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REGULATORY

NEWSLETTER N.35
July - September 2021

CROMSOURCE is an international provider of outsourced services to the pharmaceutical, biotechnology and medical device industries, specialised in clinical development and staffing solutions.

Contents

MEDICINAL PRODUCTS/DRUGS

Europe

News from the European Commission

The European Commission Adopts Adequacy Decisions for the UK

The European Commission adopted two adequacy decisions for the United Kingdom - one under the General Data Protection Regulation (GDPR) and the other for the Law Enforcement Directive. This decision contains talking about a fundamental right of data information European Union (EU) citizens that Britain have a duty to protect. The UK is also subject to the jurisdiction of the European Court of Human Rights and it must adhere to the European Convention of Human Rights for the Protection of Individuals.

The UK's data protection system continues to be based on the same rules that were applicable when the UK was a Member State of the EU. The UK has fully incorporated the principles, rights and obligations of the GDPR and the Law Enforcement Directive into its post-Brexit legal system.

For the first time, the adequacy decisions include a so-called 'sunset clause', which strictly limits their duration. This means that the decisions will automatically expire four years after their entry into force. After that period, the adequacy findings might be renewed. Should the Commission decide to renew the adequacy finding, the adoption process would start again.

The Commission also found that any transfer of data to be carried out in the context of its implementation has to comply with the data protection requirements of the transferring party (for the EU, the requirements of the GDPR and the Law Enforcement Directive).

The UK Government has stated that transfers of data from the UK to the EEA are permitted.

The UK is England, Scotland, Wales, and Northern Ireland. It does not include Crown dependencies or UK overseas territories, including Gibraltar. The UK government will allow transfers to Gibraltar to continue.

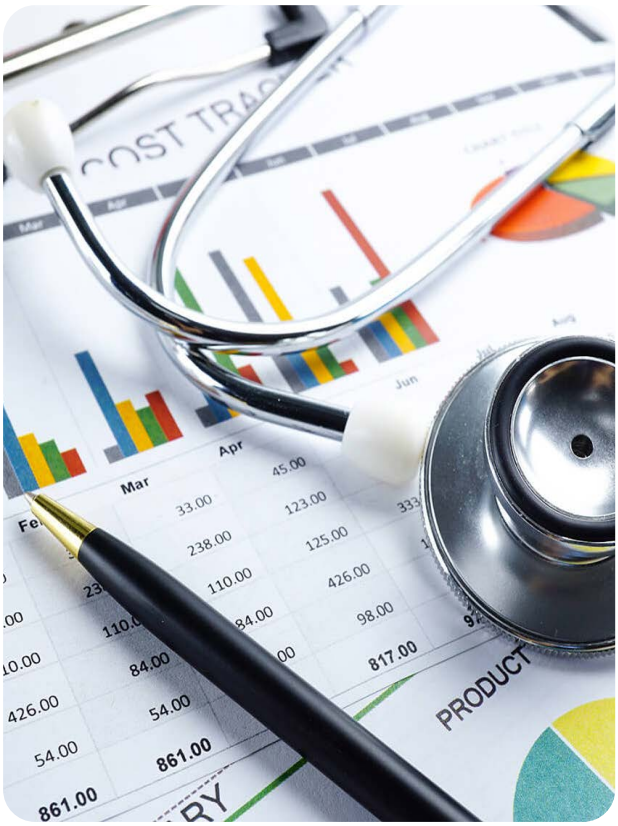
Moreover, the Health Research Authority (HRA), the organization which regulates the health and social care research in England, in the UK and approves clinical trials, informed that, no action is required by sponsors of clinical trials or participating sites.

News from the European Medicines Agency (EMA)

The source of each news item below is the EMA website: https://www.ema.europa.eu/

New EU Clinical Trials Regulation Date of Application

The European Commission confirmed 31 January 2022 as the date of entry into application of the Clinical Trials Regulation (EU) No 536/2014 (EU CTR) and the go-live of Clinical Trials Information System (CTIS). The EU CTR will replace the existing Clinical Trials Directive No. 2001/20/EC (CTD) and national legislation that was put in place to implement it.



The EU CTR will also replace the Voluntary Harmonization Procedure (VHP) which was a repository of the Regulation throughout 12 years and gave stakeholders and Member States the opportunity to experience international harmonization of clinical trials in the Europe Union (EU).

The EU CTR will automatically apply to all Member States on the Date of Application (DoA) 31 January 2022, even if not transposed into local law. However, there will also be a 3-year transition period that starts on the CTIS go-live date, 31 January 2022.

During the first year starting from CTIS go-live date until 31 January 2023, sponsors will be able to choose whether to apply for a new Clinical Trial Application (CTA) under the regime of the CTD including using EudraCT or to apply under the new EU CTR using CTIS.

During the second and third year until 31 January 2025 the EudraCT will not be available for new CTAs. From 31 January 2023 all new CTAs must be submitted under the EU CTR using CTIS. CTAs that were submitted under the CTD prior to 31 January 2023, will be able to continue to run and complete under that Directive for an additional two years maximum.

By 31 January 2025 trials submitted under the CTD must either have ended in the EU/European Economic Area (EEA) or have been transitioned to the EU CTR via CTIS. If sponsors are running trials that they expect to continue beyond 31 January 2025, sponsors will need to transition them to the EU CTR before the transition period expires.

