Clinical Trials in Human Medicines: Management of Clinical Trials Impacted by the War in Ukraine

On 31 March 2022 the FDA published the advice to sponsors on management of clinical trials impacted by the war in Ukraine.

Sponsors can adjust the way they run clinical trials that have been affected by the war in Ukraine using the experience gained during the COVID-19 pandemic. They can also apply the approaches and flexibilities agreed in the context of the pandemic.

The European Commission, EMA and the Heads of Medicines Agencies (HMA) issued this initial advice for sponsors on 30 March 2022.

The Clinical Trials Coordination Group (an HMA group uniting clinical trials experts) is developing additional recommendations for sponsors.

EMA is developing recommendations on the methodological aspects relating to data from clinical trials that have been affected by the war.

EMA advises sponsors to also check any guidance available at national level.

Read more online

Emergency Use Authorization for Vaccines to Prevent COVID-19

On 31 March 2022 the FDA published final guidance for industry.

FDA is issuing this guidance to provide sponsors of requests for Emergency Use Authorization (EUA) for COVID-19 vaccines with recommendations regarding the data and information needed to support the issuance of an EUA under section 564 of the FD&C Act (21 U.S.C. 360bbb-3) for an investigational vaccine to prevent COVID-19 for the duration of the COVID-19 public health emergency. This document supersedes the guidance of the same title issued in May 2021 (which superseded the guidance of the same title issued October 2020 and reissued February 2021).

Read more online

ICH Guideline E14/S7B: Clinical and Nonclinical Evaluation of QT/QTc Interval Prolongation and Proarrhythmic Potential —Q&A Step 5

On 24 March 2022 the EMA published the ICH Q&A guideline E14/S7B.

This Q&A guideline concerns the clinical evaluation of QT/QTc interval prolongation and proarrhythmic potential for non-antiarrhythmic medicinal products. It addresses the electrocardiogram methodology, gender, positive control, study design, use of concentration response modeling of QTc data and electrocardiogram monitoring in late stage clinical trials.

Read the pdf

Announcement on the Release of Guidelines for the Preparation of Annual Self-inspection Reports for Medical Device Quality Management Systems (No. 13 of 2022)

On 24 March 2022 the Chinese NMPA announced the release of guidelines on annual self-inspection reports for medical device quality management systems effective 1 May 2022.

In order to strengthen the supervision of medical device production and ensure the safety and effectiveness of medical devices, according to the second paragraph of Article 35 of the Regulations on the Supervision and Administration of Medical Devices, the State Drug Administration organized and revised the compilation of the annual self-inspection report on the medical device quality management system.

Read more online

"Measures for the Supervision and Administration of Medical Device Production" and "Measures for the Supervision and Administration of Medical Device Operation"

On 23 March 2022 the Chinese NMPA published two guidelines on medical device production and operation.

The Chinese State Administration for Market Regulation issued the revised guidance on "Measures for the Supervision and Administration of Medical Device Production" and "Measures for the Supervision and Administration of Medical Device Operation", effective May 1, 2022.

Read more online

An Acceptable Circular of Information for the Use of Human Blood and Blood Components

On 22 March 2022 the FDA published final guidance for industry.

FDA, Center for Biologics Evaluation and Research, are recognizing as acceptable for use by manufacturers of blood and blood components intended for transfusion, the document entitled “Circular of Information for the Use of Human Blood and Blood Components,” dated December 2021 (December 2021 Circular). The December 2021 Circular provides specific

labeling instructions for the administration and use of blood and blood components intended for transfusion. We believe that the December 2021 Circular will assist you in complying with labeling requirements under 21 CFR 606.122. The requirements under 21 CFR 606.122 specify that a circular of information must be available for distribution with blood and blood components intended for transfusion. Section 606.122 further specifies the information that is required in the circular of information. This guidance supersedes the guidance of the same title updated December 2017.

Read more online

Certain Ophthalmic Products: Policy Regarding Compliance With 21 CFR Part 4

On 22 March 2022 the FDA published final guidance for industry.

