Regulatory & Pharma News Update March 2018

REGULATORY NEWS

MHRA Publishes GXP Data Integrity Guidance and Definitions

In July 2016 the Medicines and Healthcare products Regulatory Agency (MHRA) published a draft guidance document on GXP Data Integrity which was open for public consultation until 31 October 2016. Following review of extensive comments received, the final guidance document - 'GXP' Data Integrity Guidance and Definitions - has now been published by the MHRA. It is intended to be a useful resource on the core elements of a compliant data governance system across all GxP sectors; it does not extend to medical devices. It addresses fundamental failures identified by the MHRA and international regulatory partners during GLP, GCP, GMP and GDP inspections, many of which have resulted in regulatory action. The guidance should be considered as a means of understanding the MHRA's position on data integrity and the minimum expectation to achieve compliance. The guidance has been harmonised with other published guidance, where possible, and is a UK companion document to PIC/S, WHO, OECD (guidance and advisory documents on GLP), and EMA guidelines and regulations. It covers the principles of data integrity, establishing data criticality and inherent integrity risk, designing systems and processes to assure data integrity, and definition of terms and interpretation of requirements.

https://www.gov.uk/government/publications/guidance-on-gxp-data-integrity

Updated Guidance Published on Summaries of Clinical Trial Results

Eudralex Volume 10 provides guidance documents applicable to clinical trials. A number of these documents are being revised to bring them in line with the new EU Clinical Trials Regulation No. 536/2014, while new guidance documents are being prepared to cover new aspects introduced by the Regulation. The Regulation requires sponsors to provide summary results of clinical trials in a format understandable to laypersons and Annex V of the Regulation sets out ten elements that must be addressed in the lay summaries. A Eudralex Volume 10 guidance document was published in January 2017 on Summaries of Clinical Trial Results for Laypersons. The document includes guidance and templates to help authors writing these lay summaries. The lay summaries will be publicly available on the lay summary section of the EU database. This guidance has been revised and version 2 was published on 22 February 2018. The revision relates to Annex I Section 7 regarding secondary endpoints.

https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-10/2017_01_26_summaries_of_ct_results_for_laypersons.pdf

Tracking Tool for EMA's Relocation to Amsterdam

The European Medicines Agency (EMA) has published a new tracking tool showing the main milestones and deliverables for the EMA's move to Amsterdam. The EMA is committed to giving stakeholders and the public full visibility of the relocation project and hence the tracking tool will allow interested parties to follow the progress made. The tracking tool gives a general overview of the main milestones agreed for each of the work streams (except for external communication) and then outlines in more detail the deliverables for each work stream, highlighting clearly if the EMA is on track to meet them. The tracking tool is a living document, in which milestones may be added as the project progresses. It will be updated each month.

http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2018/03/news_detail_002916.jsp&mid=WC0b01ac058004d5c1

EMA Adopts Revised Guideline on Clinical Trials for Alzheimer's Disease

The EMA's Committee for Medicinal Products for Human Use (CHMP) has adopted a revised guideline on clinical studies for medicines that target Alzheimer's Disease. Alzheimer's Disease is the most common cause of dementia in the elderly. 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 before clinical symptoms start to appear. Currently available medicines for Alzheimer's Disease only treat its symptoms. However, a number of therapies under development are targeting the biological mechanism of the disease to try and modify its course. The revised guideline builds on scientific advice provided by the EMA to medicine developers on specific products and methodologies, such as the qualification of biomarkers for use in clinical trials and a longitudinal model describing changes in cognition in patients with mild or moderate Alzheimer's Disease. The EMA's new guideline addresses, among others:

- Impact of new diagnostic criteria for Alzheimer's disease, including early and even asymptomatic disease stages, on clinical trial design;
- Factors to be considered when selecting parameters to measure trial outcomes at the different disease stages in Alzheimer's.
- Potential use of biomarkers in the various stages of medicine development;
- Design and analysis of efficacy and safety studies.

The guideline will become effective from 1 September 2018.

http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2018/02/news_detail_002913.jsp&mid=WC0b01ac058004d5c1

FDA Issues New Guidance Document on ICH E6 (R2)

Although the integrated addendum to ICH E6 Guideline for Good Clinical Practice (i.e. ICH E6 (R2)) was adopted by ICH in November 2016 and was implemented in the EU on 14 June 2017, by the end

of 2017 it had yet to be implemented in North America. However, on 01 March 2018, the US Food and Drug Administration (FDA) announced the availability of the guidance titled "E6(R2) Good Clinical Practice: Integrated Addendum to ICH E6(R1)", which amends the guidance "E6 Good Clinical Practice: Consolidated Guidance (E6(R1))". The target date for full implementation of ICH E6(R2) by Health Canada is 01 April 2018; on 29 May 2017 Health Canada announced the interim implementation of ICH E6(R2).

https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM464506.pdf

FDA Publishes Final Rule on Acceptance of Data From Clinical Investigations for Medical Devices

The FDA is amending its regulations on acceptance of data from clinical investigations for medical hdevices. The amended regulations are via a final rule, effective 21 February 2018, titled "Human Subject Protection; Acceptance of Data From Clinical Investigations for Medical Devices". The final rule requires that data submitted from clinical investigations conducted outside the US intended to support an investigational device exemption (IDE) application, a premarket notification (510(k) submission, a request for De Novo classification, a premarket approval (PMA) application, a product development protocol (PDP) application, or a humanitarian device exemption (HDE) application be from investigations conducted in compliance with good clinical practice (GCP). The final rule updates the criteria for FDA acceptance of data from clinical investigations conducted outside the US to help ensure the quality and integrity of data obtained from these investigations and the protection of human subjects.

