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REGULATORY

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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 Pharmaceutical Strategy for Europe for Upcoming Years

On 25 November 2020, the European Commission adopted a Pharmaceutical strategy for Europe.

The strategy plan covers four specific pillars, which include legislative and non-legislative action:

- "Ensuring access to affordable medicines for patients, and addressing unmet medical needs (e.g. in the areas of antimicrobial resistance, rare diseases);
- Supporting competitiveness, innovation and sustainability of the EU's pharmaceutical industry and the development of high quality, safe, effective and greener medicines;
- Enhancing crisis preparedness and response mechanisms, diversified and secure supply chains, address medicines shortages;
- Ensuring a strong EU voice in the world, by promoting a high level of quality, efficacy and safety standards."

Plans to Give the European Medicines Agency (EMA) New Powers in Case of Crisis

On 11 November 2020, the European Commission published the proposal of Regulation on a reinforced role for the EMA in crisis preparedness and management for medicinal products and medical devices.

The new powers envisaged for the EMA would enable it to:

- Ensure a high level of human health protection by strengthening the Union's ability to manage and respond to public health emergencies;
- Contribute to ensuring the smooth functioning of the internal market medicinal products and medical devices during public health emergencies;
- Monitor and mitigate potential and actual shortages of medicinal products and medical devices considered as critical in order to address a given public health emergency or, for medicinal products, other major events which may have a serious impact on public health;
- Ensure timely development of high quality, safe and efficacious medicinal products with a particular focus on addressing a given public health emergency;
- Ensure smooth functioning of expert panels for the assessment of some high-risk medical devices and avail of essential advice in crisis preparedness and management with regard to the use of medical devices.

EU CTR - Harmonisation Guidance Published

The European Commission has published Harmonisation guidance to the website EudraLex - Volume 10 - Clinical trials guidelines. The guidance document has been developed and endorsed by the EU Clinical Trials Expert Group to comply with Clinical Trials Regulation (EU) No 536/2014 (EU CTR) and support sponsors of clinical trials when submitting Part II elements of the application under EU CTR. Part II covers aspects typically examined by Ethics Committees and will be conducted separately by each Member State Concerned (MSC) individually for its own territory. The aim of this guidance is to set of harmonised documents such as Investigator Curriculum Vitae (CV), declaration of interest, site and facilities suitability, recruitment and informed consent procedure, payment of compensation. Using documents templates applicable across all EU will facilitate the clinical trials application process. Sponsors are encouraged to use the harmonised templates, however sponsors are advised to also refer to national guidance when submitting an application in each Member State.

In Introduction, the Expert Group underlines that this guidance is also relevant under Directive 2001/20/EC and may be used in advance of the EU CTR becoming applicable.

First Authorisations of COVID-19 Vaccines

The UK's Medicines and Healthcare products Regulatory Agency (MHRA) as a first in Europe granted temporary authorization to Pfizer and BioNTech's mRNA-based BNT162b2 COVID-19 vaccine, Comirnaty. Following the MHRA an authorisation has been issued in the US, Europe by EMA , Canada and Singapore. Other vaccine COVID-19 candidates like for example mRNA-1273, Moderna, type: mRNA based vaccine; AZD1222, University of Oxford/AstraZeneca COVID-19 Vaccine, type: adenovirus vaccine completed third phase of clinical trials and companies applied for its authorisation in the particular countries and regions of the word.

In addition, the EMA provided guidance for developers of potential COVID-19 vaccines on the clinical evidence to include in marketing authorisation applications.

Published also: EMA safety monitoring plan and guidance on risk management planning for COVID-19 vaccines.

Regulatory Affairs Professionals Society (RAPS) COVID-19 vaccine tracker.

Updated Guidance on Data Protection by Design and by Default

The European Data Protection Board (EDPB) has published its updated Guidelines 4/2019 on Article 25 Data Protection by Design and by Default (DPbDD), version 2.0 dated 20 October 2020. The guidance document focuses on controllers' implementation of DPbDD based on the obligation in Article 25 of the Regulation 2018/ /1725 (GDPR). DPbDD is an obligation for all controllers, irrespective of size and varying complexity of processing. To be able to implement the requirements of DPbDD, it is crucial that the controller understands the data protection principles and the data subject's rights and freedoms. The EDPB provides recommendations on how controllers, processors and producers of products, services and applications can cooperate to achieve DPbDD. It encourages the controllers in industry, processors, and producers to use DPbDD as a means to achieve a competitive advantage when marketing their products towards controllers and data subjects. It also encourages all controllers to make use of certifications and codes of conduct.

News from the European Medicines Agency (EMA)

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

European Union Clinical Trials Regulation Update

The application of Regulation (EU) No. 536/2014 (EU Clinical Trial Regulation) (EU CTR) is conditional on the conduct of an independent audit to verify that the Clinical Trials Information System (CTIS) have achieved full functionality and meet the functional specifications.

