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REGULATORY

NEWSLETTER N.34
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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

European Commission Guidance on COVID-19

All the European Union (EU) countries are affected by the pandemic. The European Commission takes every measure to ensure availability of vaccines, medicines and equipment to support Member States in their efforts to address the COVID-19 pandemic. Latest updates include: EU vaccines strategy to accelerate the development, manufacturing and deployment of safe and effective vaccines against COVID-19; EU strategy on COVID-19 therapeutics ensuring access to and swift approval if large-scale clinical trial in the EU.

In addition, the European Commission identified five promising candidate therapeutics, all of which are under rolling review or have applied for a new indication for an existing medicine to the European Medicines Agency (EMA). The Commission will draw up a portfolio of at least ten potential COVID-19 therapeutics by October 2021, building on the work of the newly established expert group on COVID-19 variants.

In June 2021, the European Commission published lessons learned report Communication on the early lessons from the COVID-19 pandemic.

Reflection Paper on Forecasting Demand for Medicinal Products in the EU/EEA

The European Commission, in cooperation with European Medicines Agency (EMA) and Heads of Medicines Agency (HMA) published Reflection paper on forecasting demand for medicinal products in the EU/EEA. The document contains recommendations to support forecasting of demand for human medicinal products across the European Union (EU) and also at the national level in exceptional situations like the COVID-19 pandemic. The document has been created based on the experience gained by EU authorities last year, during the first wave of the pandemic, and presents a common methodology to predict the demand of medicines for use in intensive care units (ICUs). It presents a practical recommendations and examples specific to the COVID-19 pandemic. Some of the general principles mentioned in the document are applicable to other emergencies which require to forecast demand for medicines.

EC Proposal on a Reinforce the Role of the EMA

On 03 June 2021, the European Commission published Proposal on a reinforced role for the European Medicines Agency in crisis preparedness and management for medicinal products and medical devices. The proposal is part of a set of three proposals "aiming to strengthen the EU's health security framework and to reinforce the crisis preparedness and response role of key EU agencies".

News from the European Medicines Agency (EMA)

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

EMA Latest Updates on the COVID-19 Pandemic

The EMA aims to expedite the development of effective medicines and vaccines to fight and prevent the spread of COVID-19. The EMA also aims to ensure that the assessment and monitoring of medicines are available for patients in Europe for all their health needs during the pandemic.

The EMA latest updates include: updating authorised COVID-19 vaccines to address SARS-CoV-2 variants; safety updates for four the COVD-19 vaccines authorised in the EU; approve a first vaccine (Comirnaty, Pfizer) for children aged 12 to 15 in the EU; evaluation the use of COVID-19 vaccine Moderna (Spikevax) in young people aged 12 to 17; reply to open letter to 'Doctors for COVID ethics' concerning COVID-19 vaccines; the EMA and the European Centre for Disease Prevention and Control (ECDC) initiative to enhance post-marketing monitoring of COVID-19 vaccines in Europe.

The EMA's Management Board Update of the CTIS Full Functionality

During the last EMA's Management Board meeting held on 21 April 2021, the Board confirmed on the basis of the independent audit report, that the Clinical Trials Information System (CTIS) including EU clinical trials Portal and EU database is fully functional and meets the functional expectations as required by Article 82(2) of the Clinical Trials Regulation (EU) No. 536/2014 (CTR). The European Commission publication of it in the Official Journal of the European Union is anticipated for 31 July 2021 and go-live version of the CTIS is currently on track for 31 January 2022.

Training Programme for the CTIS Users

To get ready for go-live CTIS, the EMA organized training programme for sponsors, Member States staff, the European Commission, small and medium-sized enterprises (SME) and Academia. The training programme has been split into several learning modules targeted for the different user groups involved in the CTIS. These modules aim to ensure a clear understanding of the different process of the system. Training session tailored for SME and Academia was held in February and March 2021. Presentations together with all eLearning recording sessions are published and available for everyone on the EMA website. On 29 July 2021 the EMA organises additional free training: Clinical Trials Information System (CTIS) webinar: How sponsor organisations can prepare for CTIS.

In June 2021, the EMA published the third number of the Clinical Trials Information System newsletter "CTIS Highlights", which is published on the page Publications/Clinical Trials Information System (CTIS) highlights of the EMA Corporate website.