https://www.federalregister.gov/documents/2018/02/21/2018-03244/human-subject-protection-acceptance-of-data-from-clinical-investigations-for-medical-devices?utm_campaign=Medical%20Device%20Acceptance%20of%20Data%20from%20Clinical%20Invest.&utm_medium=email&utm_source=Eloqua

Further EU Member States Benefit from EU-US Mutual Recognition Agreement for Inspections

In November 2017, the Mutual Recognition Agreement (MRA) between the EU and US, allowing the recognition of each other's Good Manufacturing Practice (GMP) inspection outcomes and hence better use of inspection expertise and resources, came into operation. At that time, the FDA confirmed the capability of eight EU Member States (Austria, Croatia, France, Italy, Malta, Spain, Sweden and United Kingdom) to carry out GMP inspections at a level equivalent to the US. On 01 March 2018, the FDA confirmed that it had added a further four EU Member States (Czech Republic, Greece, Hungary and Romania) to this list, making a total of 12 EU Member States whose inspection results the FDA can rely on to replace their own inspections. Plans for the agreement to be operational in all EU Member States by 15 July 2019 are on track. This agreement is underpinned by robust evidence on both sides of the Atlantic that the EU and the US have comparable regulatory and procedural frameworks for inspections of manufacturers of human medicines.

http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2018/03/news_detail_002915.jsp&mid=WC0b01ac058004d5c1

New Resources Published for TMF Reference Model

The Trial Master File (TMF) Reference Model was devised by the Drug Industry Association (DIA) and provides a framework for the content of the TMF to include all essential documents that collectively permit the evaluation of the conduct of a trial and the quality of the data produced. It is not intended to be taken and used "off-the-shelf" but can be adapted to an electronic or paper TMF and does not require any specific technology. TMF Reference Model V3.0 is the current version, which was released in June 2015. On 24 February 2018, the TMF Reference Model Project released a TMF Plan Template V1.0, which can be downloaded for free from the TMF Reference Model website. The purpose of the TMF Plan is to outline the processes and procedures that all involved parties (sponsors and CROs/vendors) will use to ensure a high-quality TMF, and to clearly define what is expected from all involved parties. The TMF Plan Template has been written to cover both sponsor and investigator TMFs but is easy to adapt if an organisation has separate, documented procedures for each type of document.

https://tmfrefmodel.com/category/news/

PHARMA NEWS

Takeda Enters into Collaboration to Develop Treatments for Neurological Disease

Takeda Pharmaceuticals announced on 20 February 2018 that it has entered into a research, development and commercial collaboration with Wave Life Sciences to develop oligonucleotides to treat genetically-defined neurological diseases, including Huntington's Disease, amyotrophic lateral sclerosis (commonly referred to as Lou Gehrig' Disease), frontotemporal dementia, and spinocerebellar ataxia type 3. Wave is developing oligonucleotide therapeutics to target diseases that have been historically difficult to treat with small molecules or biologics. Their molecules are designed to reduce the expression of disease-promoting proteins or to transform the production of dysfunctional mutant proteins into the production of functional proteins, with the potential of treating the targeted disease. This collaboration with Wave is part of Takeda's overall partnership strategy and deepened commitment in neuroscience.

PPD and Acurian Launch Patient Concierge for Clinical Trials

The global Contract Research Organisation (CRO), PPD and Acurian – a subsidiary of PPD and full-service provider of global patient enrolment and retention solutions – have announced a new patient concierge service designed to make it easier for patients and their caregivers to participate in clinical trials and to help pharmaceutical and biotechnology companies retain patients. The patient concierge serves as a single point of contact to guide a patient through trial participation and manage trial logistics. Concierges are assigned to patients for the duration of a study and check in with them regularly. Some of the specific amenities the patient concierge provides include: appointment reminders and follow-ups; trial experience feedback; trial information; device training and assistance; transportation and reimbursement support; and medication reminders. While the patient concierge service can be used with a wide range of studies, the level of support provided by the service is extremely valuable in therapeutic areas, such as for rare diseases, in which the patients

and their caregivers are navigating especially challenging trial logistics or in which complex travel arrangements to sites must be made.

Novartis Expands Alliance with Science 37

Novartis has announced that it is expanding its strategic alliance with Science 37 – a leader in decentralised clinical trial technology and design – to initiate up to 10 new clinical trials over the next three years. The studies will blend virtual and traditional models, with increasing degrees of decentralisation towards a mostly "site-less" model. These decentralised, or virtual, trials will harness digital technology to allow some or all aspects of a clinical trial to be carried out at a trial participant's home or local physician's office, rather than at a central trial site such as a large hospital. The aim is to decrease the burden of clinical trial participation on patients and trial centres, such as long journeys or extensive time spent at hospitals or trial sites. Currently, Novartis is in the process of selecting specific indications and trials where it will deploy the decentralised approach, which will use Science 37's technology to enable patient participation using mobile devices and telemedicine services. The trials are expected to begin later this year in the US in the areas of dermatology, neuroscience and oncology.