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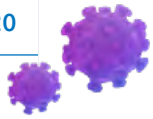
REGULATORY

NEWSLETTER N.29
January - March 2020

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

SUMMARY



CORONOVIRUS (COVID-19) OUTBREAK

On 11 March 2020 the World Health Organization (WHO) has officially declared the outbreak of novel coronavirus disease, COVID-19, a global pandemic. The European Commission (EC), all the European Union (EU) Members States, US government and other government authorities throughout the world started to cooperate more closely to slow down spreading the virus and protect businesses.

The WHO website publishes guidance and information about an impact of COVID-19 on world. It includes Questions & Answers on coronavirus, what everybody needs to do in case of travel and other advice or trainings. The website is updated daily.

Europe

In March, the European Medicinal Agency (EMA), the European Commission (EC) and national competent authorities in the Member States have organised the first meeting of the EU Executive Steering Group on shortages of medicines caused by major events. The aim of the meeting was to discuss the potential impact of COVID-19 on the supply of medicinal products for human and veterinary use in the EU and to work with pharmaceutical industry associations, companies and manufacturers in the EU. The group will also ensure that patients and healthcare professionals across the EU are kept informed in a consistent and transparent manner about the risks and the remedial actions taken.

At the EU's Response to COVID-19 webpage the EC informs about taken preventions by EU, cooperation with China and answers to many questions related to COVID-19.

In addition, the European Commission launched a special call for expressions of interest to support research on COVID-19 vaccine development, treatment and diagnostics with an initial budget of €10 million, furthermore, up to € 45 million in Horizon 2020 funding will support additional research through the Innovative Medicines Initiative (IMI).

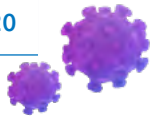
EMA published several guidance for stakeholders during coronavirus pandemic and advices for health professionals and patients on current treatments and vaccines on COVID-19.

EMA in agreement with the Clinical Trials Expert Group (CTEG) of the European Commission, the Clinical Trials Facilitation and Coordination Group (CTFG) and the GCP Inspectors' Working Group published guidance on the management of clinical trials during the COVID-19 (coronavirus) pandemic.

The guidance has been issued without prior public consultation due to rapidly evolving situation and new versions of the guidance are possible. The EMA underlines that guidance is a recommendation for sponsors, investigators and the health authorities but specific national legislation and guidance take priority over offered guidance.

The guidance instructs how to proceed with ongoing trials during COVID-19 pandemic, ongoing recruitment and continued involvement of participants in the trial, or on starting of new trials needs to be considered. It is recommended to consider phone or video visits rather than physical visits. In case an impact on subject's safety to be submitted a temporary halt of the trial to national Competent Authorities and Ethics Committees. In some clinical trials to be considered suspension or slowdown of recruitment, or extending of the duration of the trial. Regarding consent forms the guidance allows to use verbal consent form from subjects in the presence of an impartial witness in accordance Art 2 (j) of Directive 2001/20/EC but in every case national and local restrictions should be considered.

The EMA underlines that in the COVID-19 situation protocol deviations are unavoidable and all such deviations must be recorded and GCP inspection will not trigger the actions required by GCP § 5.20.



The European Union national competent authorities (NCAs) and ethics committees (ECs) also published in their press releases or announcements instructions on conducting clinical trials with medicinal products and medical devices during COVID-19 pandemic. The regulatory requirements are different from country to country but NCAs and ECs explain mostly an implications of COVID-19 on methodological aspects of ongoing clinical trials, their accessibility during pandemic, communication with them, supply of study medication to patients and possible monitoring activities (e.g. cancellation, postponement or extension on-site monitoring visit or use various electronic systems for monitoring).

Examples of guidance informing about the changes in management of clinical trials during coronavirus pandemic published recently by EU countries:

- Austria
- Bulgaria
- Belgium
- Cyprus
- Czech Republic
- Denmark
- Estonia
- Finland
- Germany PEI
- Germany BfArM
- Greece
- Hungary
- Ireland
- Italy
- Latvia
- Lithuania
- Malta
- The Netherlands
- Norway
- Poland
- Portugal
- Romania
- Slovakia
- Slovenia
- Spain
- Switzerland swissmedic
- Switzerland swissethics
- Sweden
- The United Kingdom MHRA
- The United Kingdom HRA
- The United Kingdom NIHR.

