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Regulatory Newsletter
January - March 2016

Introduction

CROMSOURCE is committed to sharing our expertise with our clients and future clients. This reflects the first part of our 'Advise Agree Deliver' motto! In this spirit we have pleasure in making available this issue of our Regulatory Newsletter.

This newsletter is put together by our expert regulatory team and tracks the changes occurring in European regulations relating to clinical research performed in both medicinal products and medical devices.

The Newsletter is a quarterly publication distributed via email and posted on the CROMSOURCE website. We hope you find this information useful, and welcome feedback, questions and suggestions. Contact us on cromsource@cromsource.com at any time.

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News from the European Medicines Agency

Update on Clinical Trials Regulation (CTR)

CTR will come into effect “by October 2018 at the latest"

In April 2014 MEPs voted by a huge majority to adopt the Clinical Trials Regulation (CTR). The CTR (EU) No. 536/2014 was published in the Official Journal of the EU in May 2014. The first stage of implementation is creation of a fully-functional single EU clinical trial portal and database. Despite this being an ambitious project the CTR was originally expected to come into effect in mid-2016 (at the earliest) at which point all EU member states were to adopt the laws into their own statutes.

At the December 18, 2015, EMA Management Board meeting, the Board endorsed an extended timeframe for the implementation of the EU clinical trial portal and database. The aim is to have the database and portal ready for independent audit by August 2017. And "if the system gets a green light from the audit, the EU Clinical Trial Regulation will come into effect by October 2018 at the latest." Aware of the disappointment this is likely to cause, the Board stressed that this is a maximum timeframe and that all possible efforts must be made to shorten it and bring the Regulation into operation as soon as possible.

According to the Board, this new timeframe will enable the robust development and testing of the system and allow resolving unforeseen difficulties and potential issues. The Board stressed that the Clinical Trials Regulation involves a very significant overhaul of the processes for authorisation and oversight of clinical trials. It will provide a single portal for submission and maintenance of clinical trial applications and authorisations, and support their coordinated assessment and supervision. The portal and database will also serve as the source of public information on the full lifecycle of all clinical trials conducted in the EU, from their initial review up to publication of their results.

Main steps in the implementation of EU portal and EU database (adapted from http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/events/2014/06/event_detail_000967.jsp&mid=WC0b01ac058004d5c3):

Activity	Date
Auditable Version released for audit	July 2017
Independent Audit completed	November 2017
Audit endorsed by EMA Management Board	December 2017
European Commission notice published in Official Journal of the European Union	March 2018
Production Version go-live	September 2018
Regulation (EU) No 536/2014 becomes applicable	October 2018
Further upgrade and enhancement of the system completed	Q3 2019
Directive on Clinical Trials 2001/20/EC no longer applicable	October 2021

Published Regulation (EU) No 536/2014:

http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=OJ:L:2014:158:FULL&from=EN

Highlights of December 2015 EMA Management Board meeting:

http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2015/12/news_detail_002452.jsp&mid=WC0b01ac058004d5c1

Delivery timeframe for the EU portal and EU database:

http://www.ema.europa.eu/docs/en_GB/document_library/Other/2015/12/WC500199078.pdf

New version of the European Clinical Trials Database launched

The European Medicines Agency has been building the publicly accessible online European Clinical Trial Database (EudraCT) since 2014. EudraCT is a database of all clinical trials which commenced in the Community from 1 May 2004, and also includes clinical trials linked to European paediatric drug development.

On 13 January 2016 a new version, EudraCT V10, was made available, marking the final step of a process through which summary clinical trial results will be made publicly available through the EU Clinical Trials Register. The summary results will be gradually made available for public access from that date, once the information has been reviewed and verified. Full access for sponsors has also been restored from that date.

Sponsors' representatives are recommended to register with EudraCT in order to become results users and before they can log into EudraCT.

