enforcement of the requirement for sponsors to retain records of all adverse events when the authorized protocol describes a selective safety data collection approach that meet the eligibility criteria.

MEDICAL DEVICES

News from the European Commission

European Commission Proposes Extended Deadline for IVDR Compliance and Changes for EUDAMED Full Functionality

On 23 January 2024, the European Commission is proposing more time for companies to apply the In Vitro Diagnostic Medical Devices Regulation (IVDR), under certain conditions. With this revision, the Commission aims to ensure patient care by improving the availability of these essential healthcare products. The Commission is also proposing measures to enhance transparency in the Medical Device sector including by speeding up the launch of some elements of the European Database on Medical Devices – EUDAMED.

Proposal for Amending Regulations (EU) 2017/745 and (EU) 2017/746

On 23 January 2024, the European Commission released the proposal for amending Regulations (EU) 2017/745 and (EU) 2017/746 regarding a gradual roll-out of Eudamed, information obligation in case of interruption of supply and the transitional provisions for certain in vitro diagnostic medical devices.

Guidance on the Investigator's Brochure Content and Appendix A of the MDCG 2024-5

In April 2024, the Medical Device Coordination Group (MDCG 2024-5) released guidance on content of the Investigator's Brochure for clinical investigations of medical devices. The Investigator's Brochure (IB) is part of the required documentation and is one of the means by which the sponsor is to fulfil the requirement in section 2.7 of Chapter I of Annex XV of the MDR which states that the investigator shall have access to technical and clinical data regarding the device that is being investigated.

The Appendix A Checklist is provided and cross-references between requirements in Annex XV chapter II of the MDR and the Clinical Investigation submission package.

Guidance on Content of the Clinical Investigation Plan (CIP) for Clinical Investigations of Medical Devices with Template for CIP Synopsis

In March 2024, the Medical Device Coordination Group (MDCG 2024-3) released guidance on content of the Clinical Investigation Plan for clinical investigations of medical devices. The clinical investigation plan (CIP) shall set out the rationale, objectives, design methodology, monitoring, conduct, record-keeping, and the method of analysis for the clinical investigation. Note that it is preferred for all necessary information to be included in the CIP. If part of the required information is provided in a separate document, it will be summarised and referenced in the CIP.

Clinical Investigation Plan Synopsis Template

MDCG 2024-3 provides Appendix A: Clinical Investigation Plan Synopsis Template. For combination studies, more details may be relevant, such as EU number of the clinical trial, name and description of investigational medicinal product or CIV-ID/SRN of performance study of an in vitro diagnostic device.

Procedures for the Updates of the EMDN

In February 2024, the Medical Device Coordination Group (MDCG 2024-2) released procedures for the updates of the European Medical Device Nomenclature. The EMDN, as established by Article 26 of Regulation (EU) 2017/745 – Medical Device Regulation (MDR) and Article 23 of Regulation (EU) 2017/746 - In Vitro Diagnostic medical devices Regulation (IVDR), will be annually reviewed and updated based on the practical use of the EMDN and feedback from its users.

Safety Reporting in Performance Studies of In Vitro Diagnostic Medical Devices under Regulation (EU) 2017/746

In April 2024, the Medical Device Coordination Group (MDCG 2024-4) released guidance on safety reporting in performance studies of in vitro diagnostic medical devices under Regulation (EU) 2017/746. Safety reporting in performance studies of in vitro diagnostic medical devices (IVDs) shall be performed in line with the requirements of IVDR.

The Appendix is provided for the Performance Study Summary Safety Reporting Form, Version 1.

Summary of Safety and Performance Template

In April 2024, the Medical Device Coordination Group (MDCG 2022-9/Rev. 1) released the Summary of Safety and Performance Template. This document provides clarification on SSP and when the safety and performance (SSP) for class C and D devices, other than devices for performance studies should be made available to patients.