Revision of Guidance on Requirements for Quality Documentation in Clinical Trials

The EMA published drafts guidance on requirements for quality documentation concerning biological investigational medicinal products in clinical trials and guidance on requirements to the chemical and pharmaceutical quality documentation concerning investigational medicinal products in clinical trials. Consultation for both guidelines is open until 31 August 2021.

These guidelines are connected to the Clinical Trials Regulation (EU) No. 536/2014 (CTR) which came into force on 20 June 2014 and is expected to be applicable in the EU on 31 January 2022. The changes in these guidelines refer to the "substantial modification" section. It is underlined that according to the CTR, "a change to investigational medicinal product (IMP)/auxiliary medicinal product quality data is either: a substantial modification, a change relevant to the supervision of the trial, a non-substantial modification (changes outside the scope of substantial modifications and changes irrelevant to the supervision of the trial)". The draft guidelines are updated to help sponsors of IMPs for new drugs and biologics decide whether manufacturing changes are considered a substantial modification needing prior approval.

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. The HRA encourages all sponsors and Contract Research Organisations (CROs) to submit new a Clinical Trials of Investigational Medicinal Products (CTIMPs) applications via the CWoW route by 01 January 2022 to get an experience of submitting via this service before the target date. The CWoW was launched to help the United Kingdom (UK) to be ready when Clinical Trial Regulation (CTR) No 536/2014 comes into effect. The main benefits of the CWoW are to get streamline and efficient application process coordinated by ethics and regulatory review leading to the Research Ethics Committee opinion and Medicines and Healthcare products Regulatory Agency (MHRA) approval delivered together. The CWoW applications must be submitted using a new part of Integrated Research Application System (IRAS) not the standard part of IRAS.

New NHS Digital System for Collecting Patient Data

The (National Health Service) NHS in England launched new NHS Digital system pooling the medical history of patients into a central database. This collection of data has started on 01 July 2021. The medical data of every patient in England, registered with a General Practice (GP) clinic, will be shared in a central system and made available to academic and commercial third parties for research and planning purposes. The NHS guarantees that data shared by new system will follow "a strict rules around privacy, security and confidentiality and the new service has been designed to the highest standards".

Italy

Update on Documentation for Initial Submission and Substantial Amendment

The Italian Medicines Agency (AIFA) has published an update concerning the documentation for the submission of Phase I, II, III and IV clinical trial applications and related substantial amendments. The requirements are applicable from 03 May 2021.

For clinical trials authorization requests submitted through the Osservatorio Nazionale per la Sperimentazione Clinica" (OsSC)-online platform, it is no longer necessary to send to the AIFA the package containing the paper documentation and the CD-ROM(s).

The specific paper copies like transmission letter, Clinical Trial Application (CTA) form (Appendix 5), Amendment form (Appendix 9), checklist, receipt of the bank transfer payment must be submitted only via OsSC. The stamp duty (costing 16 Euro) required for every transmission letter is available as a digital revenue stamp purchase through the "ebollo' online service. New models of transmission letters have been published.

The AIFA informed that the submission in transitory paper mode is permitted in the cases illustrated in the AIFA press release dated 20 December 2018 ("Procedures to be followed in the event of OsSC malfunction").

Clinical Trial Involving the Use of Artificial Intelligence (AI) or Machine Learning (ML) systems-AIFA Guidance

In May 2021, the AIFA published Guide to the submission of a request for authorisation of a Clinical Trial involving the use of Artificial Intelligence (AI) or Machine Learning (ML) systems, version 1.0.

This document contains a collection of information, recommendations and references to standards, documents and publications, and represent a general guide, a useful tool for Sponsors to optimize the documentation supporting the submission of a request for authorization of Clinical Trials (CTs) involving the use of AI or ML systems. The guidance underlines that before submitting a request for authorisation of a CT in Italy, it is always necessary that sponsor checks the regulatory framework of the AI models or ML. If the AI/ML system be classified as medical device software, the Competent Authority will be the Italian Ministry of Health (MoH), not the AIFA. The document provides links to the relevant European and Italian guidance to be consulted by the sponsors/applicants. It presents general submission workflow of a CT that is impacted by AI/ML and two case studies: one where medicinal product's regulatory framework needs to be consulted and another one for medical device regulatory framework where the MoH should be contacted.