Further information on EudraCT:

https://eudract.ema.europa.eu/

The registration process is described in the Help section and is accessed here:
https://eudract.ema.europa.eu/results-web/

Policy on the publication of clinical data now available

Transparency will be at the heart of the new Clinical Trials Regulation. Historically, when a commercial trial was completed, the sponsor of the trial would clean the data, lock the database and present this to the regulatory agency. Subsequently the sponsor was able to maintain stringent control over the database, granting access permissions and deciding what information went into the public domain in the form of scientific publications.

The policy on the publication of clinical data for medicinal products for human use (Policy 0070) was developed by the EMA in accordance with Article 80 of Regulation (EC) No 726/2004. Policy 0070 was adopted by the EMA Management Board on 2nd October 2014 and subsequently published on the EMA website. Policy 0070 is composed of two phases. Phase 1, which entered into force on 1st January 2015, pertains to publication of clinical reports contained in all marketing-authorisation applications submitted on or after this date. Phase 2, which will be implemented at a later stage, pertains to the publishing of individual patient data (IPD). Clinical reports and IPD are collectively referred to as "clinical data".

On March 3 2016 the EMA published detailed guidance for pharmaceutical companies on the requirements to comply with its policy on the publication of clinical data. The detailed set of guidance has been finalised following an extensive consultation with all stakeholders concerned throughout 2015. The guidance consists of four chapters. The first is an overarching introduction with information on the scope and definitions used throughout the text. The second chapter details procedural aspects on the submission of clinical reports including the concrete processes. The third chapter gives guidance to companies on how to anonymise clinical reports for the purpose of publication. The guidance does not single out one specific anonymisation method yet gives recommendations to companies on how to best balance data utility for researchers with a minimal risk of re-identification. Companies will need to provide a report explaining their approach to the anonymisation of the data, which will be reviewed and published by the EMA.

The fourth chapter focuses on the identification and redaction of commercially confidential information (CCI) in clinical reports submitted to the EMA for the purpose of publication. The guidance makes clear that the vast majority of the information contained in clinical reports is not considered CCI. However, in the limited circumstances in which clinical reports might contain CCI, companies will need to submit to EMA for review a table justifying why such data has been redacted.

To further ensure that companies are well prepared for the proactive publication of clinical data, the EMA will now start reaching out to companies which are concerned by the first wave of publication, i.e. those for which the decision-making process has been finalised since the policy entered into force. In addition, EMA will organise a webinar in the second quarter of 2016 to allow companies to ask any outstanding practical questions. This webinar will be a live broadcast and will be available for future reference on the EMA website.

Guidance for the publication of clinical data:

http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2016/03/news_detail_002481.jsp&mid=WC0b01ac058004d5c1

Guidelines/Recommendations

Draft guideline on evaluation of anticancer medicinal products

On 15 March 2016 the EMA published a new draft guidance on the evaluation of anticancer medicines in humans. The purpose of this guidance is to provide guidance on all stages of clinical drug development for the treatment of malignancies, including drug resistance modifiers or normal tissue protective compounds. Developers of anticancer medicinal products need to be guided in their efforts since, as EMA has observed “A very large number of anti-cancer compounds are being developed, though only a minority have obtained marketing authorization“.

Alongside conventional aims such as defining the proper dose(s) and schedule(s), the importance of identifying a target population with optimised benefit risk is emphasised in Section 6: Exploratory Studies. Guidance is also provided on combination studies. Combinations of drugs with minimal activity as monotherapy, but synergistic effects when combined, as well as combinations of conventional cytotoxics, are also discussed.

The guideline notes that convincingly demonstrated favourable effects on overall survival are from both a clinical and methodological perspective the most persuasive outcome of a clinical trial. Prolonged progression-free or disease-free survival are in most cases considered relevant measures of patients benefit, but the magnitude of the treatment effect should be sufficiently large to outbalance toxicity and tolerability problems. In order to capture possible negative effects on the activity of next-line therapies and also treatment related fatalities, informative data on overall survival compatible with a trend towards favourable outcome are normally expected at time of submission.