The independent audit of the EU Portal and Database (EUPD), which are part of CTIS, was initiated in September 2020, the first field work started on 18 November 2020 and ended on 8 December 2020 with the summary of preliminary findings expected in the third week of December 2020. In 2021, the EMA plans to focus on the findings of a system audit, improving usability, quality and stability of the CTIS and knowledge transfer to prepare users and their organisations for CTIS. The CTIS Go-Live date is the end of the six months after the European Commission publishes its notice in the Official Journal. It means that, if no unexpected issue with CTIS, the EU CTR will be fully applicable in December 2021.

EMA Guideline on the Clinical Evaluation of Anticancer Medicinal Products

In October 2020, the EMA's Committee for Medicinal Products for Human Use (CHMP) adopted for release for consultation guideline on the clinical evaluation of anticancer medicinal products. The document aims to provide guidance on all stages of clinical drug development for the treatment of malignancies. It replaces guideline on the evaluation of anticancer medicinal products in man' EMA/CHMP/205/95 Rev 5. The guidance is in a draft version and will be under consultation until 15 February 2021.

EMA New Online Platform for Scientific Advice

The EMA has announced its new IRIS Regulatory & Scientific Information Management Platform for developers of human and veterinary medicines to request scientific advice. The IRIS platform provides a single space for applicants and EMA to submit requests, communicate, share information and deliver documents concerning each scientific advice procedure. The IRIS Platform is applicable from 19 October 2020.

Reflection Paper on the Pharmaceutical Development of Medicines for Use in the Older Population

The EMA's Committee for Medicinal Products for Human Use (CHMP) has adopted Reflection paper on the pharmaceutical development of medicines for use in the older population. This comes into effect on 01 May 2021. The reflection paper mainly applies to any new applications for a marketing authorisation (MA) or variation to an existing MA, and for all application types including full and abridged MAs (i.e. new medicinal products, generics, well established use). The guidance also states that the reflection paper may also be of interest to other "stakeholders such as physicians, pharmacists and patients because of topics such as patient adherence, medication safety and practical medication problems." The reflection paper may be also considered "during the clinical trial phases and in the post-authorisation phase as part of the product lifecycle management".

News from Individual Countries

The United Kingdom

New Fast-Track Research Ethics Review Pilot

On 04 January 2021, the Health Research Authority (HRA) launched the fast-track research ethics review pilot, which will run until 31 March 2021. The pilot is open to global clinical trials and phase I trials, whether the sponsor is commercial or non-commercial. Clinical trials involving a gene therapy medicinal product are excluded. The aim of the pilot program is to get a shorter time period between submission and the Research Ethics Committee (REC) meeting, review by one dedicated experienced REC and faster turn-around of correspondence with applicants. Before entry into the pilot, all applicants first must contact fasttrack.rec@hra.nhs.uk, book the slot of REC and provide basic information about the study. The submission of application is via Integrated Research Application System (IRAS) and REC uses standard validation criteria.

Removal of Commercial Organisation Information Document from IRAS Application

The HRA informed that for new submissions from 12 November 2020, the commercial Organisation Information Document (OID) will no longer be required as part of the application process through IRAS. The commercial (OID) was initially introduced across the UK with the implementation of the UK Local Information Pack in June 2019 . Until 12 November 2020 it was mandatory to complete the document by the sponsor or authorised delegate and submit with the IRAS application. The change has been made of the request from stakeholders and it has been agreed across the four UK nations.

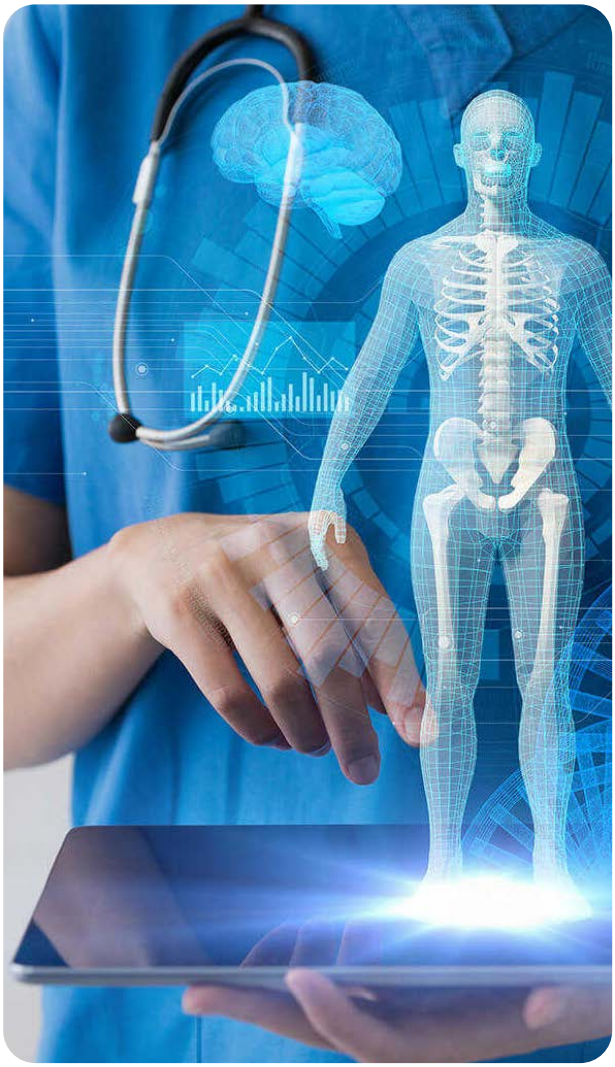
NIHR CRN Portfolio Application Form No Longer Required