North America

United States of America

FDA Encourages Inclusion of Patients with Incurable Cancers in Oncology Clinical Trials Regardless of Prior Therapies

The Food and Drug Administration (FDA) issued a draft guidance on 24th June 2021 entitled Cancer Clinical Trial Eligibility Criteria: Available Therapy in Non-Curative Settings encouraging industry to include patients with incurable cancers (when there is no potential for cure or for prolonged/near normal survival) in cancer clinical trials, regardless of whether they have received existing alternative treatment options. Historically, many clinical trials have required that participating patients previously received multiple therapies.

The FDA believes patients with incurable cancers, if provided adequate information to make an informed decision, should be eligible to participate in oncology clinical trials. If there is no scientific rationale for excluding these patients, then clinical trial eligibility criteria should be broadened to include these patients, with appropriate informed consent.

This draft guidance is part of the FDA's broader initiative to encourage rational expanded patient eligibility for oncology clinical trials. When finalized, the guidance will provide sponsors with recommendations regarding including patients who have not received available therapy/therapies, such as evaluating these patients in separate cohorts from patients who have received available therapies.

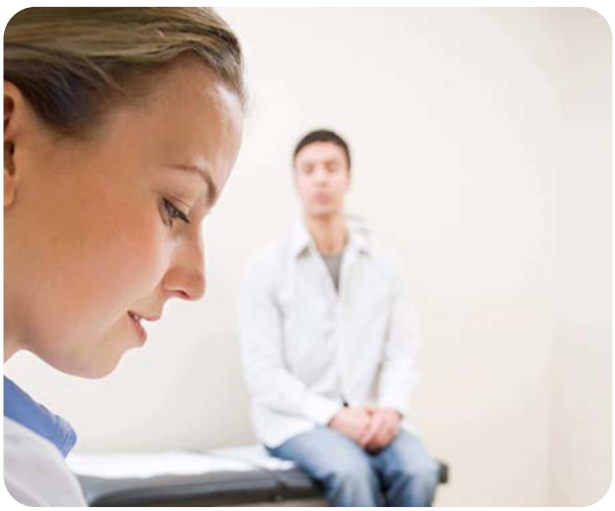
Canada

Canada's Biosimilar Initiative: Mandatory Biosimilar Switching Policy in 4 Provinces

Mandatory biosimilar switching program has been initiated in 4 provinces of Canada - British Columbia, Alberta, New Brunswick, and Quebec, which could facilitate improved access to the patients for biosimilar products. The decision is taken in consultation with different stakeholders, including prescribers and physicians from different fields. Savings from increasing the utilization of biosimilar products will be reinvested to support coverage of new therapies and improve patient access to more medications.

A biosimilar biologic drug, or biosimilar, is a drug demonstrated to be highly similar to a biologic drug that was already authorized for sale. Health Canada evaluates all the information provided to confirm that the biosimilar and the reference biologic drug are similar and that there are no clinically meaningful differences in safety and efficacy between them. Health Canada's rigorous standards for authorization mean that you can have the same confidence in the quality, safety and efficacy of a biosimilar as any other biologic drug.

www.biosimilarscanada.ca, Biosimilar biologic drugs in Canada: Fact Sheet



MEDICAL DEVICES

EUROPE

News from the European Commission

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.

European Commission Proposal on Artificial Intelligence Act

In April 2021, the European Commission published a proposal for a regulation laying down harmonised rules on artificial intelligence (AI) (Artificial Intelligence Act). The proposal sets:

- "harmonised rules for the placing on the market, the putting into service and the use of artificial intelligence systems ('AI systems') in the Union;
- prohibitions of certain artificial intelligence practices;
- specific requirements for high-risk AI systems and obligations for operators of such systems;
- harmonised transparency rules for AI systems intended to interact with natural persons, emotion recognition systems and biometric categorisation systems, and AI systems used to generate or manipulate image, audio or video content;
- rules on market monitoring and surveillance".

European Union-Switzerland Mutual Recognition Agreement (MRA) for Medical Devices

On 26 May 2021, the European Commission published a Notice to stakeholders informing about issuing a new MRA between the European Union (EU) and Switzerland. Until 26 May 2021, Switzerland has been participating in the EU internal market for medical devices through a specific chapter of the EU-Switzerland MRA. Since 26 May 2021, with the full application of the Medical Devices Regulation (EU) 2017/745 (MDR) and in the absence of an institutional agreement reached, Switzerland has become a "third country" for the EU. On 31 May 2021, the European Commission published a message to stakeholders that the Commission is working on an amendment to the MRA with Switzerland established on 26 May 2021.