In addition, several European Union member states offer fast-track review of clinical trials with medicinal products, medical devices or vaccines to initiate for COVID-19 trials and ensure that this kind of research can start as soon as possible. This means that researchers and sponsors receive approval to begin the clinical trials with a products to be used for COVID-19 treatment much more quickly than the usual timelines, sometimes in a matter of hours. The health authorities, ethics committees, agencies, scientists, health care providers and funders work in close collaboration to start pre-clinical trials, feasibility and clinical trials for COVID-19 treatment.

North America

United States of America

FDA issues Letter to Sponsors, Applicants and Regulated Entities on COVID-19 issued on 30 April 2020. This FDA letter further clarifies and updates FDA's operations from those described in the letter issued on April 24, 2020. FDA is leveraging technology to host teleconferences rather than in-person meetings. The Document Control Center (DCC) will not process any submissions received by mail or courier including submissions provided on paper and electronic media (e.g., CDs, USB drives) after Wednesday, April 29, until further notice. Extension of response due dates for device marketing applications currently on hold and more.

https://www.fda.gov/media/136501/download

Summary of FDA & EMA Global Regulators Meeting on Data Requirements Supporting First-in-Human Clinical Trials with SARS-CoV-2 Vaccines issued on 18 March 2020. The teleconference of global regulators convened jointly by the European Medicines Agency (EMA) and US Food and Drug Administration (FDA) under the auspices of the International Coalition of Medicines Regulatory Authorities (ICMRA) discussed regulatory considerations related to the development of SARS-CoV-2 vaccine candidates and preclinical data requirements to support proceeding to first-in-human (FIH) clinical trials.

https://www.fda.gov/news-events/fda-meetings-conferences-and-workshops/summary-fda-ema-global-regulators-meeting-data-requirements-supporting-first-human-clinical-trials

In March 2020, FDA issued new guidance entitled Notifying FDA of a Permanent Discontinuance or Interruption in Manufacturing Under Section 506C of the FD&C Act, Guidance for Industry. FDA has been closely monitoring the medical product supply chain with the expectation that it may be impacted by the COVID-19 outbreak, potentially leading to supply disruptions or shortages of drug and biological products in the United States.

https://www.fda.gov/regulatory-information/search-fda-guidance-documents/notifying-fda-permanent-discontinuance-or-interruption-manufacturing-under-section-506c-fdc-act

FDA Guidance on Conduct of Clinical Trials of Medical Products during COVID-19 Public Health Emergency issued in March 2020. FDA issued this guidance to provide general considerations to assist sponsors in assuring the safety of trial participants, maintaining compliance with good clinical practice (GCP), and minimizing risks to trial integrity during the COVID-19 public health emergency. The appendix to this guidance further explains those general considerations by providing answers to questions that the Agency has received about conducting clinical trials during the COVID-19 public health emergency.

FDA Guidance on Conduct of Clinical Trials of Medical Products during COVID-19 Pandemic: Guidance for Industry, Investigators, and Institutional Review Boards.

Canada

Health Canada issues notification entitled Management of clinical trials during the COVID-19 pandemic: Notice to clinical trial sponsors on 3 April 2020. Notification addresses management of Clinical Trial Applications (CTA) during the COVID-19 pandemic.

Management of Clinical Trials during the COVID-19 pandemic: Notice to Clinical Trial Sponsors - Canada.ca

MEDICINAL PRODUCTS/DRUGS

Europe

News from the European Commission

EDPB Statement on the Processing of Personal Data in the Context of the COVID-19 Outbreak

The European Data Protection Board (EDPB) made a public statement on 19 March 2020. The statement informs that EU data protection law permits "competent public health authorities and employers to process personal data in the context of an epidemic, in accordance with national law and within the conditions set therein." EDPB says that emergency measures are permissible, but only for the duration of the emergency like during epidemic circumstances. The adequate security measures and confidentiality policies need to be in place. Anonymous use of mobile location data is also permissible but should be avoided, if possible. For the processing of personal data, including special categories of data by competent public authorities, "the EDPB considers that articles 6 and 9 GDPR enable the processing of personal data, in particular when it falls under the legal mandate of the public authority provided by national legislation and the conditions enshrined in the GDPR."

