TMQA Regulatory News Update October 2016

MHRA GCP Symposium 2016

The annual MHRA GCP Symposium was held in Birmingham last month and was attended by approximately 450 delegates from commercial and non-commercial organisations over two days. MHRA GCP inspectors presented on areas of non-compliance continually identified during inspections and how to improve compliance. Some of the discussion points presented at the symposium included the following:

- An update on the EU Clinical Trials Regulation – a number of guidance documents have already been released for public consultation and some are yet to be released, e.g. Trial Master File (TMF) and Serious Breaches. These public consultations are published on the EU Commission and EMA websites. User acceptance testing of the portal is now underway.
- TMF – issues still being encountered by inspectors in relation to provision of the TMF and how it is not always in accordance with Regulation 31A of the UK Statutory Instrument (SI) 2004/1031 were presented. Inspections are still being impeded by the TMF being incomplete, despite numerous guidance being available. Organisations should be aware of all documents that comprise the TMF and where they are located. If located in different locations, then the locations should be formally specified and the TMF reviewed in its entirety as to how it will be presented to inspectors and how the documents will be archived as a complete TMF.
- Reference Safety Information (RSI) – current issues seen in relation to the use and control of RSI were presented. It is important that the RSI is clearly defined within the quality system and there are processes to control the RSI and ensure updates are approved by the MHRA as a substantial amendment prior to implementation.
- Sponsor Oversight – the importance of sponsor oversight and how this can be achieved was presented. Evidence of oversight should be retained within the TMF. Delegation of duties does not negate the fact that the sponsor has overall responsibility for the trial.
- Effective CAPA – a presentation on how to produce effective CAPA and ensure that findings/issues are truly resolved was delivered. An ineffective CAPA can result in findings being upgraded at the next inspection, therefore, it is important to identify the root cause and perform an impact assessment.
- Data Integrity – a session on data integrity and how this can be achieved was presented. Data integrity is becoming an increasing focus of the inspectorate with the use of more computerised systems in order to conduct clinical trial activities. The inspectors are reviewing audit trails on inspection and identifying issues which the sponsor was unaware of. The MHRA inspectorate currently has a draft GXP document on data integrity released for public consultation.

https://mhrainspectorate.blog.gov.uk/2016/10/18/mhra-gcp-symposium-2016/

MHRA Inspectorate Blog – Who Inspects the Inspectors?

This month the MHRA Inspectorate published a blog on who inspects the inspectors. In October 2015, the MHRA was audited under the Joint Audit Programme (JAP) for EEA GMP inspectors. The audit programme is sponsored by the Head of Medicines Agencies (HMA) and is focused solely on GMP. The two main drivers for the process are to verify equivalence and consistency of the implementation of European legislation and the practical application of GMP standards by national inspection agencies across the EEA and also to preserve confidence in the equivalence of EEA GMP systems to all member states and to EU Mutual Recognition Agreement (MRA) partner countries. The audit was conducted over five days by a team of three assessors from Finland, France and Spain and was also observed by the US FDA who were taking part under the Mutual Reliance Initiative looking to establish equivalence between Europe and the US. The detailed inspectorate processes and practices in the MHRA were assessed with the aid of a checklist of 78 indicators plus an EC legislation transposition guide. It also included two on-site GMP inspections being observed, using the JAP guidelines that describe the items normally necessary to initiate, plan, conduct, report upon and follow-up an observed inspection.

https://mhrainspectorate.blog.gov.uk/2016/10/05/who-inspects-the-inspectors/

MHRA and Swissmedic Sign MoU

The MHRA has signed a Memorandum of Understanding (MoU) with its Swiss counterpart, Swissmedic, the Swiss Agency for Therapeutic Products. The MoU was signed as part of the 11th Summit of the Heads of Medicines Regulatory Agencies, which was held in Switzerland and organised by Swissmedic. It was attended by around 75 agency representatives from 23 countries. The objective of this annual meeting is to promote information sharing and improve networking among agencies. The topics on the agenda of the 11th summit meeting included regulatory transparency, as well as best practise in cooperation and dialogue with stakeholders. Following many months of discussions, the central understandings of MoU include a shared approach to complex challenges as well as promotion of each other's regulatory frameworks, requirements and processes. Significant outcomes will include the facilitation and exchange of information, which will help make sure the regulators are better equipped to protect the health of their respective publics.

https://www.gov.uk/government/news/improving-international-collaboration-mhra-and-swissmedic-sign-mou