The Sponsor handbook informs that transition applications will usually take up to 60 days to be assessed and approved, or less, as these trials have already been approved under the Directive. However, Member States Concerned (MSC) are permitted to raise Request for information (RFI) on the transition application.

Transition applications can be submitted at any time during the 3-year transition period.

Once a clinical trial has switched to the EU CTR, all the requirements of the EU CTR will apply from the date of approval of the transition application under the EU CTR.

The main objectives of the EU CTR are harmonization of the Clinical Trial Application (CTA) process across the European Union, greater transparency in clinical processes and data, and enhanced safety and efficacy of drugs.

The new Regulation will bring certain key changes to the clinical trial application process in the EU like:

- Harmonised dossier - Part I (Scientific, Global) and Part II (Ethic, National)
- Centralised system for submission managed by EMA - Clinical Trials Information System
- Strictly defined timelines (transparent, reliable, short (maximum 12 calendar days to respond by Sponsor on RFI)
- Work sharing between "Reporting Member State (RMS)" and "Member States Concerned (MSC)"
- Process for "single decision" is within the remit of the MSC (National Competent Authority and Ethics Committee)
- Fully electronic CTA process
- Documents and information public by default

Further information of latest updates regarding *EU CTR* is provided in section OTHER 'HOT' TOPICS IN EUROPE.

Reflection Paper on Statistical Methodology for the Comparative Assessment of Quality Attributes in Drug Development

The EMA adapted a reflection paper that identifies specific areas where the quantitative comparative evaluation of drug product quality characteristics plays an important role from the regulatory perspective.

This document focussed on methodological aspects in relation to statistical data comparison approaches for pre- and post-manufacturing changes, biosimilar development, and generics' development. These comparative data are aimed at analyses to demonstrate that two drug products (or drug substances) stemming from two different manufacturing processes are similar with regard to relevant Quality Attributes (QAs).

The outcome of such comparative investigations has an impact on decisions concerning subsequent development steps. This paper aims to reflect under which circumstances, and to what extent, the implementation of inferential statistical methodology can assist comparative evaluation of QA data.

A two-step problem description approach is introduced: firstly, consideration needs to be given to what would constitute an agreeable 'similarity condition' based on assumed underlying data distributions; subsequently, a suitable similarity criterion needs to be identified and chosen to assess whether the similarity condition truly holds.

EMA Adopts Guideline on Quality Documentation for Drug-Device Combination Products

The EMA published guidance on requirements for quality documentation for medicinal products when used with a medical device. The guidance will come into effect on 01 January 2022.

This guideline describes the information that should be presented in the Quality part of a marketing authorisation dossier for a medicinal product when it is used with a medical device, or device part, and submitted following Directive 2001/83/EC and/or Regulation (EC) 726/2004.

They have described here clarification regarding documentation for medicinal products in respect of a marketing authorisation application (MAA) or post-authorisation applications. It considers the requirements, as laid down in Directive 2001/83/EC, /or Regulation (EC) 726/2004 and Medical Devices Regulation (EU) 2017/745 (MDR).

Some of the general principles mentioned in the document are related to medicinal products where the medical device and/or device part and the medicinal product form an integrated product that is not reusable (called integral) and where the action of the medicinal product is principal; medicinal products placed on the market by the Marketing Authorisation Holder (MAH), where the medical device is packed together with the medicinal product; and medicinal products, where the product information refers to a specific medical device to be used with the medicinal product, and the medical device is obtained separately by the user of the medicinal product.

News from Individual Countries

The United Kingdom

Combined Ways of Working (CWoW) Mandatory from 01 January 2022

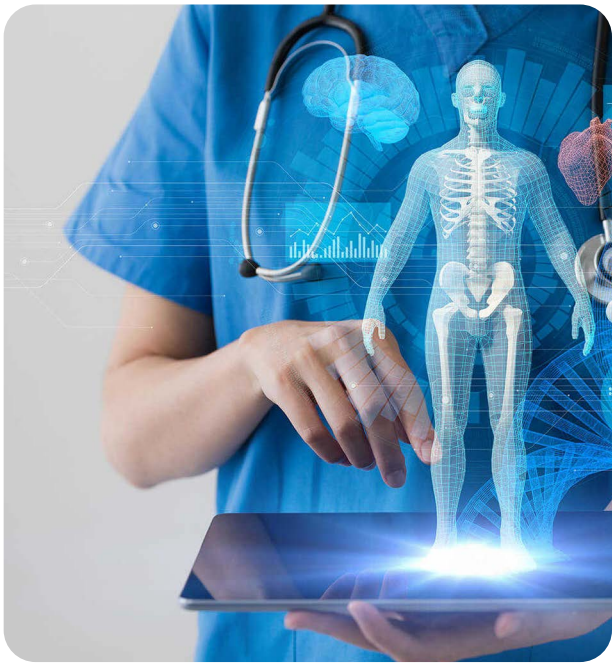
The Health Research Authority (HRA) informed that combined review service of clinical trials, formerly known as Combined Ways of Working (CWoW) will be mandatory from 01 January 2022. Combined review offers a single application route and co-ordinated review leading to a single UK decision for Clinical Trials of Investigational Medicinal Products (CTIMPs).