https://edpb.europa.eu/our-work-tools/our-documents/other/statement-processing-personal-data-context-covid-19-outbreak_en

https://www.unich.it/sites/default/files/edpb_guidelines_202003_healthdatascientificresearch-covid19_en_1.pdf

Revision of Annex 21 of EU GMP Guide

European Commission published a draft guideline on Annex 21 of European Union Good Manufacturing Practise (GMP) which sets out the principles and guidelines of good practice requirements applicable to a manufacturing and importation authorisation (MIA) holder, which imports medicinal products (human and veterinary) through the EU/European Economic Area (EEA) borders. The EC encourages all stakeholders in the supply chain of medicinal products to send the comments to draft consultation document. The consultation end date is 20 June 2020.

News from the European Medicines Agency (EMA)

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

EU Post Authorisation Studies (PAS) Register FAQ

The European Medicines Agency has released Frequently Asked Questions (FAQs) about the European Union (EU) post authorisation studies (PAS) register. The EU PAS Register is a publicly available register of non-interventional post-authorisation studies (PAS). All non-interventional PAS regardless of whether they are initiated, managed or financed by a marketing authorisation holder (MAH), or whether they are conducted by a research centre that is a partner of the European Network of Centres for Pharmacoepidemiology and Pharmacovigilance (ENCePP) network or any other research centre, including from outside the European Union, should be registered in EU PAS register. In addition, EU PAS Register has been technical upgraded with new functionalities like date of first registration or delayed protocol publication. There are additional possibilities to search by different categories: by country, by (primary) lead investigator or by EU PAS Register study number.

Mandatory Use of the ISO ICSR Format for Reporting Side Effects in Patients Across the World

In January 2020, the EMA's Management Board announced for the mandatory use of a consistent international format, the International Organization for Standardization (ISO) Individual Case Safety Report (ICSR) format, for reporting individual cases of suspected side effects in patients across the world. The ISO ICSR is prepared based on ICH E2B(R3) modalities. The EMA agreed to use also ISO standard terminology on pharmaceutical dose forms and routes of administration for adverse reaction reporting in the EU.

The use of the new international standard will become mandatory as of 30 June 2022 for all reporting to EudraVigilance, the European database of suspected side effects with medicines authorised in the European Economic Area (EEA). Currently, ICSRs are also accepted in the previous ICH E2B(R2) ICSR format and are converted to the ISO ICSR format (defined in ICH E2B(R3)) upon receipt in EudraVigilance.

European Union Clinical Trial Regulation-EMA Management Board Update

In March 2020, the EMA's Management Board endorsed the audit methodology for Clinical Trials Information System (CTIS) enabling the process for the selection of the supplier for the audit of the system to commence. EMA with CTIS providers will firstly assess the critical items prior to the audit and then focus on a further operational assessment (including of the public portal) to determine the full scope of the auditable version. The audit of the system should commence by end of December 2020.