An assessment of benefit/risk should encompass all relevant data on efficacy and safety, also taking into account uncertainties as well as external data of relevance in relation to the experimental compound and the disease to be treated.

The requirements of the characterisation of the safety profile have changed with the emergence of molecularly targeted agents, immunomodulating drugs and other non-cytotoxic agents. These agents may have other types of toxicity and are often dosed differently to conventional chemotherapy. The dose-finding process and concepts such as dose limiting toxicity may therefore need to be addressed differently than for standard cytotoxic agents.

The full guideline may be found here:
http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2016/03/WC500203320.pdf

The guidance is available for comment through 15 September. Email address for submissions:
oncwp@ema.europa.eu

Guideline on evaluation of medicines for autism

On 4 March 2016 the EMA released a guideline on the clinical development of medicines for the treatment of autism spectrum disorder (ASD) for a 6-month public consultation. This is the first guidance document issued by the Committee for Medicinal Products for Human Use (CHMP) for developers of medicines targeting autism. It is based on recent progress in the understanding of the pathological mechanisms behind ASD. The guideline also builds on EMA scientific advice for development plans for Autism Spectrum Disorder, as well as the qualification letters of support for the selection of patients in clinical trials.

The draft guideline provides advice on: diagnosis and inclusion criteria for the selection of patients; methods for assessment of the efficacy of medicines; design of clinical trials; and evaluation of clinical safety.

Further information:

http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2016/03/news_detail_002483.jsp&mid=WC0b01ac058004d5c1

Stakeholders are invited to send their comments by 31 August 2016 to cnswpsecretariat@ema.europa.eu. Comments received during the consultation will be taken into account during the finalisation of the guideline.

Revised guideline on development of medicines for Alzheimer's disease

On 1 February 2016 the EMA released a revised guideline on medicines for the treatment of Alzheimer's disease and other types of dementias for a six-month public consultation.

The EMA considers dementia as a key public health priority. According to the World Health Organization, 35.6 million people have dementia worldwide and this number is expected to double by 2030. Recent progress in understanding the pathophysiology of Alzheimer's disease suggests that the biological changes associated with the disease start to occur as early as 10 to 20 years prior to the emergence of clinical symptoms. Experimental medicines should therefore be evaluated in earlier disease stages as certain treatments may be more effective at that stage than later in the illness.

The EMA follows a multi-stakeholder approach to facilitate research and development of more effective medicines for Alzheimer's disease. The revised guideline specifically addresses the:

- impact of new diagnostic criteria for Alzheimer's disease, including early and even asymptomatic disease stages, on clinical trial design;
- choice of parameters to measure trial outcomes and the need for distinct assessment tools for the different disease stages in Alzheimer's (different signs and symptoms, differences in changes over time, severity);
- potential use of biomarkers and their temporal relationship with the different phases of Alzheimer's disease at different stages of medicine development (mechanism of action, use as diagnostic test, enrichment of study populations, stratification of subgroups, safety and efficacy markers etc.);
- design of long-term efficacy and safety studies.

The full guideline may be found here:

http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2016/02/WC500200830.pdf

Stakeholders are invited to send their comments by 31 July 2016 to cnswpsecretariat@ema.europa.eu. Comments received during the consultation will be taken into account in the finalisation of the guideline.

Draft guideline on development of medicines for chronic heart failure

On 11 February 2016 the EMA issued a draft guideline on clinical investigation of medicinal products for the treatment of chronic heart failure. This guideline addresses the EU regulatory position on the clinical development of new medicinal products in the treatment of patients with chronic heart failure.