As of 05 November 2020, the Portfolio Application Form (PAF) is no longer required to apply for National Institute for Health Research (NIHR) Clinical Research Network (CRN) support, and the option to create a PAF has been removed from the Integrated Research Application System (IRAS).

Applications to be considered for NIHR CRN support should still be made by selecting 'yes' to question 5b of the IRAS project filter through IRAS, or where HRA Approval is not required, through the relevant Local Clinical Research Network.

Restricted Access to Electronic Health Records (EHRs) in Clinical Trials

On 26 November 2020, the Medicines and Healthcare products Regulatory Agency (MHRA), the HRA and the Information Commissioners Office (ICO) have published joint guidance on access to electronic health records (EHRs) in clinical trials. Where EHRs have not been designed to allow restricted access, additional safeguards are required.



Spain

New Royal Decree on Observational Studies

The Spanish Agency of Medicines and Medical Products (AEMPS) informed about new Royal Decree 957/2020 of 03 November 2020 on observational studies with medicines for human use. The new Decree came into force on 2 January 2021.

The Royal Decree changed a definition of observational studies. Instead of EPA (post-authorization observational study) it has been used definition "observational study with drugs" and "observational study with prospective follow-up drugs". Due to that change, as of 02 January 2021, applicants do not have to request the AEMPS for classification of observational studies. The observational studies classified by the AEMPS before 02 January 2021 must continue to meet the requirements established by the previous regulations (ORDER SAS / 3470/2009 and Chapter VI of the Royal Decree 577/2013), including obtaining authorisation by the AEMPS and Autonomous Communities. Observational studies that are proposed to be carried out in Spain after 02 January 2021 must obtain only the favourable opinion of an accredited Ethics Committee for investigation with medicinal products (CEIm) and a contract with the investigational site.

It is possible that the Autonomous communities will develop their local legislation with additional requirements.

Publication of information in the Spanish Registry of Clinical Studies (REec) is:

- Mandatory for "observational study with prospective follow-up drugs"
- Voluntary for other observational studies with drugs.

Observational studies with drugs are exempted from the obligation of having an insurance.

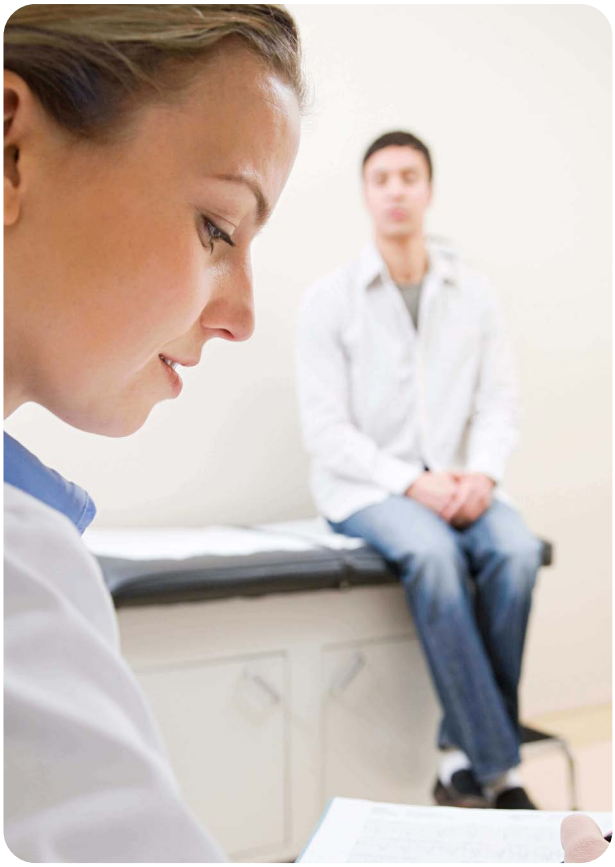
The AEMPS published also Questions and answers about the entry into force of Royal Decree 957/2020 explaining how applicants should proceed with submissions and amendments after 02 January 2021 for studies classified before that date and new studies, how to proceed in case of Post authorisation Safety Studies (PASSs) and how to report suspected adverse reactions. Q&A document also provides guidance on the monitoring of observational studies.