This guidance is intended to provide information to applicants and manufacturers regarding compliance with the requirements in part 4 (21 CFR part 4) for ophthalmic drugs packaged with eye cups, eye droppers, or other dispensers. This guidance applies to products with pending applications, approved products, and products marketed pursuant to section 505G of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 355h) without an approved application under section 505 of the FD&C Act (21 U.S.C. 355) (commonly referred to as over-the-counter (OTC) monograph drugs).

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Updated EMA Post-authorization Procedural Advice for Users of the Centralized Procedure

On 18 March 2022 the EMA updated the EudraVigilance registration manual.

This guidance document addresses a number of questions which marketing authorization holders (MAHs) may have on post-authorization procedures. It provides an overview of the Agency's position on issues, which are typically addressed in discussions or meetings with MAHs in the post-authorization phase.

Read the pdf

Updated EMA EudraVigilance Registration Manual

On 17 March 2022 the EMA updated the EudraVigilance registration manual.

To set-up a new organization in EudraVigilance Production or XCOMP (Test system), a series of steps need to be followed. Once the QPPV or RP is registered for the Production EudraVigilance system they will automatically also be registered for an XCOMP test account for the same organization.

Read the pdf

Should you be interested in a partnership where you will add your personal or your company's technical and professional expertise, please contact any of the Partners as a starting point of a dialogue or write an e-Mail to info@wsqms.com.

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Bioavailability Studies Submitted in NDAs or INDs – General Considerations

On 14 April 2022 the FDA published final guidance on general considerations for bioavailability studies submitted in NDAs or INDs.

This guidance provides recommendations to sponsors and applicants submitting bioavailability (BA) information for drug products in investigational new drug applications (INDs), new drug applications (NDAs), and NDA supplements. This guidance contains recommendations on how to meet the BA requirements set forth in 21 CFR part 320 as they apply to dosage forms intended for oral administration. These dosage forms include tablets, capsules, solutions, suspensions, conventional (e.g., immediate-release (IR) drug products) and modified-release (MR) (e.g., extended-release (ER), delayed-release (DR)) drug products. The guidance is also applicable to non-orally administered drug products when it is appropriate to rely on systemic exposure measures to determine the BA of a drug (e.g., transdermal delivery systems and certain vaginal, rectal, and nasal drug products).

The guidance provides recommendations on conducting BA studies during the investigational period for a drug intended to be submitted for approval in an NDA and bioequivalence (BE) studies during the postapproval period for certain changes to drug products with an approved NDA.

Read more online

Points to Consider on the Impact of the War in Ukraine on Methodological Aspects of Ongoing Clinical Trials

On 13 April 2022 the EMA published guidance on actions for ongoing clinical trials affected by the war in Ukraine.

This guidance covers actions that sponsors of ongoing clinical trials affected by the war in Ukraine can take to help ensure the integrity of their studies and the interpretation of the study results while ensuring the safety of trial participants is a top priority.

EMA strongly encourages sponsors to capture data affected and unaffected by the war, and to use the 'estimand framework' described in the ICH E9 (R1) guideline for dealing with events impacting the trial.

Read the pdf

Detailed Guidance on ICSRs in the Context of COVID-19

On 13 April 2022 the EMA published updated guidance revision 3, clarifying the validity and coding of ICSRs linked to COVID-19.

This detailed guidance document provides recommendations relevant to the processing and submission of Individual Case Safety Reports (ICSRs) associated with medicinal products used for the treatment or prevention of COVID-19 infection, taking into account:

- the Notice to stakeholders published by the European Commission;
- the guidance regarding COVID-19 related terms published by the MedDRA MSSO; and
- the introduction of COVID-19 related terms since the updated MedDRA version 23.0.

Read the pdf

Questions and Answers Document – Regulation (EU) 536/2014

On 13 April 2022 the European Commission published Q&A guidance on Clinical Trials Regulation (EU) 536/2014, version 6.

This document aims at informing on the technical aspects of Commission Clinical Trials Regulation (EU) No 356/2014 with a view to facilitating its implementation. It sets out frequently-asked 'questions and answers' regarding the implementation of the rules on clinical trials. All updates to this questions and answers document are presented and discussed within the “Expert group on clinical trials” and reflects the view of the group. This group is chaired by the Commission and is composed of representatives of all EU Member States and EEA contracting parties.