From 01 January 2022, the combined review service will also become the way for all combined trials of an investigational medicinal product and an investigational medical device.

The CTIMP applications via combined review must be submitted using a new part of the Integrated Research Application System (IRAS) and should not be started in the standard part of IRAS. More information and step by step guide to use IRAS for combined review are available here.

Updated Guidance for Remote Monitoring

The Medicines and Healthcare products Regulatory Agency (MHRA) updated guidance for remote monitoring for clinical trials during Coronavirus (COVID-19).



Switzerland

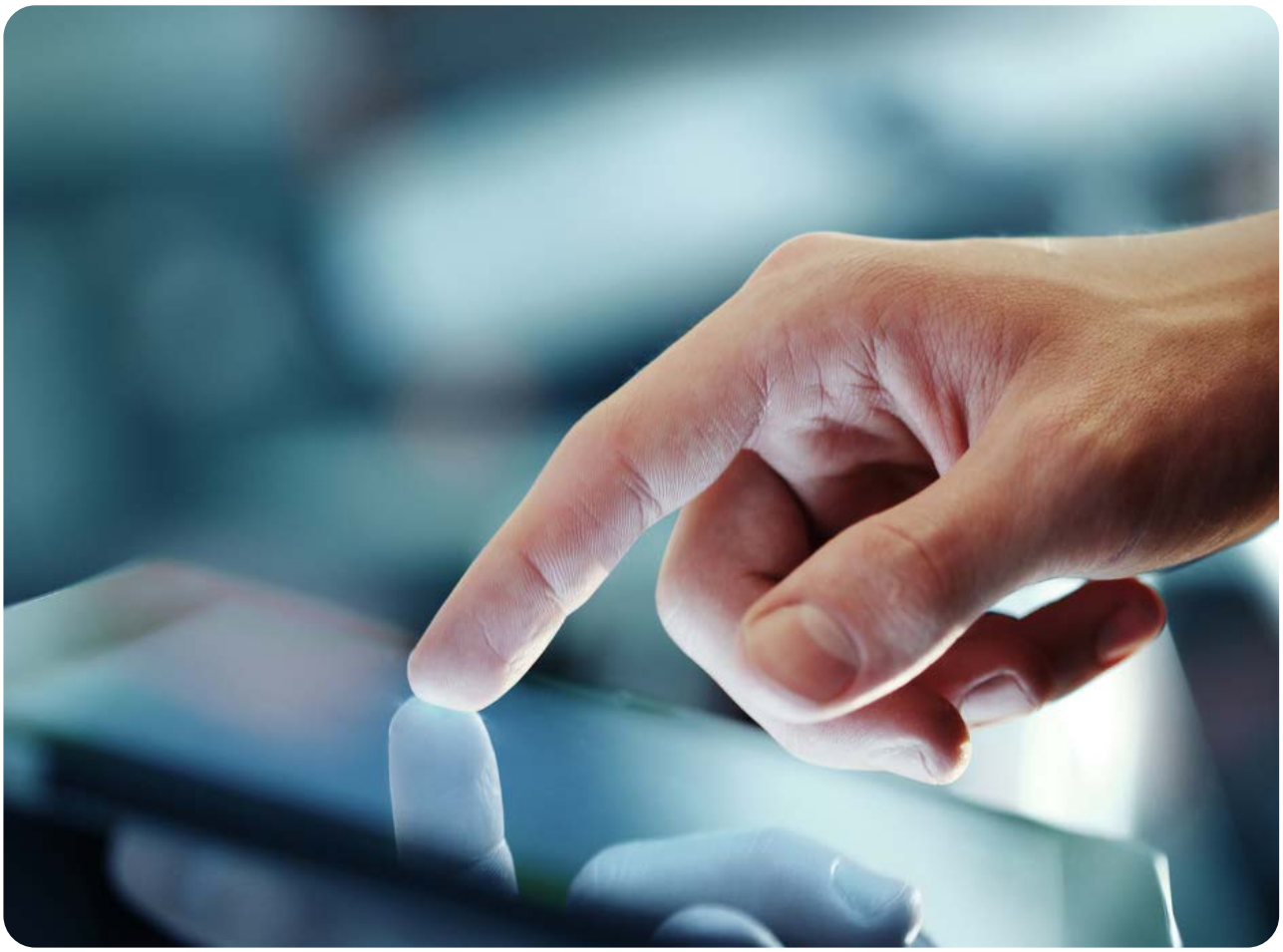
New Format for Authorisation Applications, Substantial Amendments, Notifications, SUSARs and Other Reports Regarding Clinical Trials with Medicinal Products

The Swissmedic, the Swiss Agency for Therapeutic Products, informed that from 13 September 2021, all new applications must be submitted using a new folder structure (eDoc-file structure), a new application form (FO submission form), and a new address for submissions. From 13 September 2021 only formal aspects of Clinical Trial Application (CTA) changed, the legal requirements remain the same.

The target of the changes is to prepare the Swissmedic for electronic submission procedure. The Agency informed that purely paperless submissions will not yet be possible as of 13 September 2021. The applicants still have to make submissions on paper and on CD even after 13 September 2021, confirming that the files on the CD are identical with the paper documents.