AEMPS Updates of Instruction Document for Clinical Trials

The AEMPS has published updated version 13 of Instruction document of the Spanish Agency for Medicines and Health Products for conducting clinical trials in Spain. The document is prepared in Questions and Answers (Q&A) format.

Questions & Answers on Regulation of ATMPs Updated

On 17 November 2020, the AEMPS updated the Questions & Answers on Regulation of Advanced Therapy Medicinal Products (ATMPs). Among others, the guidance explains what kind of procedures are considered by AEMPS as 'non substantial manipulation' in ATMPs. The AEMPS advises consultation, if there are doubts about the type of manipulation and/or the classification of the product as an ATMP.



The Netherlands

Procedure for Submitting a Local Feasibility Statement

The Central Committee for Research Involving Human Subjects (CCMO) informed about the change of procedure for submitting a statement of local feasibility for medical scientific research. In the new procedure, the current Research Statement has been replaced by the Certificate of Suitability for Research Institution (VGO). From 01 December 2020 to 01 June 2021, a transition period applies and applicants can choose whether to use the VGO or the current Research Statement to assess the suitability of the participating centres. If an applicant wants to use new procedure using VPO he/she must submit a signed part A of the VGO and use new the Dutch Clinical Research Foundation (DCRF) model of research contract. Use of the VGO will be mandatory from 01 June 2021.

France

ANMS Updates Guidance on COVID-19 Ongoing Clinical Trials

The National Agency for the Safety of Medicine and Health Products (ANSM), the French competent authority updated the guidance COVID-19 – Ongoing clinical trials. The ANMS says: "If it is necessary to reactivate in the same way transitional measures already authorised during the 1st wave and then suspended, information from the ANSM and the Ethic Committee is requested (substantial modification for information). Notification of an urgent safety measure followed by a substantial modification for authorisation is not required. " In addition, the ANSM brought to the attention of sponsors some certain elements related to the management of clinical trials in the current situation like resumption interrupted clinical trials due to the COVID-19 context; management of follow up visits; delivery of investigational products directly to patients and safety reporting for COVID-19 clinical trials.

Switzerland

Guidance on the Management of Clinical Trials During the COVID-19 Pandemic-Revision

In December 2020, Swissmedic, the Swiss competent authority published Joint Guidance of Swissmedic and swissethics on the management of clinical trials with medicinal drug products in Switzerland during the COVID-19 pandemic . The Swissmedic revised the chapter on "Monitoring". It further clarifies details on remote source data verification (SDV) and communication with the Lead Ethics Committee and the Swissmedic.

Slovakia

Guidance on Procedure for the Submission for the Authorisation of a Clinical Trial

State Institute for Drug Control (SUKL) , the Slovak national competent authority revised the Procedure for the submission for the authorisation of a clinical trial. The guidance is applicable to be followed by applicants from 01 October 2020.

Other Initiatives

VHP Involving Clinical Trials on GMO

The Clinical Trials Facilitation and Coordination Group (CTFG) - a working group on clinical trials of the Heads of Medicines Agencies has published version 5 of the guidance document : Guidance document for sponsors for a Voluntary Harmonisation Procedure (VHP) for the assessment of multinational Clinical Trial Applications. The main change in version 5 is the addition to the VHP clinical trials with medicinal products containing or consisting of genetically modified organisms (GMOs). In the case of clinical trials on GMO, a standard VHP dossier should be provided, the VHP assessment can take 108 days excluding a request for VHP and national step. The sponsors should take into account that there are specific national requirements for this kind of clinical trials and in some countries additional authorities decisions have to be collected before starting clinical trial or for national step. The submission of clinical trial with GMO will be limited to those Member States which agreed to participate in VHP for such studies.

CTFG Guidance on National Pilot Projects

In October 2020, the CTFG updated the guidance document on national pilot projects in support of the transition to the new Clinical Trial Regulation EU 536/2014. The guidance document lists the European Union Member States (MSs) have already started pilots projects at national level. The description of the processes in each MSs and hyperlinks to read more detailed information prepared by MSs have been revised.

North America

United States of America

FDA Releases Artificial Intelligence/Machine Learning Action Plan

On 12 January 2021, the U.S. Food and Drug Administration released the agency's first Artificial Intelligence/Machine Learning (AI/ML)-Based Software as a Medical Device (SaMD) Action Plan. This action plan describes a multi-pronged approach to advance the Agency's oversight of AI/ML-based medical software.

"This action plan outlines the FDA's next steps towards furthering oversight for AI/ML-based SaMD," said Bakul Patel, director of the Digital Health Center of Excellence in the Center for Devices and Radiological Health (CDRH). "The plan outlines a holistic approach based on total product lifecycle oversight to further the enormous potential that these technologies have to improve patient care while delivering safe and effective software functionality that improves the quality of care that patients receive. To stay current and address patient safety and improve access to these promising technologies, we anticipate that this action plan will continue to evolve over time."