Guidance for Applicants on a Pilot for Simultaneous National Scientific Advice

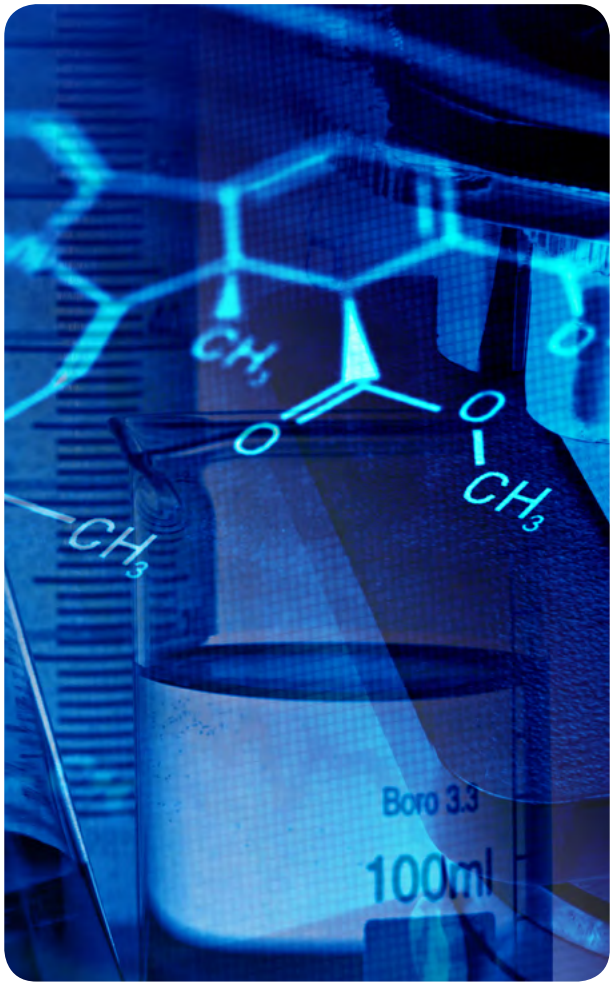
The EMA in cooperation with the Heads of Medicines Agency (HRA) launched pilot program for developers of medicinal products or medical devices and other technologies seek national scientific advice or regulatory advice in European Union countries. The program is called Simultaneous National Scientific Advice (SNSA) and establishes that in one single step national scientific and/or regulatory advice can be requested with two National Competent Authorities (NCA) simultaneously. Currently ten NCAs participate in the SNSA and offer several SNSA procedures for example questions on quality, safety and efficacy of medicinal products for human use, questions to clinical trial applications/concepts including questions on study design and statistical aspects or scientific advice requests related to drug-device combination products. Implementation of the pilot project has started on 1 February 2020. The SNSA will be widened in a next project phase to have more than two NCAs participating in the advice process and will be opened for new NCAs to join.

ICH M9 guideline on Biopharmaceutics Classification System-Based Biowaivers

The guideline has been adapted by the European Medicinal Agency (EMA) and will come into effect on **30 July 2020**. This guideline is proposed to address biopharmaceutics classification system (BCS)-based biowaivers. This guideline provides recommendations to support the biopharmaceutics classification of medicinal products and provides recommendations to support the waiver of bioequivalence studies. This will result in the harmonization of current regional guidance and support streamlined global drug development.

ICH E9 (R1) Addendum on Estimands and Sensitivity Analysis in Clinical Trials to the Guideline on Statistical Principles for Clinical Trials

The ICH E9 (R1) addendum has been adapted by the EMA in January 2020 and will come into effect in the European Union on 30 July 2020. The addendum provides clarification on some of the concepts explained in ICH E9. It presents a structured framework for clinical trials planning, conduct, data collection and interpretation of data analyses. The addendum also refines the role of sensitivity analysis to explore robustness of conclusions from the main statistical analysis, both aligned to the same estimand.



News from Individual Countries

The United Kingdom

Combined Ways of Working (CWoW) Pilot – Next Steps

The Medicines and Healthcare products Regulatory Agency (MHRA) and the Health Research Authority (HRA) informed that Combined Ways of Working (CWoW) pilot programme has reached another significant milestone, a total of 100 applications authorised across whole United Kingdom. The 100 approvals cover every phase of development, including first-in-human studies, with applications from both commercial and non-commercial sponsors. The main points of the CWoW is to develop a single application route and a coordinated ethics and regulatory review leading to a single UK decision on a clinical trial. The CWoW will help the UK to be ready when Clinical Trial Regulation (CTR) No 536/2014 comes in to effect. The CWoW reached next step and starting of 2 March 2020 a new automated technical solution has been launched. This means that the CWoW will be opened for more applicants, generate more feedback and move to the next phase of systems development.

Belgium

Fees Updated

Federal Agency for Medicines and Health Products (FAMHP), the Belgian Competent Authority has updated its fees for 2020. Information on the update can be found here.

Estonia

Medicinal Products Act amended

The Medicinal Products Act (MPA) in Estonia has been revised and updated version implemented. The MPA is applicable from 1 January 2020. It regulates the handling of medicinal products, issue of medical prescriptions, granting of marketing authorisations, clinical trials and advertising of medicinal products, and supervision over and responsibility in the area of medicinal products for the purpose of ensuring the safety, quality and efficacy of medicinal products used in Estonia and promoting the use of medicinal products for their intended purposes.