The amendment is under preparation and the change will apply only to existing medical devices and its existing certificates issued in Switzerland before 26 May 2021. It is negotiated that these medical devices will have the same transitional validity as the new MDR grants to certificates issued in the EU. The MRA will not be updated with regard to new certificates issued under the new MDR. For new MDs and its certificates, the Swiss Manufacturers must appoint the European Authorised Representative to export their devices to Europe. At the same time, the European Manufacturers must designate a Swiss Authorised Representative to export their products to Switzerland.

Update of the EU-Turkey Customs Union for Medical Devices

On 25 May 2021, the European Commission informed about signing an updated the EU-Turkey Customs Union for medical devices by both parties and at the same time confirming Turkey's alignment with the Medical Devices Regulation (EU) 2017/745 (MDR). This confirms the continued integration of Turkey to the EU market on medical devices and the facilitation of trade. A similar alignment to enable the continuation of EU-Turkey customs union for in-vitro diagnostic devices will follow.

News from Individual Countries

Austria

New Application Form

The Austrian Federal Office for Safety in Health Care (BASG), issued new BASG application form for clinical investigations with medical devices. The form is mandatory from 26 May 2021. Application forms for already notified or ongoing clinical investigations can continue to be updated.

Belgium

Submission Processes of Clinical Investigations According to MDR

The Federal Agency for Medicines and Health Products (FAMHP), the Belgian Competent Authority (CA) has updated its already published guidance in the context with the Medical Devices Regulation (EU) 2017/745 (MDR): Guideline on Submission Processes of Clinical Investigations according to MDR in Belgium, (version 5.0, 08 July 2021) and Clinical Investigations-Guidance on Dossier Content, (version 2.0, 07 June 2021). The Competent Authority provides also new templates of application form, annexes to the initial application form referring to the templates recommended by the European Commission's Medical Device Coordination Group.

Germany

Medical Device Law Implementation

The Federal Institute for Drugs and Medical Devices (BfArM), the German Competent Authority published amended the German Medical Device Law Implementation Act and other Laws dated 12 May 2021 in the context of the Medical Devices Regulation (EU) 2017/745 (MDR).

France

New Guidance and Infographic for Clinical Investigations Applicants

The French National Agency for the Safety of Medicine and Health Products (ANSM) updated all their guidance for clinical investigations (CIs) with medical devices authorisation and created new webpage. The ANSM webpage provides detailed guidance to be considered at each step of clinical investigations for ongoing trials and new to be submitted after 26 May 2021. It also includes an infographic of the initial submission process depending on the CIs categories, substantial modifications and other required submissions during CI and at the end.

Italy

New Guidance and Instructions for Applicants

The Ministry of Health (MoH), the Competent Authority for medical devices in Italy published all relevant guidance and instructions to be followed by an applicants after 26 May 2021 - the date of application of the Medical Devices Regulation (EU) 2017/745 (MDR):

- Post Market Clinical Follow-up (PMCF) clinical investigation notification with invasive or burdensome supplementary procedures
- Notification of the initiation of Post Market Clinical Follow-up (PMCF) clinical investigations
- Authorization for clinical investigation relating to non-invasive class I or class IIa or IIb medical devices not bearing the CE marking for the intended use
- Authorization for clinical investigation relating to invasive class IIa or IIb medical devices or class III not bearing the CE marking for the intended use

Spain

Update on the Guidance on Clinical Investigations under the MDR

The Spanish Agency of Medicines and Medical Products (AEMPS) updated the guidance document related to the authorisation of clinical investigations under the Medical Devices Regulation (EU) 2017/745 (MDR). The AEMPS informs that new Royal Decree which will regulate medical devices in Spain and will implement the MDR provision is under preparation. Until its publication clinical investigations with class I investigational medical devices (MDs) or class IIa and IIb non-invasive MDs will have one month of evaluation. It is underlined that until publication of new Royal Decree, the national provisions from Royal Decree 1591/2009 and Royal Decree 1616/2009 will continue to be applicable in those aspects that do not oppose to the MDR. The AEMPS is also preparing new instructions for clinical investigations with medical devices to help sponsors/applicants in the presentation of applications and to clarify different aspects.