The AI/ML-Based Software as a Medical Device Action Plan outlines five actions that the FDA intends to take, including:

- Further developing the proposed regulatory framework, including through issuance of draft guidance on a predetermined change control plan (for software's learning over time);
- Supporting the development of good machine learning practices to evaluate and improve machine learning algorithms;
- Fostering a patient-centered approach, including device transparency to users;
- Developing methods to evaluate and improve machine learning algorithms; and
- Advancing real-world performance monitoring pilots.

Canada

Health Canada Explains Plans for COVID-19 Interim Orders and Forthcoming Regulatory Amendments

Health Canada (HC) announced its intention to leave several Interim Orders (IO) relating to COVID-19 in place until at least the fall of 2021. By this time, the agency plans to have regulatory amendments in place that will maintain a balance between flexibility and regulatory oversight. In the weeks following this initial announcement, HC has released more information about the Interim Orders and its long-term plans.

In a note issued to stakeholders, Health Canada stated that it will issue a second Interim Order maintaining the provisions of Interim Order Respecting the Importation and Sale of Medical Devices for Use in Relation to COVID-19 until at least the fall of 2021. The current IO is scheduled to expire on 18 March, 2021.

HC issued an additional notice advising stakeholders on its plans to maintain the effects of the Interim Order Respecting Clinical Trials for Medical Devices and Drugs Relating to COVID-19 after the fall of 2021. This is to be accomplished through regulatory amendments that will allow sponsors to continue conducting clinical trials authorized under the IO and to utilize this pathway for new or later-phase COVID-19 clinical trials.

MEDICAL DEVICES

EUROPE

News from Individual Countries

Italy

National Contract Template for the Conduct of the Clinical Investigation on Medical Devices

The National Coordination Centre of the Territorial Ethical Committees for clinical trials on medicinal products for human use and on medical devices established by AIFA, the Italian Medicines Agency, published a national contract template to be negotiated with the sites involved in clinical trials with medical devices. Use of the contract template is highly recommended for a contract negotiation with Italian sites. It contains the minimum content and in case of specific study needs the template may be integrated. The national contract template became effective at the moment of its publication by Coordination Centre in November 2020.

The Netherlands

New Version of the Investigational Medical Device Dossier (IMDD) Model

The Central Committee for Research Involving Human Subjects (CCMO), the Dutch competent authority for clinical investigations with medical devices, has published new version of the Investigational Medical Device Dossier (IMDD) model. The IMDD specifies all items that must be covered for the application to the review committee (accredited Medical Research Ethics Committee (MREC or CCMO)) for non-CE-marked medical devices intended for clinical investigation. The new version is an update of the previous version from September 2019 and is in the line with the requirements of the EU Medical Devices Regulation (MDR).

Guidance of a Clinical Investigation with a Medical Device under MDR

The CCMO published guidance Review of a clinical investigation with a medical device - guidance document for MRECs. The guidance document is written in English and focuses on the quality and safety of medical devices to be used in clinical investigations and on the new procedures for the submission, assessment and conduct of clinical investigation as a result of the EU Medical Device Regulation (Regulation (EU) no 2017/745), applicable as of 26 May 2021.

Other Initiatives

IMDRF's Proposed Update to Guidance on Post-Market Clinical Follow-Up Studies

A proposed document on Post-Market Clinical Follow-up Studies (PMCF) has been released by the International Medical Device Regulators Forum (IMDRF) Medical Devices Clinical Evaluation Working Group. The update outlines when a PMCF study is indicated, the general principles of PMCF studies for medical devices, the design and implementation of studies, and the use of the clinical information. The consultation closed on 11 December 2020.

North America

United States of America

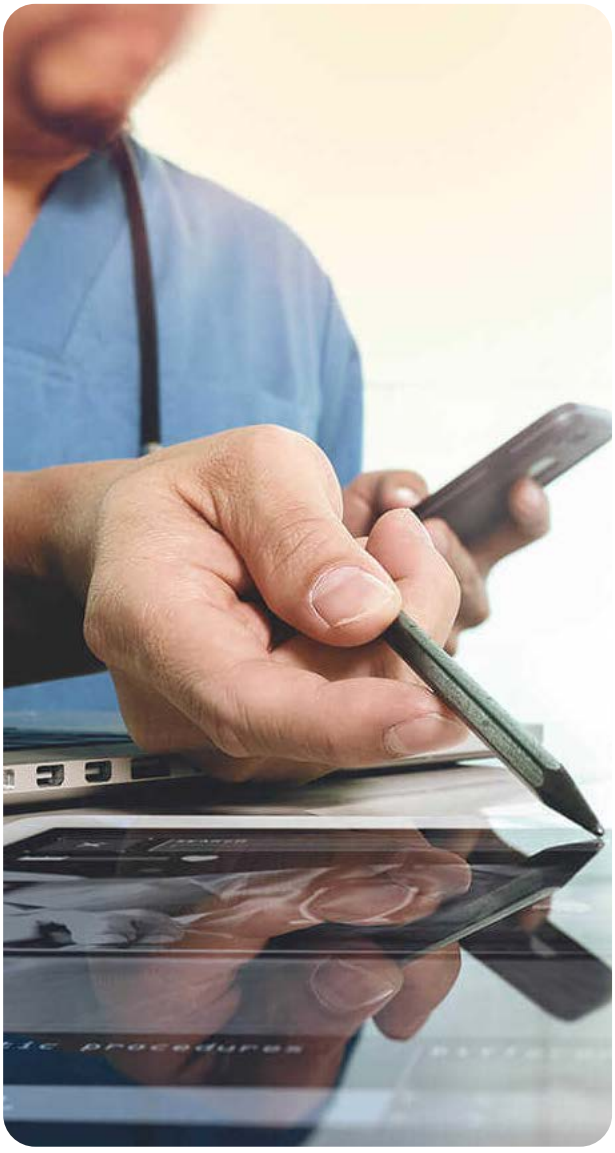
FDA Takes Steps to Provide Clarity on Developing New Drug Products in the Age of Individualized Medicine