Denmark

Executive Order on Fees for Clinical Trials

Danish Medicines Agency (DMA) have been updated the fees covering clinical trials. The fees have been changes for commercial sponsors. Clinical trials with medicinal products in development stage phase I along with non-commercial trials, will still no longer be subject to DMA application fees.

Switzerland

The Guideline Amendments in Clinical Trials

Swissmedic revised the guideline amendments in clinical trials to introduce the new form „VO Form Administrative Changes". This new form includes the notification of changes concerning sponsorship, changes concerning the Swiss representative and other administrative changes.

North America

United States of America

News from FDA

Providing Regulatory Submissions in Electronic Format – Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications Guidance for Industry

Implements the electronic submission requirements of section 745A(a) of the FD&C Act for the electronic format of the content submitted in new drug applications (NDAs), abbreviated new drug applications (ANDAs), certain biologics license applications (BLAs), and certain investigational new drug applications (INDs).

https://www.fda.gov/regulatory-information/search-fda-guidance-documents/providing-regulatory-submissions-electronic-format-certain-human-pharmaceutical-product-applications-0

Purple Book: Database of Licensed Biological Products

The US Food and Drug Administration (FDA) launches the first version of its searchable online database of biological product information, known as the Purple Book.

Guidance Document Update

Between January 2020 and 27 March 2020, FDA published guidance documents, both draft and final, for Industry. The list below contains links to the documents that may be of interest to CROMSOURCE and its customers.

- Clinical Drug Interaction Studies – Cytochrome P450 Enzyme- and Transporter-Mediated Drug Interactions Guidance for Industry | FDA
- In Vitro Drug Interaction Studies – Cytochrome P450 Enzyme- and Transporter-Mediated Drug Interactions Guidance for Industry | FDA
- Regulatory Considerations for Use of Minimal Residual Disease in Development of Drug and Biological Products for Treatment
- Pediatric Study Plans for Oncology Drugs: Transitional Information until full Implementation of FDARA Section 504- draft
- Chemistry, Manufacturing, and Control (CMC) Information for Human Gene Therapy Investigational New Drug Applications (INDs)
- Demonstrating Substantial Evidence of Effectiveness for Human Drug and Biological Products.

Canada

News from the Health Canada Other initiatives

The Revised ICH E8: A Guide to New Clinical Trial Requirements

The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) was proposing a modernization of ICH E8 and reached third step of implementation process. The revision covers:

- Identify a basic set of critical-to-quality factors that can be adapted to different types of trials to support the meaningfulness and reliability of trial results and to protect human subjects;
- Address a broader range of trial designs and data sources;
- Provide an updated cross-referencing of all other relevant ICH Guidelines that should be referred to when planning clinical studies.

The modernisation of ICH E8 is the first step towards the GCP Renovation plan.

MEDICAL DEVICES

EUROPE

News from the European Commission

Harmonised Standards for Demonstrating Conformity Of Medical Devices

In order to demonstrate the conformity of a medical device with the essential requirements laid down in Directives 85/16/EC, 90/385/EEC, 93/42/EEC and 98/79/EC, 95/ the medical device manufacturer must use harmonised standards as adopted by the European Union. A harmonized standard is defined as a standard developed by a recognized European standards organization, such as the European Committee for Standardization (CEN), the European Committee for Electrotechnical Standardization (CENELEC) or the European Telecommunications Standards Institute (ETSI).

On 25 March, the EC adopted decisions on harmonised standards which will allow manufacturers of critical devices such as medical face masks, surgical drapes, gowns and suits, washer-disinfectors, sterilisation to place them faster on the market with less expensive conformity assessment procedure. The updated list of the harmonised standards to be used was published in the Official Journal of the European Union on 25 March 2020.

Delay the Implementation of the Medical Devices Regulation (MDR) by one year – EC proposal

The European Commission has adopted a proposal to postpone the application date of the Medical Devices Regulation (MDR) for one year in response to the COVID-19 outbreak.

The proposal still requires the approval of the European Parliament and EU member states before it goes into effect. If approved, as expected, implementation of the MDR would be delayed until 26 May 2021.

News from Individual Countries

Denmark

New Enhanced Reporting Requirement

As of 3 March 2020, the Danish Medicines Agency (DMA) may impose an enhanced reporting requirement on doctors, nurses, dentists and other healthcare professionals if serious or non-serious incident, which may have potential failure or deficiencies in a particular type of medical device, occurs. This is to give the DMA the possibility of ensuring that all incidents are investigated thoroughly before any corrective actions are taken.