In addition, as of 13 September 2021, the usage of USB-Sticks is prohibited, and it is not possible anymore to perform a submission or application via e-mail. Moreover, electronic documents should be transferred via a specific personal account of the Filetransfer Service tool which if not already in possession by the applicant, the contact with the Swissmedic at ct.medicinalproducts@swissmedic.ch is required.

As of 13 September 2021, any submissions according to the old submission procedure will be deemed to be formally deficient by the Agency.



North America

United States of America

FDA Provides New Draft Guidance on Premarket Submissions for Device Software Functions

As of 03 November 2021, the US Food and Drug Administration (FDA) is making available the draft guidance Content of Premarket Submissions for Device Software Functions intended to provide information regarding the recommended documentation to include in premarket submissions for the FDA to evaluate the safety and effectiveness of device software functions.

The proposed recommendations in this draft guidance document pertain to device software functions, including both software in a medical device (SiMD) and software as a medical device (SaMD), and describe a subset of information that would be typically generated and documented during software design, development, verification and validation.

When final, this guidance will replace the FDA's Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices issued on 11 May 2005 and will update the FDA's recommendations on the appropriate documentation for the review of device software functions in premarket submissions.

The FDA committed to publish this draft revised version of the "Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices" as part of the MDUFA IV Digital Health commitments.

Canada

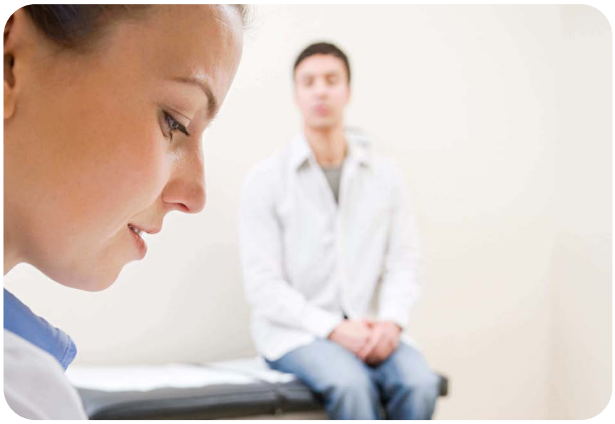
Alignment of Clinical Trial Records Retention Timelines

Health Canada proposes to reduce the current records retention requirements in the Food and Drug Regulations and the Natural Health Products Regulations from a minimum of 25 years to a minimum of 15 years, with certain exceptions, for all clinical trials of drugs involving human subjects. This is described in Health Canada's Forward Regulatory Plan: 2021-2023.

The regulatory amendments would reduce the regulatory burden on the industry conducting clinical trials in Canada, encouraging this sector to develop innovative drugs in Canada by providing cost savings as an incentive. This proposed amendment would reduce regulatory burden to better support the conduct of clinical trials in Canada without compromising the health and safety of Canadians.

This regulatory initiative was identified in the Fall 2018 Economic Statement and by Health Canada in its Health and Biosciences Sector Regulatory Review Roadmap. This proposal would improve alignment of the records retention requirements for clinical trials in Canada with international standards prescribed by other global health regulators regarding oversight and public access to information on clinical trials.

This proposal would not limit any provincial or territorial law or regulation, including any professional regulations enacted in accordance with a provincial or territorial enabling statute as part of the practice of medicine that may require longer records retention timeframes.



MEDICAL DEVICES

EUROPE

News from the European Commission

The European Commission Proposal Amending IVDR as Regards Transitional Provisions for Certain in vitro Diagnostic Medical Devices and Deferred Application of Requirements for in-House Devices

The European Commission published a proposal for a Regulation of the European Parliament and of the Council amending Regulation (EU) 2017/746 as regards transitional provisions for certain in vitro diagnostic medical devices and deferred application of the in-house device requirements. This Regulation aims to amend the transitional provisions, allowing the requirements of the Regulation to be phased in, for exceptional reasons in the context of the COVID-19 pandemic.

The new Regulation (EU) 2017/746 on in vitro diagnostic medical devices (IVDR) will enter into force on 26 May 2022 and will amend the existing Directive 98/79/EC and also implement significant changes in the in vitro diagnostic medical device sector. One of the main changes will be the introduction of inspections of in vitro diagnostic medical devices by notified bodies. The European Parliament has called on the Commission to present an urgent legislative proposal to extend the existing transitional period for devices certified under Directive 98/79/EC in order to facilitate the transition to the new regulatory framework and ensure the availability of in vitro diagnostic medical devices on the EU market. The proposal outlines the legal basis, subsidiarity and proportionality, and furthermore presents market research conducted in 2021 that demonstrates the need for legislative action. The proposal also ensures that the proposed action has no budgetary impact.

The new Regulation proposal does not change the date of application of IVDR which remains the same, i.e., 26 May 2022. See also a press release and Q&A.

Further information of latest updates regarding Medical Device Regulation (MDR) and In Vitro Diagnostic Medical Device Regulation (IVDR) is provided in section OTHER 'HOT' TOPICS IN EUROPE.