Advances in scientific knowledge and drug development technology have provided an opportunity for new approaches to drug development, including the development of drugs for the treatment of rare diseases. These advances have contributed to an increase in development and approval of drugs for the treatment of rare diseases in recent years. In fact, in the past eight years, the U.S. Food and Drug Administration (FDA) has approved more than twice as many drugs for rare diseases, often referred to as orphan drugs, as in the previous eight years.

For genetic diseases, recent approaches to testing and molecular diagnosis have allowed FDA to pinpoint, in some cases, the exact cause of a patient's disease. For a patient with a very rare genetic disease, development of a drug product that is tailored to that patient's specific genetic variant may be possible. This is an important advance in treatment for those with very rare genetic diseases, especially those for which there are no adequate therapies available to treat the disease.

At this time, development of individualized genetic drug products is most advanced for antisense oligonucleotide (ASO) products. Therefore, we are taking the first steps in bringing clarity to this emerging area of individualized drug development by releasing a new draft guidance on investigational new drug (IND) submissions for individualized ASO drug products.

The guidance addresses the following points: 1) the approach to obtaining feedback from the FDA; 2) the expectations and process for making regulatory submissions to the FDA; 3) recommendations about the requirement for Institutional Review Board (IRB) review of the protocols within, and 4) how to obtain informed consent.



OTHER "HOT" TOPICS IN EUROPE

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

The application of the Medical Device Regulation (EU) 2017/745 (MDR) will come into force in the EU on 26 May 2021 and In Vitro Diagnostic Medical Devices Regulation (EU) 2017/746 (IVDR) on 26 May 2022.

Actor Registration Module of EUDAMED Available

On 01 December 2020, the European Commission made the EUDAMED Actor registration module available to Member States and economic operators (including manufacturers, system/procedure pack producers, authorised representatives (ARs) and importers) established within the EU 27 countries, Iceland, Liechtenstein and Norway. Economic operators from the United Kingdom, Switzerland and Turkey will not be able to submit Actor registration requests in EUDAMED.

Every operating regulator requesting the Actor registration in EUDAMED will receive their company Single Registration Number (SRN) issued by the Competent Authority (CA) that has validated the request. The SRN is an unique number which will be used by economic operators in every relevant official documents and related reports.

The Actor module is the first of six EUDAMED modules. The module on Unique Device Identifier (UDI)/device registration (second module) and the module on Certificates and Notified Bodies (third module) will become available by May 2021. Other modules will be made available on a gradual basis as soon as they are functional. The European Commission is not in a position to require the use of the Actor registration module until EUDAMED is fully functional in May 2022 and additional national requirements on registrations can therefore not be excluded.

Moving forward, the European Commission has created new web page providing information on how to get SRN, description of Actor registration process, Actor roles, Actor users' access request, EUDAMED User Guide, list of documents to be provided with the Actor registration request and other useful information.

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

- MDCG 2020-18 Position Paper on UDI assignment for Spectacle lenses & Ready readers; December 2020
- MDCG 2020-17 Questions and Answers related to MDCG 2020-4: "Guidance on temporary extraordinary measures related to medical device notified body audits during COVID-19 quarantine orders and travel restrictions"; December 2020
- MDCG 2020-16 Guidance on Classification Rules for in vitro Diagnostic Medical Devices under Regulation (EU) 2017/746; November 2020

Published also: Ongoing guidance development and other relevant work within MDCG Subgroups

MedTech Europe Reflection Paper for Class D Devices under IVDR

MedTech Europe has published a reflection paper on the readiness of the In Vitro Diagnostic (IVD) Regulation Framework for Class D medical devices. The paper "aims to identify and raise awareness of those devices that are currently self-declared under IVD Directive and will become Class D under the IVDR. These devices are especially vulnerable to the IVDR transition period, because they cannot benefit from the so-called "grace period" that extends to 27 May 2024. MedTech Europe has called for an urgent discuss with the European Commission, National Competent Authorities (NCAs) and stakeholders and other relevant parties, to identify actions to ensure smooth transition these devices to the IVDR and safeguard continued access to these high-risk IVD devices.