Post-Market Surveillance and Vigilance (PMSV)

In January 2024, the Medical Device Coordination Group (MDCG 2024-1) released guidance on the vigilance system for CE-marked devices, including DSVG 00 Device Specific Vigilance Guidance (DSVG) Template. The aim of the DSVG is to harmonise vigilance reporting and provide guidance for manufacturers of Specific Devices. It provides further clarification for vigilance reporting of specific Devices to the relevant Competent Authority and should be read in conjunction with the requirements of Regulation (EU) 2017/745 on medical devices (MDR) and Regulation (EU) 2017/746 on in vitro diagnostic medical devices (IVDR).

This DSVG does not replace or extend any of those requirements.

MDCG 2024-1	Device Specific Vigilance Guidance (DSVG) Template	January 2024
MDCG 2024-1-1	DSVG 01 on Cardiac ablation	January 2024
MDCG 2024-1-2	DSVG 02 on Coronary stents	January 2024
MDCG 2024-1-3	DSVG 03 on Cardiac implantable electronic devices (CIEDs)	January 2024
MDCG 2024-1-4	DSVG 04 on Breast implants	January 2024

Overview of Language Requirements for Manufacturers of Medical Devices for the Information and Instructions that Accompany a Device in a Specific Country

On 17 January 2024, the European Commission and Member States have created MDR and IVDR tables. These tables aim to help manufacturers of medical devices and in vitro diagnostic medical devices, particularly small and medium-sized ones, understand the language requirements for the information and instructions that accompany a device in a specific country.

The tables provide an overview of the language requirements for each Member State. The Table provided for MDR - language requirements for manufacturers, Rev. 1 was updated in March 2024.

The United Kingdom

Roadmap Towards the Future Regulatory Framework for Medical Devices

The Medicines and Healthcare Products Regulatory Agency (MHRA) intends to introduce new regulations for medical devices that prioritise patient safety, give patients access to the medical devices they need and ensure the UK remains an attractive market for medical technology innovators. The approach to this reform was outlined in the government response to the 2021 consultation on the future regulation of medical devices in the UK. The government will ensure that there is a proportionate, phased approach to the implementation of the future regulatory framework, which supports system readiness and minimises the risk of supply disruption for UK patients. This guidance has been updated with a Roadmap towards the future regulatory framework for medical devices (published 9 January 2024) which sets out intended timescales for delivery of the future core regulations. The regulations will be delivered through four Statutory Instruments. It is intended that priority measures to enhance post-market surveillance will be put in place first in 2024, with core elements of the new framework expected to be in place in 2025.

The blog entitled Med Tech Regulatory Reform: The first steps towards a new framework for medical devices in the UK was published on 13 February 2024.

North America

United States of America

FDA Issues Draft Guidance on Select Updates for the Premarket Medical Device Submission on Cybersecurity

On 12 March 2024, the FDA issued the draft guidance Select Updates for the Premarket Cybersecurity Guidance: Section 524B of the FD&C Act. This draft guidance proposes updated recommendations to industry on quality system considerations for cyber devices and for documentation in device premarket submissions. This will apply to the premarket application or submission under any of the following pathways including 510(k), PMA, PDP, De Novo, or HDE for a device that meets the definition of a "cyber device," as defined in section 524B(c) of the FD&C Act.

FDA Published New Paper on Artificial Intelligence and Medical Products

On 15 March 2024, the FDA published its new paper, "Artificial Intelligence and Medical Products: How CBER, CDER, CDRH, and OCP are Working Together," which outlines specific focus areas regarding the development and use of AI across the medical product lifecycle. The paper helps further align and streamline the agency's work in AI. Read more about the agency's AI initiatives at the website. Artificial intelligence (AI) has the potential to revolutionize health care by advancing medical product development, improving patient care, and augmenting the capabilities of health care practitioners.