It is recognised that chronic heart failure encompasses heterogeneous groups of patients with a wide spectrum of symptoms and different causes, resulting from an abnormality of cardiac structure or function. Within this spectrum, patients may either have heart failure with reduced ejection fraction or heart failure with a moderately reduced or largely preserved ejection fraction. The aim of this guideline is to update the *Note for guidance on clinical investigation of medicinal products for the treatment of*

cardiac 59 *failure (CPMP/EWP/235/95, Rev. 1)*. The principal changes from the previous document relate to: differentiation of types of heart failure between reduced and preserved ejection fraction; inclusion of patients that are clinically stable early after hospitalisation for heart failure; description of ways to measure morbidity; assessment of efficacy criteria and the need for morbidity and mortality trials.

Full text of the guideline:

http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2016/02/WC500201772.pdf

Consultation end date 31 August 2016. Email address for submissions: vswpsecretariat@ema.europa.eu

Reflection paper on assessment of drugs' cardiovascular safety profile

On 25 February 2016 the Committee for Medicinal Products for Human Use (CHMP) issued a reflection paper on assessment of cardiovascular safety profile of medicinal products. The purpose of this reflection paper is to provide recommendations for the evaluation of the cardiovascular safety profile of new (non-generic, non-biosimilar) medicinal products that are intended for long-term treatment of certain cardiovascular and metabolic diseases (diabetes, obesity, hypertension, lipid disorders). This paper aims to clarify the requirements for these medicinal products at the time of assessment of the marketing authorisation application with respect to data needed for the evaluation of the cardiovascular safety profile.

For the evaluation of medicinal products in other therapeutic areas, the same principles of data generation and assessment may apply if a detailed evaluation of their cardiovascular safety profile becomes necessary.

"Reflection paper on assessment of cardiovascular safety profile of medicinal products" (full text):

http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2016/03/WC500203804.pdf

Guidance for users of centralised pre-authorisation procedure

Regulation (EC) No 726/2004 of the European Parliament and of the Council lays down a centralised Community procedure for the authorisation of medicinal products, for which there is a single application, a single evaluation and a single authorisation allowing direct access to the single market of the Community. A marketing authorisation granted under the centralised procedure is valid for the entire Community market, which means the medicinal product may be put on the market in all member states.

On 31 March 2016 the EMA issued a guidance entitled "European Medicines Agency pre-authorisation procedural advice for users of the centralised procedure". This guidance addresses a number of questions which users of the centralised procedure may have. It provides an overview of the EMA's position on issues, which are typically addressed during the course of pre-submission meetings. It will be updated regularly to reflect new developments, to include guidance on further pre-authorisation

procedures and to reflect the implementation of the new European legislation. Revised topics will be marked by “New” or “Rev” upon publication.

Pre-submission meetings (which should take place approximately 7 months prior to the anticipated date of submission of the application) are a vital opportunity for applicants to obtain procedural, regulatory and legal advice from the EMA.

Full text:

http://www.ema.europa.eu/docs/en_GB/document_library/Regulatory_and_procedural_guideline/2009/10/WC500004069.pdf

Initiatives

Launch of PRIME (PRIority MEdicines) scheme

On 7 March 2016 the EMA launched its new PRIME (PRIority MEdicines) scheme to strengthen support to medicines that target an unmet medical need. The scheme focuses on medicines that may offer a major therapeutic advantage over existing treatments, or benefit patients with no treatment options. These medicines are considered priority medicines within the EU.

PRIME was developed in consultation with the Agency's scientific committees, the European Commission and its expert group on Safe and Timely Access to Medicines for Patients (STAMP) as well as the European medicines regulatory network. The main principles of PRIME were released for a two-month public consultation in 2015 and the comments received were taken into account in the final version.

PRIME builds on the existing regulatory framework and tools already available such as scientific advice and accelerated assessment. By engaging with medicine developers early on, PRIME is aimed at improving clinical trial designs so that the data generated is suitable for evaluating a marketing-authorisation application. Early dialogue and scientific advice also ensure that patients only participate in trials designed to provide the data necessary for an application, making the best use of limited resources. This means that developers of a medicine that benefitted from PRIME can expect to be eligible for accelerated assessment at the time of application for a marketing authorisation.