IVD Symbols Titles Translations to comply with IVDR

MedTech Europe has published new In Vitro Diagnostic (IVD) symbols in order to comply with the In Vitro Diagnostic Medical Devices Regulation (IVDR). The IVDR requires 'devices intended for self-testing', 'devices for near-patient testing' and specific tests for not self-testing to state these facts on their labels. IVD symbols titles have been translated in 27 EU languages and they are strongly recommended to use.

Notified Bodies Officially Designated in Europe

The 18th Medical Devices (MDs) Notified Bodies were officially designated under the MDR and included in the European Commission NANDO database. The 5th notifications were noticed under the IVDR.

Key Brexit Updates

On 24 December 2020, the United Kingdom (UK) and the European Union (EU) have agreed a post-Brexit Trade and Cooperation Agreement. It is mean that hard Brexit has been avoided and new free trade cooperation between the UK with the EU has started. Brexit came into force on 01 January 2021.

Amended UK Statutory Instruments Applicable from 1 January 2021

Following the end of the transition period (31 December 2020), the UK Statutory Instruments have been further amended by:

- The Human Medicines (Amendment etc.) (EU Exit) Regulations 2019 (SI 2019 No. 775)
- The Human Medicines and Medical Devices (Amendment etc.) (EU Exit) Regulations 2019 (SI 2019 No. 1385)
- The Medicines for Human Use (Clinical Trials) (Amendment) (EU Exit) Regulations 2019 (2019 No.744)
- The Human Medicines (Amendment etc.) (EU Exit) Regulations 2020 (SI 2020 No. 1488)
- The Medical Devices (Amendment etc.) (EU Exit) Regulations 2019 (SI 2019 No. 791)
- The Blood Safety and Quality (Amendment) (EU Exit) Regulations 2020 (SI 2020 No.1304)
- The Human Tissue (Quality and Safety for Human Application) (Amendment) (EU Exit) Regulations 2020 (SI 2020 No.1306)

MHRA Post Transition Period Guidance

The Medicines and Healthcare products Regulatory Agency (MHRA) has published on 31 December 2020 post-transition period guidance for industry and organisations to follow from 01 January 2021. It replaces previously published guidance. The revised guidance refers to clinical trials, devices, importing and exporting, IT systems applicable in the UK from 01 January 2021, applicable legislation in GB (England, Scotland and Wales) and Northern Ireland, procedures in licensing of medicinal products, medical devices, orphan drugs, biosimilars and e-cigarettes, guidance on pharmacovigilance and paediatric requirements. More about each of guidance is available here.

Guidance Note on Good Pharmacovigilance Practices Specific for the UK

The MHRA published the guidance note titled Exceptions and modifications to the EU guidance on good pharmacovigilance practices that apply to UK marketing authorisation holders and the licensing authority. The guidance note provides an overview of the modifications to the EU Good Pharmacovigilance Practices (GVP). The key changes are highlighted in the summary section for each module, there are additions to the UK legislative references, deleted sections that no longer apply for GB (England, Scotland and Wales). This replaces for the specific paragraphs comparing to EU GVP. Note that sections which are not mentioned in the guidance still apply in full in the UK.

EMA Questions & Answers (Q&A) Guidance on Implementation of Northern Ireland Protocol

The European Medicines Agency (EMA) has published a practical guidance on the applicable rules in Northern Ireland after the transition period with respect to EMA activities. The Protocol on Ireland/Northern Ireland is part of the EU Withdrawal Agreement. The Protocol introduces new arrangements whereby the Northern Ireland (NI) market must continue to conform to European Union law, including medicinal products and medical devices licensing for sale or supply.

The guidance informs that the Qualified Person of a clinical trial can be established in NI. In case a sponsor is in NI, it is mandatory for the sponsor to nominate a legal representative in EU/EEA (European Economic Area). A legal representative cannot be established in NI and needs to be in an EU/EEA country.

From 01 January 2021 the UK authorities will have partial access to EudraVigilance database. Question and answer 4.1 explains the process and which country code should be used for UK (NI) and GB.

Third country reporting rules apply to all clinical trial SUSAR cases occurring in the UK including NI, therefore the country code "GB" should be used for all reportable SUSARs occurring in the UK.

The guidance document provides information on requirements for UK and NI, among others, on electronic application form (eAF), Periodic Safety Update Report (PSUR) repository, manufacturing and distribution, dossier submission and product information.

Regulation of Medical Devices in Northern Ireland

The MHRA has updated the guidance on regulating devices from 01 January 2021. The update provides more information on the regulation of medical devices in Northern Ireland (NI) under the terms of the Ireland/Northern Ireland Protocol.

