What's New in Clinical Development Practices & Regulations Quarter 4 – 2018

BREXIT

Brexit and Patient Protection

UK health service and industry representatives are asking the government and the EU to ensure cooperation on medicines safety and regulation is a clear priority in the final version of the Brexit Agreement.

http://www.abpi.org.uk/media-centre/news/2018/november/nhs-pharma-and-biotech-industries-call-on-government-to-protect-patients-in-future-uk-eu-relationship

European Medicines Agency (EMA) and Brexit

On 01 October, the EMA's Brexit Preparedness Business Continuity Plan (BCP) officially entered Phase 3. The aim is to safeguard its core activities as it prepares for relocating to Amsterdam in March 2019 and deals with associated significant staff losses whilst at the same time managing the consequences of UK's exit from the EU.

https://www.ema.europa.eu/documents/other/ema-brexit-preparedness-business-continuity-plan-phase-3-implementation-plan_en.pdf

Brexit and the EU Clinical Trial Regulation (CTR)

The planned implementation of the new EU CTR is scheduled to coincide with the transition period that will be in place as the UK exists the EU.

The Medicines and Healthcare products Regulatory Agency (MHRA) has issued a statement on the implementation of the EU CTR following Brexit.

https://www.gov.uk/government/news/clinical-trials-regulation?utm_source=4cc78e9c-3d0c-4205-84d1-0bb04058c0af&utm_medium=email&utm_campaign=govuk-notifications&utm_content=immediate

MHRA guidance on Brexit

The MHRA has provided guidance relating to the Brexit implementation period and an Exit no-deal contingency legislation for the regulation of medicines and medical devices.

https://www.gov.uk/guidance/technical-information-on-what-the-implementation-period-means-for-the-life-science-sector?utm_source=a96e5c8e-0a3c-4305-863e-1a8f733e1fbc&utm_medium=email&utm_campaign=govuk-notifications&utm_content=daily

https://consultations.dh.gov.uk/mhra/mhra-no-deal-contingency-legislation-for-the-regul/

CLINICAL TRIAL DATA SHARING

Study Subjects Supportive of Clinical Trial Data Sharing

The *New England Journal of Medicine* has published findings from a survey which show that patients understand and value the positive benefits of data sharing. The benefits include:

- Clinicians and patients are able to make best-informed decisions.
- It may prevent/uncover inaccurate reporting of data.
- It may facilitate efficiencies and innovation in drug development.

The negative side relate to the potential risks, in particular regarding privacy and data re-identification.

https://www.nejm.org/doi/full/10.1056/NEJMsa1713258

Clinical Trial Registries – Incorrect and Incomplete

The European Commission's (EC's) requirement is for all trials on the EU Clinical Trials Register to have their results posted within 12 months of completion. Recent analyses show errors and contradictory entries in the data posted.

The research also identifies features associated with non-compliance and it ranks sponsors according to their compliance.

https://www.bmj.com/content/362/bmj.k3218

EUROPEAN AGENCIES

EC Consults on Draft Good Clinical Practice (GCP) Guidelines for Advanced Therapy Medicinal Products (ATMPs)

This draft guidance was issued for consultation in order to collect relevant evidence and information to enable the EC to further develop the guideline.

https://ec.europa.eu/health/sites/health/files/files/advtherapies/2018_gcp_atmp_en.pdf

EMA Releases Guidance on Data Monitoring Committees (DMC)

This consultation continues until 31 July 2019 and addresses topics such as whether a DMC's recommendation is binding for the sponsor and whether a DMC can stop a study or change the study design. The guidance will be in a Question and Answer format.

https://www.ema.europa.eu/documents/scientific-guideline/draft-questions-answers-data-monitoring-committees-issues_en.pdf

European Agencies Aim to Boost the Development of Paediatric Medicines

In October 2018, the EC and EMA published a joint action plan to support the development of medicines for children. The plan aims to increase the efficiency of paediatric regulatory processes and boost the availability of medicines for children.

In addition, a new EMA guideline on Good Pharmacovigilance Practice (GVP) for paediatric populations came into effect 08 November.

https://www.ema.europa.eu/documents/report/european-medicines-agency-european-commission-dg-health-food-safety-action-plan-paediatrics_en.pdf

https://www.ema.europa.eu/documents/scientific-guideline/guideline-good-pharmacovigilance-practices-gvp-product-population-specific-considerations-iv_en-0.pdf

CLINICAL TRIAL DESIGN DEVELOPMENT AND METRICS

UK – New Guidance on Electronic Informed Consent

The National Health Service Health Research Authority and the MHRA have issued a joint statement describing the legal and ethical requirements for obtaining informed consent using electronic methods.

https://www.hra.nhs.uk/about-us/news-updates/hra-and-mhra-publish-joint-statement-seeking-and-documenting-consent-using-electronic-methods-econsent/

UK – 2018 Metrics on Clinical Trial Applications (CTAs) and Substantial Amendments

The MHRA reviewed on average 85 CTAs and 368 substantial amendments per month. The vast number of substantial amendments has a huge implication on the cost of clinical drug development.

https://journals.sagepub.com/doi/abs/10.1177/2168479016632271?journalCode=dijc

https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/763248/11_November_2018.pdf

Food and Drug Administration (FDA) – New draft Guidance on Adaptive Trial Design

An adaptive clinical trial design has the potential to provide a better chance of detecting the true drug effect, while reducing the number of subjects exposed to ineffective investigational treatments.

The FDA has released draft guidance that describes the principles for designing, conducting and reporting the results from adaptive clinical trials.

https://www.fda.gov/ucm/groups/fdagov-public/@fdagov-drugs-gen/documents/document/ucm201790.pdf

ONCOLOGY CLINICAL TRIALS

Encouraging Trends in Modern Phase I Oncology Trials

A recent survey questioned the perception that only 5% of patients in Phase I oncology trials experience a benefit. This 5% relates to a genuine clinical benefit (tumour shrinkage). In addition, reported data suggested that phase I oncology patients may have unrealistic high expectations of the likely clinical benefits of trial participation.

The survey was of more than 200 Phase I oncology trials and suggests an overall beneficial response of nearer 20%. This is published in the *New England Journal of Medicine* by French researchers.

https://www.nejm.org/doi/full/10.1056/NEJMc1803837

New Oncology Guidance

- FDA Draft Guidance on Placebos and Blinding in Oncology Trials - https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM617931.pdf
- FDA Draft Guidance on Master Protocols for Cancer Treatments - https://www.fda.gov/ucm/groups/fdagov-public/@fdagov-drugs-gen/documents/document/ucm621817.pdf
- FDA Draft Guidance on Expansion Cohorts in First-In-Human Oncology Trials - https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM616325.pdf?utm_campaign=CDER%20New%208%2F13&utm_medium=email&utm_source=Eloqua&elqTrackId=74dc985536ea41b097d0f6e2d89a6a4e&elq=9fb78fc7bc7647a99c9195c1e4eb247b&elqaid=4615&elqat=1&elqCampaignId=3664

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