Regulatory & Pharma News Update November/December 2018

REGULATORY NEWS

MHRA Inspectorate Blog: GCP Expectations for Dose Escalation Trials

On 26th November 2018 the Medicines and Healthcare products Regulatory Agency (MHRA) Inspectorate published a new blog post discussing their expectations in relation to dose escalation (DE) trials. The publication contains references to European Union (EU) Directives and United Kingdom (UK) Regulation relating to DE topics. It highlights the need for DE practices to be the same regardless of trial phase e.g. first in-human or first in-patient clinical trial and reiterates that DE is a major safety decision and therefore should be based on accurate information. The document states that for DE to be GCP compliant, there should be a formalised procedure detailing the dose escalation process (in the form of standard operating procedures and transparency in the protocol). It is additionally noted that MHRA inspectors expect to see:

- 'evidence that the relevant data has been collated, verified for accuracy and provided to the DE committee
- the DE meeting minutes
- the DE decision agreed by the DE committee (including the PIs)
- circulation of the DE decision to all relevant team members'

Examples of DE issues identified by the MHRA inspectors as well as inspectors' thoughts on potential reasons why the issues occurred are described in the publication.

https://mhrainspectorate.blog.gov.uk/2018/11/26/dose-escalation-is-it-gcp-compliant/

MHRA GPvP Inspectorate Pharmacovigilance Inspection Metrics Report

The MHRA Good Pharmacovigilance Practice (GPvP) inspectorate on 03rd December 2018 published their inspection metrics for the period from April 2017 to March 2018. This report contains data relating to 22 inspections of marketing authorisation holders conducted during the period. As stated in the report, the purpose of these inspections was to examine compliance with existing EU and national pharmacovigilance regulations and guidelines. A total of four critical, 89 major and 69 minor findings were identified during the period. Critical findings were categorised into the following topic areas: two risk management, one quality management system and one ongoing safety evaluation. The report includes a summary of each critical finding. Risk management was the topic with the highest proportion of major findings (25%) and the next highest was in relation to noncompliance in the quality management system (21%). These topics are discussed in more detail in the report.

https://mhrainspectorate.blog.gov.uk/2018/12/04/pharmacovigilance-inspection-metrics-april-2017-to-march-2018/

https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/761289/GPvP_Metrics_2017-18_.pdf

Expansion of EU-US Mutual Recognition Agreement for Inspections

Since 1st November 2017, EU Member States and the European Medicines Agency (EMA) can rely on inspection results from the United States (US) Food and Drug Administration (FDA). The mutual recognition agreement between the EU and the US forms the basis of accepted inspections of manufacturing sites for human medicines conducted in their respective territories since the EU and the US have comparable regulatory and procedural frameworks.

In the most recent update, five additional countries are now included; Belgium, Denmark, Finland and Latvia on 16th November and Estonia on 28th November 2018. The agreement is now operational between 20 EU Member States and FDA. It is the stated intention of the EMA and FDA that the agreement will include all EU Member states by 15th July 2019.

https://ec.europa.eu/newsroom/sante/newsletter-specific-archive-issue.cfm?archtype=specific&newsletter_service_id=327&newsletter_issue_id=11972&page=1&fullDate=Thu%2029%20Nov%202018&lang=default
https://ec.europa.eu/health/sites/health/files/eu_world/docs/c2017_1323_en.pdf

https://www.ema.europa.eu/en/human-regulatory/research-development/compliance/good-manufacturing-practice/mutual-recognition-agreements-mra

FDA Guidance for Industry on Data Integrity and Compliance with Drug CGMP

On 12th December 2018, the FDA published their guidance in the form of 'Questions and Answers' on data integrity and compliance with current good manufacturing practice (CGMP) for drugs. The document represents the current thinking of the FDA on the topic and aims to clarify the role of data integrity in CGMP for drugs, as required by 21 CFR parts 210, 211, and 212.

https://www.fda.gov/downloads/drugs/guidances/ucm495891.pdf

EMA Management Board: Highlights of December 2018 Meeting

On 14th December 2018 the EMA published a summary of their December 2018 meeting including:

The temporary premises in Amsterdam are on track to be fully operational on 1st January to allow for final preparations for the move to Amsterdam in March 2019. Work on the permanent premises is progressing as planned and should be completed by mid-November 2019.

The EMA expects to lose approximately 25 per cent of its overall workforce, however, all core activities related to the evaluation and supervision of medicines are expected to continue without any interruption or delays.

Work programme and budget for 2019 and a preliminary draft programme and budget for 2020 were adopted. Draft budget has decreased slightly (by 1.4 per cent) for 2019 compared to 2018. It is currently intended that the budget and work programme for 2019 should be published on the EMA website in Q1 2019.