According to Vytenis Andriukaitis, EU Commissioner for Health and Food Safety the launch of PRIME is a major step forward for patients and their families that have long been hoping for earlier access to safe treatments for their unmet medical needs, such as rare cancers, Alzheimer’s disease and other dementias. Through enhanced scientific support this scheme could also help, for example, to accelerate the development and authorisation of new classes of antibiotics or their alternatives in an era of increasing antimicrobial resistance.

To be accepted for PRIME, a medicine has to show its potential to benefit patients with unmet medical needs based on early clinical data. While PRIME is open to all companies on the basis of preliminary clinical evidence, micro-, small- and medium-sized enterprises (SMEs) and applicants from the academic sector can apply earlier on the basis of compelling non-clinical data and tolerability data from initial clinical trials. They may also request fee waivers for scientific advice. Since SMEs and academia often

lack experience with the regulatory framework, they can benefit in particular from earlier scientific and regulatory advice.

Source:

http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2016/03/news_detail_002484.jsp&mid=WC0b01ac058004d5c1

Additional information on the PRIME scheme:

http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000660.jsp&mid=WC0b01ac05809f8439

Consultation on a major revision of GVP module V

On 29 February 2016 the EMA published a revision of module V of the good pharmacovigilance practices (GVP) on risk management systems for public consultation. GVP module V, released in 2012, advises developers of medicines, marketing authorisation holders and regulators on the design of effective risk management systems and plans. Risk management is a major component of the safety monitoring of medicines. Risk management entails putting in place measures to minimise potential risks and to fill knowledge gaps for medicines (e.g. through post-authorisation data). The goal is to ensure that throughout its lifespan the benefits of a particular medicine exceed the risks by the greatest achievable margin. Marketing authorisation holders are required to present the proposed activities in a risk management plan (RMP) that needs to be approved by the regulators before a medicine can be authorised.

This first major revision of GVP module V clarifies the activities a risk management plan should focus on during the life cycle of a product. This will help to ensure that a risk-proportionate planning of activities directs resources to areas where the need for additional information and risk minimisation is greatest.

Good pharmacovigilance practices are a set of measures drawn up to facilitate the performance of pharmacovigilance in the EU. GVP apply to marketing-authorisation holders, the European Medicines Agency and medicines regulatory authorities in EU Member States. They cover medicines authorised centrally via the Agency as well as medicines authorised at national level. The guideline on GVP is a key deliverable of the 2010 pharmacovigilance legislation. This legislation, which came into effect in July 2012, was the biggest change to the regulation of human medicines in the European Union (EU) since 1995. It had significant implications for applicants and holders of EU marketing authorisations, as well as for patients, healthcare professionals and regulators. The development of the pharmacovigilance legislation was based on the observation that adverse drug reactions (ADRs), 'noxious and unintended' responses to a medicine, caused around 197,000 deaths per year in the EU.

Source:

http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2016/02/news_detail_002479.jsp&mid=WC0b01ac058004d5c1

Pharmacovigilance Legislation:

http://www.ema.europa.eu/ema/index.jsp?curl=pages/special_topics/general/general_content_000491.jsp&mid=WC0b01ac058058f32d

Good Pharmacovigilance Practices:

http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/document_listing/document_listing_000345.jsp&mid=WC0b01ac058058f32c

Consultation ends 31 May 2016. Email address for submissions: gvp@ema.europa.eu

EudraVigilance information day

On 11 March the EMA announced that a EudraVigilance information day will be held on 21 June 2016 at the EMA office, London, UK. The information day will provide a forum to update stakeholders about latest developments with regard to EudraVigilance in the context of the implementation of the pharmacovigilance legislation. It further aims to facilitate change management as part of the Agency's pharmacovigilance programme and the planning of modifications to business processes by regulatory authorities and pharmaceutical companies.