UK EU Life Sciences Transition Programme

Following the outcome of the EU Referendum, the former UK Life Sciences Minister announced the formation of the UK EU Life Sciences Steering Group to oversee and manage the transition of the life sciences sector and consider how the UK can seize the opportunity to define a new relationship with the EU. The Association of the Pharmaceutical Industry (ABPI) and the BioIndustry Association (BIA) were asked by the Steering Group to set up and support a UK EU Life Sciences Transition Programme to do this and to provide a starting point for engagement with the Government. The key objective of the Programme is to determine how to create a world-leading life-sciences environment in the UK outside of the EU. This includes:

- Identifying optimal position for the life sciences sector against potential exit scenarios, and generating ideas for agile approaches to overcome barriers and mitigate risks;
- Identifying opportunities to make the UK domestic landscape as strong and as attractive as possible for the life sciences industry;

- Providing options for how the UK can negotiate with the EU and relevant EU life sciences bodies to obtain the optimal outcome for UK and European industry, health systems and patients;
- Ensuring a framework for a continued dialogue between the life science industry and the government on these issues.

Over 50 hours of working group meetings were held in July and August focusing on: regulation, people, manufacturing and supply, R&D, Intellectual property and fiscal and trade; the MHRA attended all workshops. On 6 September 2016, the UK Life Sciences industry presented a report from the outcome of these meetings to Ministers and the UK EU Life Sciences Steering Group, which identified the following four priority areas: funding for scientific research, trade, regulation and talent.

http://www.bioindustry.org/policy-and-regulation/eu-referendum/

Highlights of EMA Management Board October 2016 Meeting

The European Medicines Agency (EMA) has issued highlights from its Management Board Meeting which was held in London on 6th October 2016. Key points from this meeting include the following:

- The EMA's new scheme to support the development of promising medicines addressing unmet medical needs (PRIME) has been successful so far with 64 applications having been received since its launch on 7th March 2016.
- The number of new applications for marketing authorisation received during the first half of 2016 was comparable to that received during the same period in 2015 (42 in the first half of 2016 compared with 45 in the first half of 2015).
- European medicines web portal was given the go-ahead:
    - The Board adopted a reflection paper on the development of a European medicines web portal, which sets out a vision for the portal and the expected benefits, and how best to achieve this vision. The multilingual website will provide access to free, reliable and unbiased information on all medicines authorised in the EU for patients, consumers, carers, healthcare professionals and academia across the EU.
    - Through the portal, comprehensive information will be provided on a medicine across its lifecycle, from clinical trial information to adverse drug reaction reports. The portal should increase the visibility of information on medicines held by the EMA and EU Member States.
    - The web portal will support high-level European initiatives on data availability providing downloadable, consumable datasets.
    - The portal is required by the 2010 pharmacovigilance legislation that came into effect in 2012. The EMA, in collaboration with EU Member States and the European Commission, will develop a multi-annual delivery plan and start scoping out IT solutions to support the project.
- A new vice-chair for the Management Board was elected. Grzegorz Cessak was elected as vice-chair for a three-year period. Dr Cessak has served on the Management Board since 2010 and is President of Poland's Office for registration of Medicinal Products, Medical Devices and Biocidal Products.

http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2016/10/news_detail_002616.jsp&mid=WC0b01ac058004d5c1

HHS Issues Final Rule on ClinicalTrials.gov Requirements

Last month the US Department of Health and Human Services (HHS) issued a final rule – the Clinical Trials Registration and Results Information Submission (42 CFR Part 11) - that clarifies and expands on the existing regulatory requirements and procedures for submitting registration and summary results information of clinical trials on ClinicalTrials.gov. These existing regulatory requirements are found in Section 801 of the Food and Drug Administration Amendments Act (known as FDAAA 801).

The final rule is intended to make it clear to sponsors, investigators and the public which trials must be submitted, when they must be submitted and whether compliance has been achieved. Some of the changes from current requirements are as follows:

- Additional data elements are required for registration and results information submission.
- Results information is required for ALL applicable clinical trials that are required to register and not just those for which the drug, biological or device products studied are approved, licensed or cleared.
- An expanded access record is required if an investigational drug product studied in an applicable drug clinical trial is available through an expanded access program.
- Some data elements must be updated more frequently than the standard 12 months.
- Responsible parties can evaluate whether a clinical trial is an applicable clinical trial based on required registration data elements.
- Corrections to submitted information will be required within 15 days (for registration information) and 25 days (for results information).

The National Institutes of Health (NIH) has also released a complimentary policy for registering and submitting summary results information to ClinicalTrials.gov.

https://clinicaltrials.gov/ct2/manage-recs/fdaaa#DevelopmentOfRegulations