Potential impact of Brexit on the supply of centrally authorised products (CAP) was assessed and the EMA has revised the number of centrally authorised products of which there are concerns of Brexit-related supply shortages to 31 (19 human medicines and 12 veterinary medicines). National competent authorities will check whether there are possible therapeutic alternatives available in their

country. All CAPs at risk of Brexit-related supply disruptions will continue to be closely monitored by EMA.

The update on the status of the development of the Clinical Trials Information System (formerly the EU clinical trial portal and database) was given as follows: the system remains in a phase of pre-testing of the auditable release (release 0.7) before user acceptance testing can start. At the same time, work to develop the safety reporting part of the system is progressing.

https://www.ema.europa.eu/documents/press-release/ema-management-board-highlights-december-2018-meeting_en.pdf

EMA: Revision of Guideline on the Environmental Risk Assessment of Human Medicines

The EMA has opened a public consultation for revision of its guideline on environmental risk assessments (ERA) of human medicines. An ERA is required for all new marketing authorisation applications for a medicinal product through a centralised, mutual recognition, decentralised or national procedure.

The EMA highlights that one of the most notable changes in the proposed revision is the introduction of the term "endocrine active substances," to include all compounds that affect development or reproduction. A further significant change provides guidance for the assessment of risk to predators eating contaminated prey (secondary poisoning).

Comments from Stakeholders on the revision are expected by 30th June 2019.

https://www.ema.europa.eu/en/news/revised-guideline-assess-risk-human-medicines-environment

https://www.ema.europa.eu/documents/scientific-guideline/draft-guideline-environmental-risk-assessment-medicinal-products-human-use-revision-1_en.pdf

December Meeting Highlights from the Committee for Medicinal Products for Human Use

On 14th December 2018, EMA released news after the latest meeting of the human medicines committee (CHMP) on 10-13 December 2018. Highlights of the meeting included:

- Seven medicines received a positive recommendation from the Committee:
  - Two new orphan medicines (one for the treatment of *polycythaemia vera* without symptomatic splenomegaly and another for the conditioning treatment prior to allogeneic haematopoietic stem cell transplantation);
  - Two new non-orphan medicines (one for the treatment of severe thrombocytopenia in adults with chronic liver disease undergoing invasive procedures and one for the treatment of opioid-induced constipation);
  - One biosimilar medicine (for the treatment of carcinoma of the colon or rectum, breast cancer, non-small cell lung cancer, renal cell cancer and carcinoma of the cervix);
  - One generic medicine for the treatment of adult patients with mild to moderate type 1 Gaucher disease;
  - One hybrid medicine for the management of chronic pulmonary infection due to *Pseudomonas aeruginosa* in patients aged 6 years and older with cystic fibrosis.
- Two applications for initial marketing authorisations have been withdrawn:

- Fyzoclad (adalimumab) was intended to be used to treat a number of inflammatory diseases;
- Canakinumab Novartis was intended to be used to prevent serious events such as stroke, heart attack or death in patients who have had a heart attack.

- Status of the review of impurities in sartan medicines:
  - The review of the blood pressure medicines containing candesartan, irbesartan, losartan, olmesartan or valsartan in relation to impurities found in some batches is still ongoing.

Full details are available at EMA's web page below.

https://www.ema.europa.eu/en/news/meeting-highlights-committee-medicinal-products-human-use-chmp-10-13-december-2018

https://www.ema.europa.eu/documents/medicine-qa/questions-answers-withdrawal-marketing-authorisation-application-canakinumab-novartis-canakinumab_en.pdf

PHARMA NEWS

Havas Lynx Group Creates 60 New Jobs

Havas Lynx Group, a healthcare communication agency, were named as Cannes Lions Healthcare Agency of the Year 2018 and saw turnover rise 23% to £31 million last year, marking a major period of growth for the business. The company has recently announced the creation of over 60 new jobs at their Manchester and London offices and plans to hire a further 20 over next three months.

The increase is intended to expand its workforce to 'keep up with a host of new campaign wins' and due to increased demand from clients such as AstraZeneca, Johnson & Johnson and Roche.

http://www.pharmatimes.com/news/havas_lynx_group_recruitment_drive_creates_60_new_jobs_1272952

https://www.havaslynx.com/news/havas-lynx-group-creates-60-new-jobs-with-largest-ever-recruitment-drive/

https://www.havaslynx.com/news/havas-lynx-scoops-healthcare-agency-of-the-year-at-cannes-lions-health-festival-2018/

Schrödinger and TB Alliance Announce Collaboration to Accelerate Tuberculosis Drug Discovery

On 11th December 2018 Schrödinger and TB Alliance announced a three-year research collaboration to increase the speed of the development of next-generation tuberculosis (TB) treatments by leveraging Schrödinger's advanced computational platform for drug discovery. The joint team will focus on the discovery of efficacious inhibitors of PknB, which is essential for the growth of Mycobacterium tuberculosis (TB).

https://www.schrodinger.com/news/year2011