Switzerland

New Requirements and Changes to the Submission Process of Clinical Investigations

The Swissmedic, the Swiss competent authority published new guidance for sponsors/manufacturers/applicants to be followed during dossier preparation and approval process in Switzerland. Due to the lack of reached Mutual Recognition Agreement (MRA) for medical devices between the European Union-Switzerland the sponsors who have headquartered in another country must specify a representative domiciled/headquartered in Switzerland to act as the direct contact for Swissmedic. Preliminary decisions, official decisions and invoices from Swissmedic will be sent to the representative. Legal and natural persons domiciled or headquartered in Switzerland can be specified as representatives, e.g., distribution companies, a lawyer or the clinical investigator.

The United Kingdom

MDR Implementation in Northern Ireland

Under the terms of the Northern Ireland Protocol, the Medical Devices Regulation (EU) 2017/745 (MDR) applies in Northern Ireland from 26 May 2021. The Medicines and Healthcare products Regulatory Agency (MHRA) published guidance explaining the rules for placing medical devices on the Northern Ireland market and also how to notify the MHRA of a clinical investigation. The rules in the Northern Ireland are differ from those applicable to Great Britain (England, Wales and Scotland). For the investigation sites in England, Wales and Scotland the submission requirements and approval timelines remain the same. In the case a clinical investigation involves a site from Northern Ireland the initial application must be submitted to the MHRA in line with the new requirements of MDR. Single application will also cover any sites proposed in Great Britain in addition to site(s) in Northern Ireland for the same clinical investigation. In case a site from Northern Ireland involved the serious adverse events (SAEs) reporting should be done by using MDCG 2020-10/2 SAE reporting table.

In addition, to support stakeholders operating in the Northern Ireland, the MHRA published Introductory guide to MDR and IVDR and other relevant instructions.

North America

United States of America

FDA Issues Final Guidance on Requests for Feedback and Meetings for Medical Device Submissions

FDA updated the final guidance "Requests for Feedback and Meetings for Medical Device Submissions: The Q-Submission Program" to include that a Q-submission is the appropriate mechanism for submission of requests for inclusion in Safer Technologies Program (STeP) for Medical Devices as well as other updates.

The early engagement with the Agency is facilitated through request for feedback or a meeting with the FDA under the "Q-Submission Program". This program enables interaction with the FDA on study and data considerations to improve quality of submissions, reduced review timelines and avoidance of unnecessary pre-clinical or clinical studies. Pre-Sub is appropriate when FDA's feedback on specific questions is necessary to guide product development and/or submission preparation.

The program is entirely voluntary on the part of the submitter. However, early interaction with FDA on planned non-clinical and clinical studies and careful consideration of FDA's feedback may improve the quality of subsequent submissions, shorten total review times, and facilitate the development process for new devices. FDA believes that interactions provided within Pre-Subs are likely to contribute to a more transparent review process for FDA and the submitter.

Specifically, the guidance discusses the different mechanisms available to device makers for requesting feedback or a meeting with FDA staff during the presubmission phase for investigational device exemption (IDE) applications, premarket approval applications (PMAs), humanitarian device exemption (HDE) applications, de novo requests, premarket notification (510(k)) submissions, Clinical Laboratory Improvement Amendments (CLIA) waivers, dual (510(k)) and CLIA waiver by application submissions, accessory classification requests and certain investigational new drug (IND) applications and biologics license applications (BLAs).

The final guidance also includes a new table in the section on processes by Q-submission types that details the corresponding method of feedback and timeframes for pre-submission, submission issue request (SIR) and information meeting Q-submissions.

Additionally, FDA has expanded the second appendix to include cybersecurity as a topic for pre-submission questions, with four questions included as examples of cybersecurity questions that could be addressed via Q-submission feedback. Examples of other pre-sub questions covering different disciplines are also provided in the final guidance.

Canada

Canadian Regulatory Amendments Introduce Expanded Postmarket Surveillance Provisions

Health Canada (HC) published SOR/2020-262 in the *Canada Gazette*, consisting of significant amendments to the Food and Drug Regulations and the Medical Devices Regulations (CMDR). The amendments aim to strengthen post-market surveillance for medical devices, in support of the life cycle amendments introduced in Vanessa's Law, by providing regulatory authorities with greater power and more tools to evaluate and monitor incidents.