Recommendations on Applications for Authorisation of Clinical Investigation of Medical Device due to the MDR

From the date of Medical Device Regulation (MDR) applications, the Danish Medicines Agency (DMA) will no longer assess applications for clinical investigation authorization under Executive order no. 1263 of 15.

The DMA recommended sponsors, who wish an authorization for clinical applications under the current executive orders, submit a complete application at least 60 days prior the date of MDR application. This is to enable the Agency to complete the clinical authorization assessment before the date of MDR applies.

Additionally, the Agency indicated that approved clinical investigations that hold authorization under the current executive orders and have started prior the date of MDR application, can be continued.

The United Kingdom

Clinical Investigations of Medical Devices - Guidance for Manufacturers

In order to be able to CE mark medical devices, manufacturers have to provide clinical data on said devices. One of the ways to provide such data is to conduct a clinical investigation.

In order to assist manufacturers on this matter, the UK Medicines and Health products Regulatory Agency (MHRA) released, on January 2020, the 5th version of their Guidance for manufacturers regarding Clinical Investigations of Medical Devices.

- https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/865135/Guidance_for_mfrs_on_clinical_trials_January_2020.pdf
- https://www.raps.org/news-and-articles/news-articles/2020/1/mhra-updates-guidance-on-clinical-investigations-o?utm_source=MagnetMail&utm_medium=E-mail%20&utm_campaign=RF%20Today%20%7C%2027%20January%202020
- https://www.gov.uk/government/collections/regulatory-guidance-for-medical-devices?utm_source=909096de-cc63-4acc-8b6b-7749cd1ea96a&utm_medium=email&utm_campaign=govuk-notifications&utm_content=immediate

Guidance for Products Without an Intended Medical Purpose (Annex XVI) under MDR

The MHRA's guidance helps manufacturers, importers and distributors of such products to understand how they will be affected by Annex XVI and how to best comply with the new rules (which are to be read alongside Articles 10, 13 and 14 of the MDR) on the UK market. Importantly, manufacturers of these products will need to demonstrate compliance with common specifications that have not yet been adopted.

- https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/748131/Guidance_leaflet_on_Annex_XVI_products_.pdf
- https://www.gov.uk/guidance/notify-mhra-about-a-clinical-investigation-for-a-medical-device
- https://www.gov.uk/guidance/medical-devices-clinical-investigations-during-the-coronavirus-covid-19-outbreak?utm_source=49d9c46a-2377-4a20-ad57-64a35eabc756&utm_medium=email&utm_campaign=govuk-notifications&utm_content=immediate

North America

United States of America

News from FDA

Due to the COVID-19 pandemic, FDA announced they are temporarily postponing all domestic and foreign routine surveillance facility inspections. These facility inspections are assigned biannually using a risk-based Site Selection Model.

Similarly, routine surveillance inspections in support of the Bioresearch Monitoring (BIMO) program are currently postponed. Postponed inspections are being prioritized for completion when travel restrictions are lifted.

Where possible, other pathways are being used to inform decisions regarding pending applications including requesting existing inspection reports from other competent authorities, requesting information from applicants, and requesting records from facilities and other inspected entities directly.

Pre-approval and for-cause assignments deemed mission-critical will still be considered for inspection on a case-by-case basis.

https://www.fda.gov/drugs/coronavirus-covid-19-drugs/manufacturing-supply-chain-and-drug-inspections-covid-19