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Updated IRIS Guide for Applicants

On 13 April 2022 the EMA published version 2.8 of the IRIS guide on how to create and submit scientific applications, for industry and individual applicants.

This guide has been produced to show applicants how to use the IRIS platform to prepare and submit an application and/or data for a scientific procedure (orphan designation application, scientific advice, ITF briefing meeting requests, marketing status reports, inspections and veterinary signal management) and related activities.

Read the pdf

Diversity Plans to Improve Enrollment of Participants from Underrepresented Racial and Ethnic Populations in Clinical Trials

On 13 April 2022 the FDA announced the availability of the draft guidance for industry.

The purpose of this guidance is to provide recommendations to sponsors developing medical products on the approach for developing a Race and Ethnicity Diversity Plan (referred to as the "Plan") to enroll adequate numbers of participants in clinical trials from underrepresented racial and ethnic populations in the United States.

Read more online

Updated Frequently Asked Questions about Parallel Distribution

On 12 April 2022 the EMA updated the FAQ/General Question No. 22.

Article 76 of Directive 2001/83/EC and Article 102 (5) of Regulation (EU) 2019/6 imposes the individual obligation on the distributor who intends to import a medicinal product from another Member State to submit the notification to the marketing authorization holder and the Agency in case of medicinal products which have been granted an authorization pursuant to Regulation (EC) No 726/2004.

However, if as a result of a merger/acquisition the parallel distributor is dissolved or if it changes the legal form, there is an assumption of continuity of the legal entity. In these situations, a notification of a bulk change ('Reassignment of notices for Parallel Distribution') would need to be submitted.

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Providing Regulatory Submissions in Electronic and Non-Electronic Format—Promotional Labeling and Advertising Materials for Human Prescription Drugs

On 11 April 2022 the FDA published the final guidance for industry.

This guidance pertains to submissions of promotional materials for human prescription drugs (drugs) to the FDA made by manufacturers, packers, and distributors (firms), whether the applicant or an entity acting on behalf of the applicant. Specifically, this guidance pertains to submissions made to the Office of Prescription Drug Promotion (OPDP) in the Center for Drug Evaluation and Research (CDER) and the Advertising and Promotional Labeling Branch (APLB) in the Center for Biologics Evaluation and Research (CBER). This guidance also explains certain aspects of electronic submission of promotional materials in module 1 of the electronic common technical document (eCTD), using version 3.3 or higher of the us-regional-backbone file.

Read more online

Draft Guidance Document on How to Approach the Protection of Personal Data and Commercially Confidential Information in Documents Uploaded and Published in the Clinical Trial Information System (CTIS)

On 8 April 2022 the EMA published draft guidance on protection of personal data and commercially confidential information in CTIS.

This guidance document focuses on the following areas:

- Description of the CTIS structure and components including a description of the functionalities and publication rules for clinical trials information submitted to the CTIS (chapter 2)
- The protection of personal data as part of the clinical trial information submitted to CTIS (chapter 3)
- The protection of commercially confidential information (CCI) as part of the clinical trial information submitted to CTIS (chapter 4)
- The protection of personal data and CCI in inspection reports (chapter 5)

Read the pdf

Cybersecurity in Medical Devices: Quality System Considerations and Content of Premarket Submissions

On 8 April 2022 the FDA published draft guidance on cybersecurity in medical devices for industry and FDA staff. Comments may be submitted until 7 Jul 2022.

This guidance is intended to provide recommendations to industry regarding cybersecurity device design, labeling, and the documentation that FDA recommends be included in premarket submissions for devices with cybersecurity risk. These recommendations can facilitate an efficient premarket review process and help ensure that marketed medical devices are sufficiently resilient to cybersecurity threats.

Read more online

General Considerations for Clinical Studies – E8(R1)

On 7 April 2022 the FDA published the final guidance on ICH E8(R1) general considerations for clinical studies.

The ICH has the mission of achieving greater regulatory harmonization worldwide to ensure that safe, effective, and high-quality medicines are developed, registered, and maintained in the most resource-efficient manner. By harmonizing the regulatory expectations in regions around the world, ICH guidelines have substantially reduced duplicative clinical studies, prevented unnecessary animal studies, standardized safety reporting and marketing application submissions, and contributed to many other improvements in the quality of global drug development and manufacturing and the products available to patients.