Source:

http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/events/2016/03/event_detail_001266.jsp&mid=WC0b01ac058004d5c3

Other news affecting EU countries

Revised ISO 13485 standard for medical devices quality systems

On 26 February 2016 a revised version of ISO 13485 was published, the first revision since the 2003 publication of the internationally recognized ISO standard. ISO 13485:2003 "Medical devices – Quality management systems – Requirements for regulatory purposes" specifies requirements for a quality management system that can be implemented by medical device companies to help demonstrate regulatory compliance, and the standard is accepted as the basis for CE marking medical devices under EU directives.

The new version has a greater emphasis on risk management and risk-based decision making, as well as changes related to the increased regulatory requirements for organizations in the supply chain. Improvements in the new version of the standard include broadening its applicability to include all organizations involved in the life cycle of the product, from concept to end of life, greater alignment with regulatory requirements and a greater focus on post-market surveillance including complaint handling. There is also a greater emphasis on having the appropriate infrastructure, particularly for the production of sterile medical devices. The new version is expected to help all organizations involved in the development, distribution and maintenance of medical devices improve their processes, manage risk better and ultimately improve the quality of what they do.

Organizations certified to ISO 13485:2003 wishing to transition to the new version can get guidance from the standard's Transition Planning Guidance document.

Source:

http://www.iso.org/iso/home/standards/management-standards/iso13485.htm

http://www.iso.org/iso/home/news_index/news_archive/news.htm?Refid=Ref2046

Transition Planning Guidance:

http://www.iso.org/iso/white_paper_-_iso_transition_planning_guidance_for_iso_13485-2016.pdf

Spain: New regulations on clinical trials go into effect

On 4 December 2015, the Spanish Council of Ministers passed a Royal Decree regulating clinical drug trials, drug-research ethics committees (RECs) and the Spanish Clinical Studies Registry in order to put in place criteria to increase transparency and simplify procedures for clinical trials. The regulations went into effect on 12 January 2016. However, due to the short transition period the CA and the ECs are not yet implementing all the instructions as explained in the updated legislation.

According to information provided by Barcelona Clinical Trials Platform (BCTP), the regulations establish that clinical trials may be approved with an evaluation and report from just one accredited ethics committee and the Spanish Agency of Medicines and Medical Devices (AEMPS), where previously they needed authorization from the ethics committees at all the participating hospitals. In addition to this simplification, there is another change that mainly favors industry-driven studies. The promoter can negotiate approval to conduct a trial with healthcare centers while simultaneously sending documents to the ethics committee and the AEMPS (to evaluate and authorize), which will shorten timelines. However, it has been reported that Asebio, the Spanish Bioindustry Association, would like a single model contract valid at all healthcare centers created because hospital bureaucracy tends to draw the process out.

The new regulations also affect the make-up of research ethics committees, which from now on must have at least one individual representing the best interests of the subjects taking part in the trial, protecting their rights and wellbeing.

Spain is the first to apply the EU Clinical Trial Regulation, which is expected to attract the global pharmaceutical industry. However, the Spanish Clinical Studies Registry is seen by some as unnecessary because it will only duplicate information if data is to be stored centrally in the EU.

The Royal Decree 1090/2015 (unofficial English translation):

http://www.aemps.gob.es/legislacion/espana/investigacionClinica/docs/Royal-Decree-1090-2015_4-December.pdf

Further information:

http://www.barcelonaclinicaltrials.org/en/spain-passes-new-regulations-clinical-trials-increase-transparency-and-simplify-procedures

The Spanish Clinical Studies Registry is available online:

https://reec.aemps.es/reec/faces/buscador/index.xhtml

Denmark: ENLI's authority is extended

DELACOUR (member of ADVOC, a leading international network of independent law firms) reported that as of 1 February 2016, the Danish Ethical Committee for the Pharmaceutical Industry (ENLI) has been given authority to control and impose sanctions on pharmaceutical companies that do not comply with the regulations pertaining to the clinical testing of pharmaceuticals and non-interventional studies. The extension of ENLI's authority is a consequence of the guidelines recently approved by The Danish Association of the Pharmaceutical Industry (Lif) for ENLI's control of and authority to impose sanctions on pharmaceutical companies' actions that are in violation of the so-called joint declaration on clinical testing of pharmaceuticals and non-interventional studies drawn up by Lif and the Organization of Danish Medical Societies. Only pharmaceutical companies which are members of Lif are subject to ENLI's authority and sanctions.