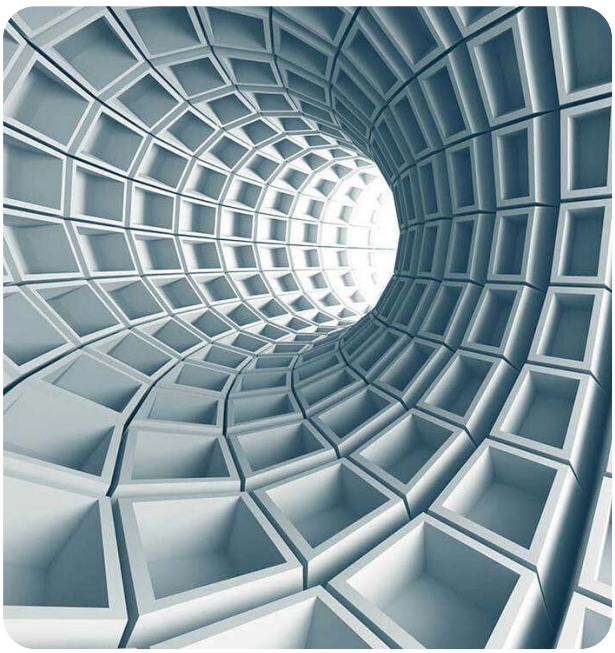
Helsinki Procedure for Borderline and Classification under MDR & IVDR

Helsinki Procedure 2021 applies to exchange of information between medical device competent authorities on borderline and classification cases. The purpose of the system is to allow consultation among competent authorities (CAs) on borderline and classification issues concerning medical devices and to ensure that appropriate guidance is published in the Manual on Borderline & Classification for Medical Devices. The main aspects of the procedure are presented in the form of a diagram. The diagram gives an overview of the procedure with flows A-F and many subsections.

Harmonised Standards for the MDR and IVDR - First Publications in the OJEU

The European Commission published in the Official Journal of the European Union (OJEU) harmonised European standards on 19 July 2021 for the Medical Device Regulation (MDR) and on 20 July 2021 for the In Vitro Diagnostic Medical Devices Regulation (IVDR). More references will be published by the Commission in the coming months.

More about harmonised European standards for medical devices is available here and MDCG 2021-5 – guidance.



News from Individual Countries

Austria

The New Fees Since 01 August 2021

The Austrian Federal Office for Safety in Health Care (BASG), the Austrian Agency informed about new fees for clinical trials with medical devices submitted in accordance with Medical Device Regulation (EU) 2017/745 (MDR). The BASG informed that the same fee will apply for academic and commercial clinical trials for initial application and substantial amendments. The fee reduction applies only for performance evaluation studies and its amendments. Fee rate - BASG

United Kingdom

Clinical Investigations Coordinated Assessment - Phase of the Pilot

The Medicines and Healthcare products Regulatory Agency (MHRA) together with the Health Research Authority (HRA) are working on a new pilot coordinated assessment pathway which will streamline the review of clinical investigations involving medical devices.

During this pilot phase, the MHRA review and the Research Ethics Committee (REC) review will be done in parallel, and information will be shared. There will be no change to the application forms or method of submission. However, anyone who is interested in taking part in the pilot, the individual needs to contact the MHRA by emailing Devices.Regulatory@mhra.gov.uk with "MHRA/HRA Coordinated assessment pathway pilot" in the subject line. The pilot pathway is intended to develop and test a coordinated review of applications to the MHRA and REC to improve efficiency, streamline approval and reduce approval time in the UK.

North America

United States of America

FDA Participates in New 'Collaborative Communities' to Address Emerging Challenges in Medical Devices

On 04 August 2021, the U.S. Food and Drug Administration (FDA) announced participation in several new collaborative communities aimed at addressing challenges in patient health care. Collaborative communities are a continuing forum where private and public sector representatives of the community work together on medical device challenges to achieve common objectives and outcomes.

The FDA currently participates in 12 collaborative communities, which are established, managed and controlled by external stakeholders. Collectively these communities are charting paths to accelerate and address regulatory science and other knowledge gaps to aid in medical device review and oversight. They may also impact the delivery of healthcare and change clinical care paradigms.

The most recent collaborations focus on topics such as: medical device development and product quality; understanding of valvular heart disease; innovations in digital pathology; reducing rates of intended self-injury and suicidal acts by people with diabetes; and strategies to increase the awareness, understanding and participation of racial and ethnic minorities in the medical technology industry. The FDA participates in these collaborative communities:

- Collaborative Community on Ophthalmic Imaging
- National Evaluation System for health Technology Coordinating Center (NESTcc) Collaborative Community
- Standardizing Laboratory Practices in Pharmacogenomics Initiative (STRIPE) Collaborative Community
- International Liquid Biopsy Standardization Alliance (ILSA)
- Xavier Artificial Intelligence (AI) World Consortium
- Case for Quality Collaborative Community
- Heart Valve Collaboratory (HVC)
- Wound Care Collaborative Community
- Pathology Innovation Collaborative Community (PICC)
- REducing SuiCide Rates Amongst IndividUals with DiabEtes (RESCUE) Collaborative Community
- MedTech Color Collaborative Community on Diversity and Inclusion in Medical Device Product Development and Clinical Research (MedTech Color Collaborative Community)
- Digital Health Measurement Collaborative Community (DATAcc)

Collaborative communities are convened by interested stakeholders and may exist indefinitely, produce deliverables as needed and tackle challenges with broad impacts. The FDA does not establish, lead or operate collaborative communities, nor are collaborative communities intended to advise the FDA. Instead, the FDA may participate in the community in order to contribute its knowledge and perspective to discussions of public health challenges and solutions.