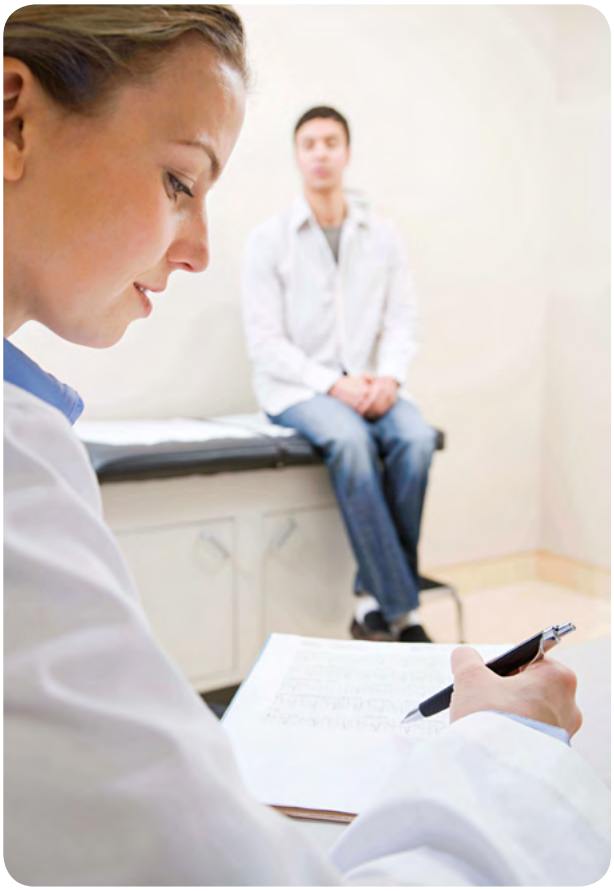
The FDA has also posted an updated COVID-19 Response At-A-Glance Summary. It contains updates on major agency activities as well as some important facts and figures.

Canada

News from the Health Canada

Vaccines and treatments for COVID-19: List of all COVID 19 clinical trials authorized by Health Canada. Currently, the treatment of COVID-19 includes supportive care and treatment of any secondary infections, such as pneumonia. There are no drugs or vaccines approved, but there are now 20 clinical trials authorized in Canada with diagnostic equipment, supportive care and/or treatments for COVID-19.

https://www.canada.ca/en/health-canada/services/drugs-health-products/covid19-clinical-trials/list-authorized-trials.html



OTHER "HOT" TOPICS IN EUROPE

MDR-latest status

Medical Device Coordination Group (MDCG) Joint Implementation/Preparedness Plan on the New Medical Devices Regulation 2017/745 (MDR)

With the 26 of May around the corner, and as response to the call from the Council of the EU (EPSCO), the MDCG (Medical Device Coordination Group) has issued a document stating the challenging joint responsibility Member States and the Commission have, together with the concerned stakeholders, to ensure that the new legislation on medical devices is operational from the aforementioned date.

Medical device shortages across the region have been chief among the concerns floated by industry and other stakeholders, particularly as there may be insufficient capacity among notified bodies. The MDCG says in its 8-page preparedness plan: "It is difficult to quantify the size of this challenge as no specific data has been presented by the industry."

And as far as only having 11 notified bodies under MDR so far, the MDCG offered few specifics but said, "It can be reasonably estimated that the number of designated notified bodies will significantly increase in 2020."

Some legacy devices that were marketed under the previous directives will be afforded a grace period until May 2024, but the MDCG explains that the 55 notified bodies designated under the current directives "have an important role in reviewing and renewing existing certificates, when necessary. Such renewals have to be finalised before 26 May 2020."

Joint Implementation/preparedness plan on the new Medical Devices Regulation 2017/745 (MDR)

Guidance on Significant Changes Regarding the Transitional Provision under Article 120 of the MDR with Regard to Devices Covered by Certificates according to MDD or AIMDD

The highly anticipated guidance provides medical device manufacturers and Notified Bodies (NB) with flowcharts to determine if devices currently covered by certificates under Medical Device Directive (MDD) or the Active Implantable Medical Device Directive (AIMDD) should consider a change in their medical device as significant when transitioning to MDR under Article 120(3).

MDCG released guidance to provide clarification on the changes to a legacy device that should be considered a "significant change in design or a significant change in the intended purpose" under MDR Article 120(3).