Aligned with its mission of protecting, promoting, and advancing public health, and building on the Agency's longstanding commitment to support innovative work in the development and regulation of medical products, the Food and Drug Administration's (FDA's) Center for Biologics Evaluation and Research (CBER), Center for Drug Evaluation and Research (CDER), Center for Devices and Radiological Health (CDRH), and Office of Combination Products (OCP) are jointly published this paper to provide greater transparency regarding how FDA's medical product Centers are collaborating to safeguard public health while fostering responsible and ethical innovation.

Fast-Tracked Approval for Medical Devices: Health Canada Expands Urgent Public Health Considerations

On 3 January 2024, the Regulations Amending the Medical Devices Regulations (Medical Devices for an Urgent Public Health Need) (the "Amended Regulations") came into force. They were accompanied by new Guidance on Medical devices for an urgent public health need("UPHN Guidance").

The Amended Regulations and UPHN Guidance enable access to the expedited authorization pathway for a medical device that addresses a public health need without relying on temporary measures. Part 1.1 of the Medical Devices Regulations (MDR) now provides an expedited authorization pathway.

OTHER "HOT" TOPICS FROM UNITED STATES

FDA Issues Revised Draft Guidance for Industry: Conducting Remote Regulatory Assessments Questions and Answers

On 25 January 2024, the FDA announced the availability of a revised draft guidance for industry titled Conducting Remote Regulatory Assessments Questions and Answers. The draft guidance, once finalized, will describe how the FDA intends to use RRAs for FDA-regulated products. The revised draft guidance reflects the FDA's consideration of comments to the July 2022 draft guidance, as well as revisions to align with recent changes in law concerning mandatory records requests.

An RRA is an examination of an FDA-regulated establishment and/or its records, conducted entirely remotely, to evaluate compliance with applicable FDA requirements. RRAs assist in protecting human and animal health, informing regulatory decisions, and verifying certain information submitted to the Agency. RRAs are a tool FDA may use to support regulatory decisions and oversight activities. However, an RRA is not an inspection.

FDA Releases Guidance on Data Monitoring Committees for Clinical Trial Management

The FDA released a proposed update to its guidance on DMCs on 13 February 2024, aiming to refine and modernize their role in this critical endeavor. The draft guidance provides recommendations to help clinical trial sponsors determine when a data monitoring committee (DMC) would be beneficial for managing clinical trials and what procedures and practices they should consider when using a DMC, significantly revising past guidance from FDA.

The draft guidance substantially revises FDA's 2006 guidance on Establishment and Operation of Clinical Trial Data Monitoring Committees and was prompted by changes in how DMCs are used in current clinical trials. Specifically, FDA notes there has been an increase in DMC use, a trend of longer and more detailed DMC charters, an expansion of DMC functions, and increased clinical trial globalization. Guidance introduces several noteworthy changes, each tailored to address specific needs, including assessing risk versus benefit, maintaining independence, and reducing bias, addressing dynamic designs, applying comprehensive documentation, unbiased statistical support and defining the analyses.

FDA Final Guidance Released on Expedited Safety Reports From IND-Exempt BA/BE Studies

FDA released on 4 April 2024, final guidance on "Electronic Submission of Expedited Safety Reports From IND-Exempt BA/BE Studies". In this guidance, instructions are provided for submitting expedited individual case safety reports (ICSRs) to FDA Adverse Event Reporting System (FAERS) from investigational new drug (IND)-exempt bioavailability (BA)/bioequivalence (BE) studies conducted to support abbreviated new drug applications (ANDAs).

About ClinChoice

ClinChoice is a global full-service CRO specializing in clinical development and functional solutions for pharmaceutical, biotechnology, medical device, and consumer health companies. We have over 28 years of proven high-quality delivery and results across all our services. With over 4,000 professionals in more than 20 countries across the Americas, Europe, and Asia-Pacific, we are positioned to fulfill our clients' business requirements locally and globally. We oer high-quality, full-service clinical development and post-marketing solutions. For our clients, it means a reliable partner and quality results.

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