Canada

Guidance Document: Classification of Products at the Drug-Medical Device Interface

Health Canada releases guidance document on 21 July 2021 entitled Updated: Guidance Document: Classification of Products at the Drug-Medical Device Interface that was first published on 30 January 2013 as "Factors Influencing the Classification of Products at the Drug-Medical Device Interface." The present revision is intended to reflect the recently implemented Ministerial Schedule, enacted through the Budget Implementation Act (BIA) in 2019.

The new authorities allow the Minister to determine a single set of regulations that would apply to a health product that simultaneously meets more than one of the definitions outlined in the Food and Drugs Act (F&DA) (i.e., drug, food, device, or cosmetic). The new Schedule is intended to improve consistency, predictability, and transparency of classification decisions for industry stakeholders.

The classification of a health product determines which set of regulations will be applied. The majority of products can be readily classified according to the definitions in section 2 of the F&DA and its associated regulations. Although, it is sometimes difficult to determine which set of regulations apply. Classification guidance documents describe the factors that influence these decisions made by Health Canada, and are intended to increase transparency and predictability.

This document addresses the classification of two health product groups (i.e., medical devices and drugs).

Health Canada's Proposal for Clinical Trials Regulatory Modernization

Health Canada opened a consultation on its proposal to modernize the regulatory framework for clinical trials related to human drugs, medical devices, non-prescription drugs, and natural health products to seek feedback from key stakeholders to validate and inform further policy development. This future policy is part of the Targeted Regulatory Review – Regulatory roadmap development under the Regulatory Review of Drugs and Devices (R2D2) initiative.

To achieve a very ambitious goal of clinical trials regulatory modernization, there is a need for significant change to the whole ecosystem of clinical research. This significant change is exactly what Health Canada is trying to achieve by proposing a single clinical trial framework for all health products.

This framework will lay out a foundation for a new regulatory regime that would provide proportional risk-based oversight with a single authorization of a trial, regulatory flexibility over the lifecycle of the trial, greater transparency, enhanced technology to improve patient recruitment, and a modernized compliance and enforcement regime.

Health Canada proposes modernization to 4 major areas. The biggest impact will be implementation of the risk-based approach, where trials that fall under Category A could be exempt from the authorization process. This will be consistent with the current process, for example, exemption of Phase IV clinical trial from Health Canada review.

Category B will allow authorization with tailored requirements for the drugs and devices where safety information is available. The high-risk devices, new drugs, and new natural health products (NHPs) will fall under Category C and will require authorization with full requirements.

As such, Health Canada intends to enable and encourage the conduct of decentralized clinical trials (DCT), where patients could participate in the trial remotely without frequent travel to the clinical site. The regulatory proposal to enable this approach includes other proposed changes as outlined in the proposal.

OTHER "HOT" TOPICS IN EUROPE

European Union Clinical Trials Regulation (EU CTR): Latest updates

The Clinical Trials Regulation (EU) No 536/2014 (EU CTR) will become applicable in the EU on 31 January 2022 and will replace the Clinical Trials Directive (CTD) No. 2001/20/EC and national legislation that was put in place to implement Directive.

The European Medicines Agency (EMA), the Clinical Trials Facilitation and Coordination Group (CTFG) and the European Commission published supporting instructions and guidance.

TRAINING AND SUPPORTING MATERIALS (EMA)

To get ready for go-live CTIS, the EMA is delivering an extensive online modular training programme for self-study to help clinical trial sponsors, national competent authorities, ethics committees, European Commission and EMA staff prepare for using CTIS.

Resources include:

- Online training modules
  Clinical Trials Information System (CTIS): online modular training programme
- A handbook for clinical trials sponsors
  CTIS Sponsor Handbook 2021
- Reference materials for sponsors and authorities
  Principles for Sponsor Organisation
  Modelling for CTIS, updated 29 October 2021
  Clinical Trial Information System (CTIS) - Sponsor user personas, updated 11 October 2021
- Training and information events

EMA is also offering training sessions in classroom format, to provide additional learning opportunities. Upcoming:

Webinar for small and medium-sized enterprises (SMEs) and academia on the Clinical Trials Regulation and the Clinical Trials Information System (CTIS) (29/11/2021)

- Online modular training programme-CTIS
  Introduction to CTIS
  Common functionalities for all registered users
  Authority workspace
  Sponsor workspace
- CTIS Progress update
  Clinical Trials Information System (CTIS) highlights - October 2021

VOLUNTARY HARMONISATION PROCEDURE (VHP)

The CTFG published a guidance document Conclusion of VHP Procedure informing of deadline for submissions to VHP in the context of the Christmas Break 2021/2022 and transition to CTIS/EU CTR starting with the EU CTR application. In order to organise a smooth transition of the VHP-Processes into CTIS and the EU CTR, all VHPs procedures should be finalised in January 2022. In order to achieve this goal and to offer clear guidance the last day for any VHP submission (initial, substantial amendment, second round) was 15 October 2021.

