EUROPEAN COMMISSION
HEALTH AND FOOD SAFETY DIRECTORATE-GENERAL

Health systems, medical products and innovation
Medicines: policy, authorisation and monitoring

PHARM 705

PHARMACEUTICAL COMMITTEE
28 April 2016

Subject: **Implementation of the Clinical Trial Regulation**

Agenda item 2iii

Three meetings were held (in November 2015, February 2016 and April 2016) with the *ad hoc* group on clinical trials (CT), established under Directive 2001/20/EC:

EU CT Portal and database

During the meeting held in February 2016 the European medicines Agency (EMA) representative gave an update on the development of the EU CT portal and database covering the following aspects:

- Timelines and milestones: a new proposal was adopted by the EMA Management Board in December 2015 and published on the EMA website. The audit has been moved to August 2017 and will be completed in November 2017, with the Regulation becoming applicable in October 2018. The current timelines are the maximum timelines; all efforts for earlier application are to be made to bring the Regulation into application as soon as possible.
- There will be an audit release as well as a production release of the system. The latter will be in time for National Competent Authorities (NCAs) to familiarise themselves with the system.
- User acceptance testing (UAT) will take place following each iteration of the system. Nominations for focal points in NCAs and stakeholders for the UAT have taken place. The objective is to create a system fit for purpose by involving a large number of testers.

CT project microsite

Following a request from IT Directors and Member States during a workshop held in October for improved communications with the Member States, EMA has developed a Clinical Trials Programme Microsite for this purpose. The microsite is a platform to share with Member State representatives technical documentation and information

regarding the EU Portal and Database and other IT systems to support the implementation of the CT Regulation. Currently the microsite still presents a general outline and can only be accessed by the Member States group. A bulletin is issued every time there is an update to the site. Additional access to the microsite can be granted by EMA if Member States request so.

Ad hoc group Work plan for 2016

During the February meeting COM presented the draft 2016 working plan for *ad hoc* group, emphasizing the heavy workload. Priority 1 projects are those required by the Clinical Trial Regulation (CTR), namely the Implementing Act on GCP Inspections, the Delegated Act on GMP for IMP and the Guidelines on GMP for IMP. All remaining guidelines fall under the second priority and are grouped under two categories: those that are to be finalized by the end of 2016, and those that are due by the middle of 2017.

Progress on Legal obligations

Following the outcome of the public consultation that closed in November 2015 the *ad hoc* group was consulted between 8 February and 15 March 2016 on the technical documents regarding the following legal obligations:

- Commission Implementing Act on detailed arrangement for clinical trials inspection procedures including the qualifications and training requirements for inspectors (Article 78(7))
- Commission Delegated Act on principles and guidelines on good manufacturing practices for investigational medicinal products for human use and inspection procedures (Article 63(1))

Next steps: Internal consultation in the Commission and a second public consultation for 1 month in summer.

With respect to the "Detailed Commission guidelines on good manufacturing practices for investigational medicinal products" (Article 63(1)) consultation with *ad hoc* group is planned to be held in Q2 2016.

Progress on new guidelines and revision of existing ones to be finalized between the end of 2016 and mid-2017

Discussions were held with the *ad hoc* group on new guidelines that are being prepared by various task groups on behalf of the *ad hoc* group in preparation for the implementation of the CTR. These included: *"Guidelines on the summary of results for lay persons"* and *"Guidelines on risk proportionate approaches in clinical trials*".

Additionally the *ad hoc* group discussed a number of existing guidelines which are being revised by various task groups on behalf of the *ad hoc* group to bring them in line with the CTR. These included: "*Guidance documents applying to clinical trials guidance on IMPs and AMPs*[1]*", "Guidance on ethical considerations for clinical trials on medicinal products conducted with the paediatric population",* and *"Guidelines on GCP*

[1] Note that AMPs were previously referred to as non-IMPs (NIMPs)

compliance in relation to trial master file (TMF) (paper and/or electronic) for content, management, archiving, audit, and inspection of clinical trials[2]*"*

Clarifications and discussions of aspects relating to procedures and rules for the implementation of the Regulation

During both meetings COM gave presentations with the aim of clarifying and discussing with delegates certain outstanding issues that have arisen during discussions held with different groups. These included clarification of the procedures regarding the addition of a Member State (article 14 of the Clinical Trial Regulation (CTR))

Preliminary discussions were held regarding what is considered to be a temporary halt and a premature end as well as which types of substantial modifications would be applicable for the submission of a single request for authorisation affecting more than one CT (of same sponsor and same IMP) as per Annex II A1 of CTR.

Regular discussions on the various aspects of the Q&A document on the Clinical Regulation, such as regarding "*Clinical trials in emergency situations (Article 35 of Clinical Trial Regulation)"*

Please note that an update on the ad hoc group meeting of April will be given orally during the meeting.

Collaboration of Member States with EMA and COM

COM would like to urge Member States to collaborate constructively with EMA and COM to advance further on the development of the EU CT portal and database not to delay further the application of the Regulation beyond the maximum timeline of October 2018 agreed during the December 2015 EMA Management Board meeting.

Any further delay in the project is not admissible. There is a huge pressure from the public and the stakeholders (and the EP) to have in place as soon as possible the new legislation, one of whose key objectives is to strengthen the attractiveness of the European clinical trial environment, benefit researchers and patients in Europe and foster innovation. The reputational risk of the EU is at stake.

Action to be taken:
For discussion/For information

[2] This guideline will replace existing Volume 10 guidance by utilising the draft reflection paper that had been developed by the GCP Inspectors Working Group