Read more online

Use of Whole Slide Imaging in Nonclinical Toxicology Studies: Questions and Answers

On 7 April 2022 the FDA published the draft Q&A guidance for industry. Comments may be submitted until 7 Jun 2022.

This guidance provides information to sponsors and nonclinical laboratories regarding the use and management of whole slide images used during histopathology assessment and/or pathology peer review performed for good laboratory practice (GLP)-compliant nonclinical toxicology studies using non-human specimens. When whole slide imaging is used as part of

a nonclinical study conducted in compliance with the GLP regulations, adequate documentation is critical. The FDA's expectations regarding documentation practices during generation, use, and retention of whole slide images have not been clearly defined and vary among nonclinical testing facilities. This question-and-answer document is intended to clarify FDA's recommendations concerning the management, documentation, and use of whole slide imaging in histopathology assessment and/or pathology peer review for nonclinical studies conducted in compliance with the GLP regulations.

Read more online

Chronic Hepatitis B Virus Infection: Developing Drugs for Treatment

On 6 April 2022 the FDA published the final guidance on developing drugs for chronic hepatitis B virus infection.

The purpose of this guidance is to assist sponsors in the clinical development of drugs and biologics for the treatment of chronic hepatitis B virus (HBV) infection from the initial investigational new drug application (IND) through the new drug application (NDA)/biologics license application (BLA) and post-marketing phases.

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M7(R2) Addendum: Application of The Principles of the ICH M7 Guideline to Calculation of Compound-Specific Acceptable Intakes

On 6 April 2022 the FDA published draft guidance on ICH M7 addendum for industry.

The ICH has the mission of achieving greater regulatory harmonization worldwide to ensure that safe, effective, and high-quality medicines are developed, registered, and maintained in the most resource-efficient manner. By harmonizing the regulatory expectations in regions around the world, ICH guidelines have substantially reduced duplicative clinical studies, prevented unnecessary animal studies, standardized safety reporting and marketing application submissions, and contributed to many other improvements in the quality of global drug development and manufacturing and the products available to patients.

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Guidance for Applicants/MAHs Involved in GMP and GCP Inspections Coordinated by EMA

On 2 April 2022 the EMA published guidance for applicants/MAHs involved in GMP and GCP inspections.

These GMP and GCP inspections are requested by the Committee for Medicinal Products for Human Use (CHMP) in order to verify compliance with Good Manufacturing Practice of sites responsible for the manufacture of centrally authorized products and to verify compliance with Good Clinical Practice for centrally authorized products.

The details of each of the inspections adopted by the Committee(s), including the contact details of the persons in the inspection services who will be involved can be found in the IRIS Industry portal.

Read the pdf

Good Clinical Practice for Medical Devices

On 2 April 2022 the Chinese NMPA issued an announcement for the GMP for clinical trials of medical devices (No. 28 of 2022).

According to the "Regulations on the Supervision and Administration of Medical Devices" (Order No. 739 of the State Council) and the "Administrative Measures for Registration and Filing of Medical Devices" (Order No. 47 of the State Administration for Market Regulation), "Administrative Measures for Registration and Filing of In Vitro Diagnostic Reagents" (Order No. 48 of the State Administration for Market Regulation), the NMPA, in conjunction with the National Health Commission, organized the revision of the "Good Clinical Practices for Medical Devices", which are hereby promulgated and effective May 1, 2022.

Read more online

Update to Guidance document "Information on PSUR / PBRER submission"

Effective 1 April 2022, Swissmedic updated the Guidance document, allowing a transition period of 30 days.

The following points have been expanded on or clarified in section 5.2:

- PSURs are generally submitted once a year as a 12-month report. It is possible to modify the submission cycle (e.g. submission every 6 months, submission every 2 years).
- In future, modification of the reporting period will be via notification with brief supporting information (not an application as previously) by the marketing authorization holder to: riskmanagement@swissmedic.ch
- As a general rule, only one PSUR/PBRER document will be accepted per application.

Clarifications in section 5.4 regarding submission of RMP Updates have also been expanded on.

This guidance document enters into force on 1 April 2022 with a transitional period of 30 days.

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