After the Christmas break in January 2022, the Sponsors may decide afterwards either to file national submission (after the VHP as usual) or to transfer the clinical trial directly to the CTIS under the EU CTR. When pursuing the latter path, the involvement of Ethics Committees or others involved in the CTRs part II assessment has to be ensured outside of VHP and in CTIS.

EUDRALEX - VOLUME 10 - CLINICAL TRIALS GUIDELINES

In September 2021, the European Commission published Draft - Questions and Answers Document - Regulation (EU) 536/2014 – Version 4.1. The Q&As document has been updated by several questions including arrangements for the transitional period. The document has been also sent to for discussion to the Expert Group on Clinical Trials. Updated versions of the document will be published progressively.

Medical Devices Regulation (MDR) and In Vitro Diagnostic Medical Devices Regulation (IVDR): Latest Updates

The Medical Devices Regulation (EU) 2017/745 (MDR) became applicable in the EU on 26 May 2021 and replaced Directive 90/385/EEC on Active Implantable Medical Devices (AIMDD) (1990) and Directive 93/42/EEC on Medical Devices (MDD) (1993) and national legislation that was put in place to implement Directives.

The In Vitro Diagnostic Medical Devices Regulation (EU) 2017/746 (IVDR) will be applicable in the EU on 26 May 2022.

The European Commission's Medical Device Coordination Group (MDCG) published several guidance documents relating to classification of medical devices (MDs), clinical investigations with MDs, EUDAMED and notified bodies.

Guidance on Classification of Medical Devices

The Medical Device Coordination Group published and endorsed a guidance document on medical device classification. This document contains the descriptions of purpose and practical relevance of medical device classification while focusing on various aspects of device compliance with regulatory requirements such as traceability, post-market surveillance, clinical evaluation and investigation and conformity assessment. The attention is also drawn to how classification is carried out, along with the presentation of definitions and terms useful for applying classification principles and rules. Based on the division of the medical devices into three categories: non-invasive, invasive and active, it is further explained the individual rules of classification followed by graphical summary and general clarification of rules, practical issues and examples.

CLINICAL INVESTIGATIONS

Instructions for Generating CIV-ID for MDR Clinical Investigations

The document describes instructions on how to use Eudamed2 for clinical investigations under the MDR the Competent Authorities (CAs) to obtain a Union-wide unique single identification number (the 'CIV-ID'). Obtaining the CIV-ID from the CA before the first submission of application/notification of clinical investigation is mandatory. The generated CIV-ID is used for subsequent submission to other Member States. Once EUDAMED, the European Database on Medical Devices is fully functional (26 May 2022), sponsors will have the possibility to generate the Single Identification Number (SIN) instead of the CIV-ID.

The whole instruction is presented graphically in a very clear form. As the main criteria for obtaining a CIV-ID is generally: 1. Search for CIV-ID; 2. Generate CIV ID; and 3. MDR-specific procedure to amend the CIV details.

EUDAMED

EUDAMED-New UDI/Devices and NBs & Certificates Modules Opened

The EUDAMED module on Unique Device Identification (UDI)/device registration and the module on Notified Bodies and Certificates have been opened. Economic operators and notified bodies can start entering data in EUDAMED on a voluntary basis.

Fully operational, EUDAMED will also include modules on clinical investigations and performance studies, vigilance and market surveillance.

Questions and Answers on Obligations and Related Rules for the Registration in EUDAMED of Actors Other than Manufacturers, Authorised Representatives and Importers Subject to the Obligations of Article 31 MDR and Article 28 IVDR

The MDCG created a guidance document concerning explanations in the form of Q&As. This Q&As is a document aimed at addressing questions relating to the registration in EUDAMED of actors other than manufacturers, authorised representatives and importers subject to the obligations of Article 31 of the MDR and/or Article 28 of IVDR. The document has clarified the cases where an Actor ID is issued instead of an SRN. The document consists of nine questions and answers, which are very thoroughly discussed.

NOTIFIED BODIES

Clarification on "first certification for that type of device" and Corresponding Procedures to be Followed by Notified Bodies, in Context of the Consultation of the expert panel referred to in Article 48(6) of Regulation (EU) 2017/746

The MDCG published guidance on requirements for class D devices, Article 48(6) of IVDR. These conditions are connected to the absence of common specifications for the class D device in question, and where it is the first certification for that type of device. It has been created to clarify the meaning of these conditions and on the corresponding procedures to be followed by the notified body. The first certification for that type of device in Article 48(6) of the IVDR should be understood as the first certification under either Directive 98/79/EC or under IVDR. The certificate also deals with the main issue like intended purpose, analysis technology and process used.

Guidance for Notified Bodies, Distributors and Importers on Certification Activities in Accordance with Article 16(4) of Regulation (EU) 2017/745 and Regulation (EU) 2017/746

This guidance document is mainly focused on activities performed by notified bodies, providing also clarification on the quality management system they are expected to assess. This guidance is also addressed to distributors and importers with respect to their quality management system to be certified by a notified body. The procedures established under the quality management system address elements related to contractual relationships.