Guidance on significant changes regarding the transitional provision under Article 120 of the MDR with regard to devices covered by certificates according to MDD or AIMDD

Medical Device Coordination Group (MDCG) Offers New Guidance:

- Guidance on BASIC UDI-DI and changes to UDI-DI
- The European Medical Device Nomenclature (EMDN) - the nomenclature of use in EUDAMED
- The CND Nomenclature - background and general principles
- Class I Transitional provisions under Article 120 (3 and 4) – (MDR)
- Implant Card relating to the application of Article 18 Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices

Other MDCG endorsed guidance:
https://ec.europa.eu/growth/sectors/medical-devices/new-regulations/guidance_en

Medical Devices: Latest Notified Body Designations

The European Commission (EC) has announced that the 10th Notified Body (NB) to be designated under Regulation (EU) 2017/745 on medical devices (MDR) is Norwegian notified body (NB) DNV GL Presafe AS, 11th and the first in Ireland is the National Standards Authority of Ireland (NSAI), 12th is CE Certiso Orvos- és Kórháztechnikai Ellenőrző és Tanúsító Kft in Hungary and first in that country.

Key Brexit Updates

The transition period ends on 31 December 2020This is enshrined in UK law. The UK will continue to stay aligned to EU law during the transition period. The House of Commons has published a briefing paper outlining the procedure for negotiations. On 5 March 2020, Michel Barnier, the European Commission's Chief Negotiator, sets out points of convergence and divergence following the first round of negotiations. Due to the coronavirus pandemic the second round of negotiation has been postponed. However, the European Commission to consider alternative ways to continue discussions, including looking at the possibility of video conferencing or conference calls.

Medicines and Medical Devices Bill 2019-21

In February, the UK government has introduced a bill to update its regulatory "to human medicines, veterinary medicines and medical devices; make provision about the enforcement of regulations, and the protection of health and safety, in relation to medical devices; and for connected purposes". The current stage of the Medicines and Medical Devices Bill has been suspended in light of the COVID-19 outbreak.

Withdrawal of the United Kingdom and EU Rules For Medicinal Products- update for Notice to Stakeholders

https://ec.europa.eu/info/sites/info/files/notice_to_stakeholders_medicinal_products.pdf

Free Trade Agreement (FTA) with the United States published by the UK

The UK has published its negotiating objectives for a Free Trade Agreement (FTA) with the United States

https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/869592/UK_US_FTA_negotiations.pdf

For more information, see also:

- https://www.ema.europa.eu/en/about-us/uks-withdrawal-eu/brexit-related-guidance-companies
- UK withdrawal from the EU on 31 January 2020 | European Medicines Agency
- MHRA

OTHER "HOT" TOPICS FROM UNITED STATES

The FDA has issued more than 35 guidance documents to provide updated policies, transparency, and regulatory flexibility to address the vital medical products and public health issues facing the U.S. during this COVID-19 pandemic. These guidances are on diagnostics, personal protective equipment, other medical devices, investigational treatment with convalescent plasma, conduct of clinical trials of medical products, blood supply, hand sanitizers, food safety and supply, telemedicine and others.

https://www.fda.gov/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/covid-19-related-guidance-documents-industry-fda-staff-and-other-stakeholders

The FDA has worked with more than 380 test developers who have said they will be submitting Emergency Use Authorizations (EUAs) for tests that detect the virus, and has been notified that more than 235 laboratories have begun testing. This includes issuing 53 individual EUAs for test kit manufacturers and laboratories and 23 additional high complexity molecular-based laboratory developed tests (LDTs) are authorized for emergency use. Among the individual EUAs are 9 serology tests to date.

There are 50 ventilators and accessories that are authorized for emergency use, and the FDA also has issued EUAs for other equipment to treat patients.

Nearly 80 COVID-19 drug development programs are in progress, with multiple candidates under investigation that may be able to effectively treat patients before a vaccine is developed. Over the coming months, the FDA anticipates receiving information from clinical trials, including:

- Antivirals intended to directly suppress or eradicate SARS-CoV-2
- Immunomodulators intended to reduce the marked inflammatory stage of the disease
- Convalescent plasma and hyperimmune globulin, with the potential to lessen the severity or length of illness for some patients

https://www.fda.gov/media/137005/download

The Emergency Use Authorization (EUA) authority allows FDA to help strengthen the nation's public health protections by facilitating the availability and use of medical countermeasures needed during public health emergencies.

A list and descriptions of the diagnostic tests and medical devices that have been authorized for emergency use.

- More information about Emergency Use Authorization (EUA) and a list of all current EUAs
- FDA Combating COVID-19 With Medical Devices

The FDA is facilitating development and availability of potential COVID-19 treatments.

- FDA Combating COVID-19 With Therapeutics

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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