Currently under the CMDR, license holders may be asked to provide post-market information on medical devices but are not required to offer detailed analysis. As a result, the information provided can sometimes be unclear and lead to delays in the evaluation of medical devices.

The amendments seek to address this problem by granting new powers to HC to compel medical device license holders to conduct a risk assessment of their own devices considering new information gathered, which should offer greater certainty to industry and ensure that critical information is conveyed to HC.

Another noteworthy change concerns foreign risk notification. License holders for Class II, III, or IV medical devices will be required to notify HC of foreign actions regarding serious risk of injury to human health (e.g., recalls, reassessments, and suspensions of authorizations) that occur in relevant foreign jurisdictions within 72 hours instead of 10 days. These provisions are to come into effect on 23 June 2021.

OTHER "HOT" TOPICS IN EUROPE

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

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 within one year on 26 May 2022.

The European Commission's Medical Device Coordination Group (MDCG) published several guidance documents relating to clinical investigations with medical devices, EUDAMED, the European Medical Device Nomenclature (EMDN), Implant Card and transitional provisions for certification of class D in vitro diagnostic medical devices.

CLINICAL INVESTIGATIONS

Regulation (EU) 2017/745-Questions & Answers Regarding Clinical Investigation

In April 2021, the MDCG published Questions & Answers on clinical investigations with medical devices in the context of the MDR. The document includes 28 questions and answers as well as two annexes providing the regulatory pathway for clinical investigations and a non-exhaustive list of substantial modifications. The guidance provides instructions for sponsors on how to choose appropriate regulatory pathway for initial application of clinical investigations under different circumstances and how to proceed with a substantial modification after 26 May 2021.

Moreover, the document informs of the validation and assessment timelines for certain regulatory pathways. The guidance explains the content of clinical investigation reports and safety reporting requirements for clinical investigations. The document may be supplemented in the future with further questions and answers.

Clinical Investigation Application/Notification Documents

The MDCG created a series of clinical investigation application/notification documents which may be used by sponsors/applicants in the absence of the European database on medical devices (EUDAMED). The documents have been published to support clinical investigation procedures with respect to the MDR. There is clinical investigation–application/notification form under the MDR which includes the same data fields to the EUDAMED system in development. It has been created an addendum to the clinical investigation application form in case of addition of investigational device(s), comparator device(s) or investigation site(s). The guidance also lists the documents supporting clinical investigation application in referring to a Chapter II of Annex XV of Regulation (EU) 2017/745 (MDR). Using the forms is not mandatory but the Competent Authorities and sponsors are encouraged to use them.

EUDAMED

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 guidance, published in Questions & Answers format, explains how EUDAMED rules apply to actors not subject to registration requirements under MDR and IVDR, including manufacturers of custom-made devices, legacy devices and "old" devices. The document clarifies the need of Actor ID and Single Registration Number (SRN). Actor ID is the identifier issued to all actors registered in EUDAMED for their identification in the system. It is automatically generated by EUDAMED and issued once the registration request is approved by the relevant competent authority.

The SRN is issued through EUDAMED to economic operators (including manufacturers, authorised representatives and importers) by the competent authority. The SRN is a unique number which will be used by economic operators in every relevant official documents and related reports. The guidance explains that registered manufacturers and authorised representatives of only custom-made devices or only legacy devices, or only "old" devices are assigned an Actor ID that is non-SRN. The obligation to register as actors in EUDAMED is applicable also to non-EU manufacturers and authorised representatives.

EU UDI Helpdesk Launched

The European Commission launched the EU Unique Device Identification (UDI) help desk to provide support to economic operators in the implementation of the obligations and requirements introduced by the new UDI system, which include UDI assignment, labelling and registration of devices. This helpdesk also provides the support as regards the use of the European Medical Devices Nomenclature (EMDN). The UDI helpdesk is prepared in the Frequently Asked Questions format and split into to five groups: definitions and basic information; specific questions; EUDAMED-related questions; dates and deadlines; documents and links.