Further information:
http://en.delacour.dk/news/2016/march/extension-of-enli-s-authority/

Poland: Site contracts no longer required for CTA submissions

Poland's attractiveness for supporting clinical investigations of medical devices has increased since a new regulation relating to contracts with sites was issued on 17 February 2016. Contract negotiation can severely slow negotiation timelines with sites and investigators, sometimes up to as much as four months in certain countries. The process is often a burden on clinical study start-up activities, given that site contracts are part of essential document collection and sites cannot be initiated until contracts are finalised. In Poland fully executed contracts with the sites had to be available for submission to the Competent Authority and the Ethics Committee, which meant that the time needed to prepare the complete documentation was prolonged noticeably. According to the new regulations, a contract for the site is no longer required for the submissions.

Resolution of Polish Ministry of Health -17.02.2016 (In Polish - English version in preparation):

http://dokumenty.rcl.gov.pl/DU/rok/2016/pozycja/209

Further information on the Competent Authority (The Office for Registration of Medicinal Products, Medical Devices and Biocidal Products) web page:

http://www.urpl.gov.pl/

France: Clinical Trial Vigilance Data Reporting (SUSARs)

From 31st of March, ANSM implements a priority processing of suspected unexpected serious adverse reactions reports (SUSARs) occurring during biomedical research on a medicinal product of Phase 1 First-in-man on healthy volunteers and subsequent trials. The transmission procedure for others SUSARs reports remains the same.

Each SUSAR must be reported in an individual email message. It should be sent to: declarationsusars@ansm.sante.fr

The subject line should be written as follows (see Explanatory Note link below for precise requirements):

SUSAR_yyyymmdd_name of substance (or trial code no.)_Worldwide unique case identification number_CT

Ex : SUSAR_20140115_SUBSTANCE_123456789_CT

Explanatory Note:

http://ansm.sante.fr/var/ansm_site/storage/original/application/58edba3672daf1e51ac33f0c53259ca5.pdf

Further information:

http://www.microsofttranslator.com/bv.aspx?from=&to=en&a=http%3A%2F%2Fansm.sante.fr%2FActivites%2FMedicaments-et-produits-biologiques%2FDeclaration-des-effets-indesirables-faits-nouveaux-et-mesures-urgentes-de-securite%2F(offset)%2F4

UK: MHRA mandates online clinical trial submissions via CESP

The Common European Submission Platform (CESP) is an online system developed by the Head of Medicines Agency (HMA), designed to be a secure means for applicants to exchange information and submissions with agencies across Europe. The purpose of the system is to:

- provide a secure method of communicating with regulatory agencies via one platform
- allow submission of an application once to reach all required agencies
- reduce the burden for both industry and regulators of submitting/handling applications on CD-ROM and DVD

On 1 February 2016 the MHRA announced that it will no longer accept submissions on physical media (CD/DVD/Letters); only submissions using the CESP will be accepted. This is in relation to any new clinical trial authorization submissions along with substantial amendments, and development safety update reports. It is expected that in the long run CEPS should be easier, quicker and more cost-effective for sponsors.

Source:

https://www.gov.uk/guidance/clinical-trials-for-medicines-apply-for-authorisation-in-the-uk

http://www.rdforum.nhs.uk/content/2016/01/08/mhra-update-cta-submission-now-only-accepted-via-cesp/

Any questions regarding CESP should be directed to the clinical trial helpline: ctdhelpline@mhra.gsi.gov.uk

Clinical trial applicants can view the MHRA Clinical Trials Guidelines document here:
https://cespportal.hma.eu/trg/training/clinicaltrialsmhra.pdf