Questions and Answers: Requirements Relating to Notified Bodies

The European Commission's MDCG created a document that presents questions and answers on requirements relating to notified bodies under MDR and IVDR. At the very beginning of the document, it discusses the organizational and general requirements. Then the document describes the process and resources requirements in every detail.

The European Commission's MDCG also published Application forms to be submitted by a conformity assessment body when applying for designation as notified body under the MDR and/or IVDR. It has been also issued Explanatory note on IVDR codes.

COVID-19 RELATED

Notice to Manufacturers and Authorised Representatives on the Impact of Genetic Variants on SARS-COV-2 In Vitro Diagnostic Medical Devices

The European Commission's Medical Device Coordination Group (MDCG) published a Notice to manufacturers and authorised representatives on the impact of genetic variants on SARS-COV-2 in vitro diagnostic medical devices. The notice underlines the manufacturers' responsibilities to continually assess the impact of newly identified genetic variants of SARS-CoV-2 on the capability of those in vitro diagnostics devices (IVDs) to meet their performance, risk and safety claims.

OTHER MDCG GUIDANCE

MDCG 2021-19 Guidance note integration of the UDI within an organisation's quality management system, July 2021

MDCG 2021-26 Questions and Answers on repackaging & relabelling activities under Article 16 of Regulation (EU) 2017/745 and Regulation (EU) 2017/746, October 2021

OTHER "HOT" TOPICS FROM THE UNITED STATES

FDA Collaborates with Health Canada and UK's MHRA to Foster Good Machine Learning Practice

As of 03 November 2021, the U.S. Food and Drug Administration (FDA), Health Canada and the United Kingdom's Medicines and Healthcare products Regulatory Agency (MHRA) jointly issued the "Good Machine Learning Practice for Medical Device Development: Guiding Principles" to identify a set of ten guiding principles that are important to be included in the development of Good Machine Learning Practice (GMLP). Good Machine Learning Practice is intended to advance high quality artificial intelligence/machine learning enabled medical device development.

These ten principles are intended to identify areas where alignment in efforts related to research, building resources and tools, regulatory policies, regulatory guidelines, international harmonization and consensus standards could be developed by the International Medical Device Regulators Forum (IMDRF), international standards organizations and other collaborative bodies to advance the maturation of GMLP.

The FDA envisions that these guiding principles could be used to either specifically tailor practices applicable to health care, create new practices for health care or adopt from practices that have been proven in other domains.

FDA Awards 11 Grants to Clinical Trials to Develop New Medical Products for Rare Disease Treatments

On 14 October 2021, the U.S. Food and Drug Administration announced it has awarded 11 new clinical trial research grants, equaling more than $25 million of funding over the next four years. The FDA's Congressionally-funded Orphan Products Grants Program awards these grants to clinical investigators to support the development of medical products for patients with rare diseases.

The Office of Orphan Products Development works to identify, examine and ultimately fill the gaps that exist within the rare disease drug development community by funding necessary and revolutionary clinical studies to determine the safety and efficacy of potential treatment options.

The grant awards support clinical studies of products that address unmet needs in rare diseases or conditions or provide highly significant improvements in treatment or diagnosis.

About CROMSOURCE

CROMSOURCE is an ISO-certified international provider of outsourced services to the pharmaceutical, biotechnology and medical device industries, specialising in clinical development and staffing solutions. CROMSOURCE was founded in 1997, almost 25 years ago. Its successful growth has been built on stability, integrity, and high levels of customer satisfaction, all of which contribute to a high rate of repeat and referral business. We have grown steadily, but responsibly, to become an organisation of over 350 organised and well-trained experts.

A well-established full service CRO, **CROMSOURCE** is unique in offering an end-to-end guarantee covering trial timelines, enrolment and contract price. This guarantees our clients that their trials are delivered on time and within the contract price with no CRO-initiated change orders. **CROMSOURCE** operates through offices across all regions of Europe and North America and delivers a comprehensive breadth of services.

CROMSOURCE supports the full spectrum of clinical development via our Pharmaceutical, Medical Device and Staffing Solutions divisions. We seamlessly move biopharmaceutical products from first-into-human conducted in our exceptional early phase unit, through all subsequent phases of pre- and post- approval research internationally.

We also support medical device projects through regulatory planning and execution, to pilot and pivotal clinical investigations in Europe and North America.

Global Reach

CROMSOURCE, with world headquarters in Verona, Italy, is a leading CRO in Europe and the US with a solid infrastructure and operational subsidiaries in Belgium, Germany, Poland, Russia, Spain, Switzerland, the UK, the Netherlands, and the US.

From our office locations across Europe and North America, **CROMSOURCE** employs experienced field-based teams around the globe to provide expert capabilities in regions including the Middle East, Africa, APAC, and South America.

It's a simple concept, really. Quality data. On time. On Budget. Guaranteed.

At CROMSOURCE we believe experts should keep their word. With nearlly 25 years of success we provide the industry's only End-to-End Guarantee™. Starting at the RFP stage with our uniquely detailed Feasibility Plus™ process we guarantee:

1. Your study will start on time
2. We will enroll 100% of the contracted patients
3. We will finish on time with a set date for database lock
4. The price you contracted is the price you pay. There will be no CRO-initiated changes-in-scope.

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