OTHER MDCG GUIDANCE

FAQ on the European Medical Device Nomenclature (EMDN)

The European Medical Device Nomenclature (EMDN) aims at supporting the functioning of the European database on medical devices (EUDAMED). Among others, it will be utilised by manufacturers for the registration of medical devices in EUDAMED, where it will be associated to each Unique Device Identifier-Device Identifier (UDI-DI). The MDCG published guidance how to assign EMDN code for a particular medical device (MD). The EMDN code is established in a seven-level hierarchical tree. It clusters medical devices into three main levels: category of medical device, group and type of MD. The access to the EMDN is free and all stakeholders such as manufacturers, patients, contract research organisations, practitioners, hospitals, pharmacies etc. may have access to it by downloading the pdf. or excel version. Second release of EMDN will be announced in Q3 2021.

Guidance on Implant Card-Device Types

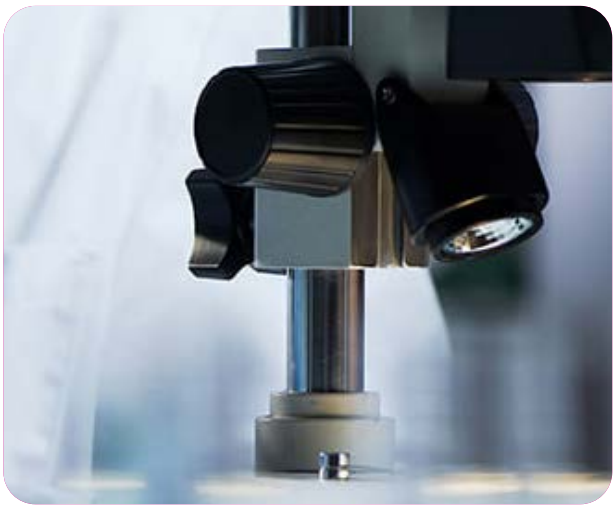
The guidance provides a non-exhaustive list of correct terms of implantable medical 'device types' which must display on the implant card for every implantable medical devices in accordance with Article 18 (a) of the MDR. The list has been created to aid manufacturers in allocating an appropriate term on its implant card.

Application of Transitional Provisions for Certification of Class D In Vitro Diagnostic Medical Devices According to Regulation (EU) 2017/746

According to Regulation (EU) 2017/746 on in vitro diagnostic medical devices (IVDR), as part of conformity assessment of class D in vitro diagnostic medical devices (IVDs), the manufacturer must submit an application to a notified body and under certain conditions may be reviewed by an expert panel and/or tested by an EU reference laboratory (EURL). This guidance provides indications for how to apply the IVDR provisions related to expert panels and EURLs during the transition period, i.e., before 26 May 2022.

The First Opinion of the Expert Panels in the Fields of Medical Devices is Published

The expert panels issued first opinion provided under the Clinical Evaluation Consultation Procedure (CECP). Notified bodies are required to consult with expert panels on the clinical evaluations of certain high-risk medical devices and performance evaluations of some high-risk IVDs. The first scientific opinion has been provided for 'General and plastic surgery and dentistry' theme.



Medical Device Coordination Group (MDCG) New Guidance or Revisions of Guidance

- MDCG 2021-09_ MDCG Position Paper on the Implementation of UDI requirements for contact lenses, spectacle frames, spectacle lenses & ready readers, May 2021
- MDCG 2021-10 - The status of Appendixes E-I of IMDRF N48 under the EU regulatory framework for medical devices, May 2021
- MDCG 2021-5, Guidance on standardisation for medical devices, April 2021

KEY BREXIT UPDATES

The Trade and Cooperation Agreement between the European Union (EU) and the United Kingdom (UK) of Great Britain and the Northern Ireland was reached on 24 December 2020 and came into force on 01 January 2021, following the end of the transition period on 31 December 2020 and entered into force on 01 May 2021. The Trade and Cooperation Agreement has been published in 23 languages.

The UK's Medicines and Healthcare products Regulatory Agency (MHRA) has released plenty of guidance documents for industry and organisations explaining how clinical trials, drugs, medical devices and importation will be regulated as of 01 January 2021.

OTHER "HOT" TOPICS FROM THE UNITED STATES

FDA Finalizes Guidance with Internationally Harmonized Recommendations to Further Support Safe, High-Quality Human Drug Products

On 11 May 2021, the U.S. Food and Drug Administration announced the availability of a final guidance for industry, entitled "Q12 Technical and Regulatory Considerations for Pharmaceutical Product Lifecycle Management."

