TMQA Regulatory News Update March 2017

MHRA Launches New Medical Regulations Blog

The MHRA has issued an official blog providing expert insight into the latest regulatory thinking and all aspects of medicines regulation. The MedRegs blog will provide an opportunity for the MHRA to connect directly with stakeholders and customers in a less formal way, helping them to avoid common and easily avoidable errors. The blog will feature posts from experts who work right across the regulatory process from clinical trial authorisations to marketing authorisation applications. Topics that will be covered include:

- Submissions – how to get them right first time
- Behind the scenes – find out more about how the regulator works
- Key issues – the inside track on emerging issues for the regulation of medicines.

https://www.gov.uk/government/news/new-medregs-blog

MHRA Publishes Data on Serious Breach Reporting

The MHRA has published data on serious breach reporting during the period Jan-Dec 2016. The data shows that of the 112 serious breaches reported in 2016, only 78 of these were considered serious breaches by the MHRA. The majority of serious breaches were reported by sponsors (83/112), while 15/112 were reported by CROs. The remainder were reported by Trusts (4), Investigators (4), HRA (2), Whistleblowers (2) and Other (2). Of all reported serious breaches, the greatest impact was on patient safety (55/112), followed by scientific value/data integrity (19). None of the reported serious breaches resulted in an urgent triggered inspection, though two resulted in a recommended triggered inspection; the outcome for the majority of reported serious breaches was in-house follow-up.

https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/600695/Referral_Metrics_2016.pdf

HRA Publishes New Proportionate Consent Guidance

The Health Research Authority (HRA) has published new guidance on how consent might be sought in pragmatic trials (i.e. those that do not normally involve any extra interventions beyond those required as part of the patient's routine care) in a way that is proportionate to the low levels of risk involved in such trials. This new guidance complements the existing HRA online guidance for consent and participant information sheets and reinforces the HRA's view that people who volunteer to take part in research should be provided with succinct, relevant, user-friendly information in a proportionate manner that better promotes genuinely informed consent and facilitates the conduct of ethical research. Procedures for seeking consent can sometimes be applied too rigidly and with too little appreciation of the risks, benefits and values that are at stake in connection with different kinds of

research. This can lead to excessively lengthy and complex participant information sheets which can inhibit, rather than promote, participant understanding and genuinely informed consent. While lengthy, complex participant information sheets covering every minor detail of the research might protect the sponsor and researcher against litigation they do not necessarily facilitate the genuine understanding and consent of potential participants, nor facilitate recruitment. Excessively long participant information sheets can also overburden the health care professional seeking consent and may even deter some health care professionals from taking part in the recruitment process at all.

http://www.hra.nhs.uk/news/2017/01/31/hra-publishes-new-proportionate-consent-guidance/

Updated EMA GCP Inspectors Q&A

The European Medicines Agency (EMA) recently updated its GCP Q&As to address several contractual arrangement 'pitfalls' with clinical trial electronic systems vendors. The new question which was added in January reads 'What are the pitfalls to be aware of regarding contractual arrangements with vendors for electronic systems in connection with clinical trials'. Sponsors contract out an increasing number of tasks in clinical trials. One area where sponsors typically lack internal knowledge or resources is development of electronic systems in clinical trials such as systems used for randomisation and IMP distribution management/accountability (interactive response technology (IRT)) and/or clinical trial data capture (eCRF and ePRO systems). An increasing number of deviations from GCP standards, relating to sub-standard contractual arrangements and related procedures, have been identified during inspections. The Q&A includes examples of deviations described as bullet points under the following headings: status of contracts; distribution of delegated tasks; standards to be followed; audits and inspections; serious breaches; compliance with the protocol; output; and exemptions.

http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/q_and_a/q_and_a_detail_000016.jsp&mid=WC0b01ac05800296c5www.eme.europa.eu

EMA GCP Inspectors Working Group – Plan for 2017

The EMA has published its GCP Inspectors Working Group (IWG) work plan for 2017. The GCP IWG was established by the EMA in 1997 and focuses on harmonisation and coordination of GCP related activities at a European level. The group's activities for 2017 have been outlined in the work plan and the priorities of the group will be:

- To provide expert support to the European Commission on GCP related matters and inspections in relation to the implementation of the new Clinical Trials Regulation
- To develop new and revise existing documents such as EMA GCP inspection procedures and guidelines in relation to the implementation of the new Clinical Trials Regulation. This includes launching a number of draft documents for public consultation such as: Guidance for the appointment of a lead Member State for the management of serious breaches; Guidance for clinical trial sponsors on what is expected to be reported as a serious breach; Guideline on GCP compliance in relation to the trial master file (paper and/or electronic) for content, management, archiving, audit and inspection of clinical trials.
- To provide training and support for EU inspectors with a focus on inspection on bioequivalence trials
- To continue to engage with stakeholders on topics such as electronic data systems, data integrity, data protection and quality risk management in clinical trials. In particular, they will continue working on the presentation of a guidance document on the use of electronic systems

and data capture systems in clinical trials and will prepare Q&A documents, as required, to clarify the inspectors' expectations with respect to certain processes and procedures, with particular focus on data integrity.

http://www.ema.europa.eu/docs/en_GB/document_library/Work_programme/2017/02/WC500222058.pdf

ICH Publishes Presentation on E6(R2) and E11(R1)

The international council for harmonisation (ICH) has published presentations on its website relating to ICH E6(R2) Good Clinical Practice and ICH E11 Clinical Investigations of Medicinal Products in the Paediatric Population. The ICH E6(R2) presentation provides a high-level overview of the addendum content which was adopted by CHMP in Dec 2016. The ICH E11 presentation provides an overview of the draft addendum which has reached step 2b in the process and is currently under public consultation. This addendum is being generated to address new scientific and technical knowledge advances in paediatric drug development.

http://www.ich.org/products/guidelines/efficacy/article/efficacy-guidelines.html

FDA Publishes BIMO Metrics for 2016

The Food and Drug Administration (FDA) has published annual inspection metrics for the compliance programs in the FDA's Center for Drug Evaluation and Research (CDER). The vast majority of these inspections are conducted by the FDA's Office of Regulatory Affairs (ORA). Inspections of clinical investigators accounted for 41% of the Bioresearch Monitoring (BIMO) inspections for 2016, while sponsor (GCP) inspections accounted for 6% (the latter included sponsors/CROs/Sponsor-Investigators). A total of 415 clinical investigator inspections were carried out in 2016. Of these, 68% were conducted in the United States, 12% in Western Europe, 9% in Eastern Europe, 4% in Asia Pacific, 2% Canada, 2% Latin America, 1% Middle East/Central Asia, 1% Australia, 1% Africa. The frequency of clinical investigator-related deficiencies was greater for domestic inspections (349 deficiencies) compared with foreign inspections (129 deficiencies). Of the 61 sponsor (GCP) inspections conducted, 37 of these were inspections of sponsors, 18 were inspections of CROs and 6 were inspections of sponsor-investigators.
https://www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/UCM438250.pdf

EU and US Agree on Mutual Recognition of Inspections

Regulators in the US and EU have agreed on mutual recognition of inspections of medicines manufacturers. Each year national competent authorities from the EU and the FDA inspect many manufacturing sites of medicinal products in the US, EU and elsewhere in the world to ensure that these sites operate under Good Manufacturing Practice (GMP). Under this new Mutual Recognition Agreement (MRA), US and EU regulators will rely on information from each other's inspections of manufacturing sites of medicinal products. This will enable the FDA and EU to avoid duplication of manufacturing site inspections, will lower inspection costs and will allow regulators to devote more resources to other parts of the world where there may be greater risk. Around 40% of finished medicines marketed in the EU come from overseas and 80% of manufacturers of active pharmaceutical ingredients (APIs) for medicines available in the EU come from outside the EU. The agreement is an annex to the EU-US MRA which was signed in 1998 but it not yet implemented. The EU already has existing experience with mutual recognition of GMP inspections, having existing MRAs

of GMP inspections with several other countries including Australia, New Zealand, Canada, Japan and Switzerland.