The rules for placing medical devices on the NI market differ from those applicable to Great Britain (England, Wales and Scotland). Unlike Great Britain (GB), the EU MDR and the EU IVDR will apply in NI from 26 May 2021, and 26 May 2022 respectively, in line with the EU's implementation timeline. When placing devices on the NI and market, GB-based manufacturers must appoint an EU or Northern Ireland-based Authorised Representative. However, most manufacturers based outside the UK (NI, England, Wales and Scotland) must have a UK Responsible Person in place to act as a regulatory point of contact within the UK and comply with the registration requirements when these begin to apply.

To place a CE marking on device for circulation in both NI and the EU, manufacturer must use an EU-recognised Notified Body to undertake any mandatory third-party conformity assessment.

How to Import and Export Goods Between Great Britain and the EU

The MHRA has published interactive guidance for anyone who is navigating importing and exporting goods between Great Britain (GB) and the EU. The guidance applies to all goods including lab kids, study samples which must be sent to the laboratories in the UK. To ensure ongoing trials can continue, investigator sites within the EU require to get an EORI (Economic Operator Registration and Identification) number for trading with organisations outside of the EU to make shipments.

Please note, additional post-Brexit new or revised guidance from MHRA is expected and will be included in future Regulatory Newsletters.

OTHER "HOT" TOPICS FROM UNITED STATES

FDA Offers Guidance to Enhance Diversity in Clinical Trials, Encourage Inclusivity in Medical Product Development

To further promote and protect public health, it is important that people who are in clinical trials represent the populations most likely to use the potential medical product. In that spirit, today the U.S Food and Drug Administration (FDA) issued final guidance with the agency's recommendations on designing and executing clinical trials of drugs and biologics that include people with different demographic characteristics (e.g., sex, race, ethnicity, age, location of residency) and non-demographic characteristics (e.g., patients with organ dysfunction, comorbid conditions, and disabilities; those at weight range extremes; and populations with diseases or conditions with low prevalence).

The final guidance issued by FDA, "Enhancing the Diversity of Clinical Trial Populations-Eligibility Criteria, Enrollment Practices, and Trial Designs," which was first issued as a draft in 2019, provides the agency's current thinking on steps to broaden eligibility criteria in clinical trials through inclusive trial practices, trial designs, and methodological approaches. The guidance aims to provide recommendations for how sponsors can increase enrollment of underrepresented populations in their clinical trials.

Additionally, this guidance provides recommendations on broadening clinical trial eligibility criteria for clinical trials of investigational drugs intended to treat rare diseases and recommendations on improving enrollment and retention of participants with rare diseases. The guidance notes that sponsors should consider early engagement with patient advocacy groups and patients to elicit suggestions for designing trials that participants would be willing to enroll in and support.

2020: A Strong Year for New Drug Therapy Approvals – Despite Many COVID-19 Challenges

Throughout 2020, the U.S. Food and Drug Administration's Center for Drug Evaluation and Research (CDER) was challenged to respond to the COVID-19 pandemic while still working to bring safe and effective new drug therapies for a range of other diseases and conditions to patients in need.

In 2020, FDA approved a wide variety of new drugs never before marketed in the United States, known as "novel" drugs, along with a range of new approvals containing active ingredients already on the market put to new and innovative uses. Many will have a positive, and even life-saving impact, on countless patients' lives. Some of the approvals included:

Advances to treat infectious disease, including the first FDA-approved medication in the U.S. for the treatment of patients with COVID-19 (hospitalized adults and adolescents). Among others, FDA also approved new treatments for HIV-1, chronic hepatitis C, hospital-acquired bacterial pneumonia and ventilator-associated bacterial pneumonia, and flu prevention.

Many new therapies for a wide array of cancers, particularly lung cancers, for which FDA approved twelve notable new treatments, two of which were also approved to treat patients with certain types of thyroid cancer. FDA also approved four new notable therapies to treat patients with various forms of breast cancer. Other advances include new therapies for patients with other forms of cancer urothelial cancer, colorectal cancer prostate cancer, and bladder cancer.

New drug therapies for patients with rare diseases are often among the most important approvals. Patients with rare diseases frequently have few or no drugs available to treat their condition – and for them, approvals of so-called "orphan" drugs can mean new hope for an enhanced quality of life, and in some cases, increased survival. In 2020, more than half (31 of 53, or 58%), of all of FDA's novel approvals were for drugs to treat patients with rare diseases.

Although regulatory processes differ widely between the FDA and those of regulatory agencies in other countries, 40 of the 53 novel drugs approved in 2020 (75%) were approved in the United States before receiving approval in any other country.

More details about CDER's new drug therapy approvals for 2020 – including many specific examples of notable new approvals for the year – are available in FDA's annual New Drug Therapy Approvals report.

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 500 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.

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