The FDA is continually working to promote drug innovation and improvement, strengthen quality assurance, safety and supply of drug products and enable more efficient use of industry and regulatory resources. Through the harmonization of requirements for drug lifecycle management, manufacturers and the FDA can meet these goals in less time through effective management of postapproval changes.

This guidance reflects just one element in the FDA's work with regulatory authorities and industry associations from around the world to promote international harmonization of regulatory requirements under the ICH (International Council for Harmonisation) guidelines. The FDA is committed to continue seeking scientifically based harmonized technical procedures for the development and manufacture of drugs.

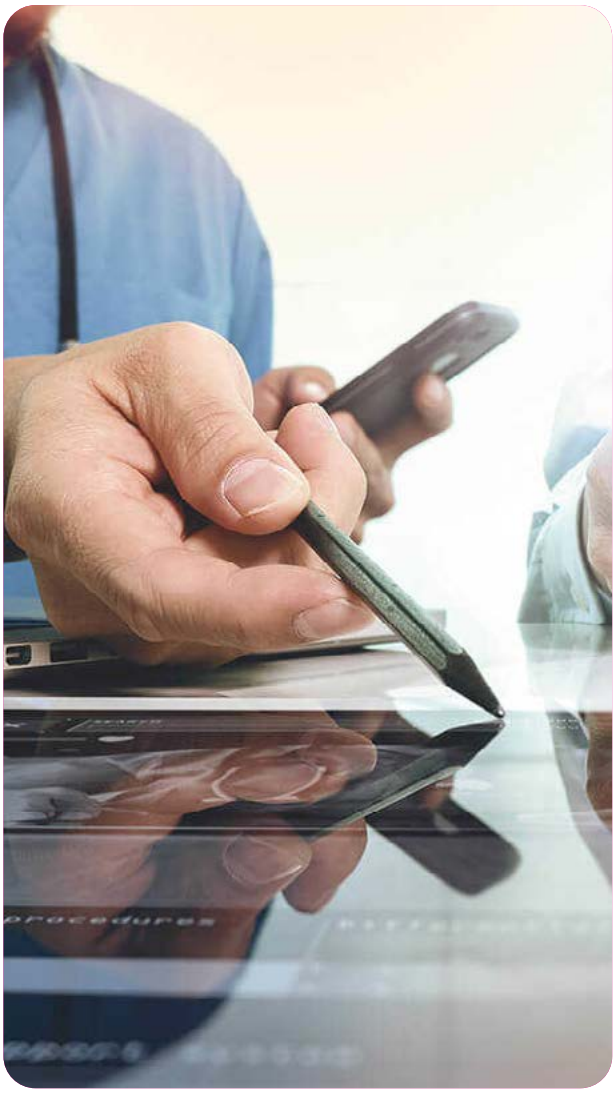
The guidance discusses how to identify the elements in an application that are considered necessary to assure product quality and therefore would require a regulatory submission if changed post approval.

FDA Final Guidance: Safer Technologies Program for Medical Devices

The U.S. Food and Drug Administration (FDA) issued final guidance outlining the Safer Technologies Program (STeP) for Medical Devices. This program will be a voluntary pathway for certain medical devices and device-led combination products that are reasonably expected to significantly improve the safety of currently available treatments or diagnostics for diseases or conditions that are less serious than those eligible for the Breakthrough Devices Program.

The Breakthrough Devices Program is a voluntary program for certain medical devices and device-led combination products that provide for more effective treatment or diagnosis of life-threatening or irreversibly debilitating diseases or conditions. The Breakthrough Devices Program replaces the Expedited Access Pathway and Priority Review for medical devices. The FDA considers devices granted designation under the Expedited Access Pathway to be part of the Breakthrough Devices Program.

FDA believes that the Safer Technologies Program will help patients have more timely access to these medical devices and device-led combination products by expediting their development, assessment, and review, while preserving the statutory standards for premarket approval, De Novo marketing authorization, and 510(k) clearance.



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 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.

1 ONE TRIAL ONE PRICE™
GUARANTEED FIXED PRICE BUDGET

FEASIBILITY PLUS™
GUARANTEED ENROLLMENT & TIMELINES

We know that budgets must be competitive, and you can rest assured that our End-to-End Guarantee™ does not come with a premium price.

As an ISO-certified organization, you can also rest easy about quality.

Don't you owe it to your project to learn more? Contact us to request more information.