Medicines & Healthcare products Regulatory Agency

MHRA

Chair of the Science and Technology committee
House of Commons
London
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Further information for questions raised by the Science and Technology committee

Dear Danielle Nash,

Thank you for the opportunity to attend and give evidence during the session on clinical trials transparency on 29 October 2019. You asked that I write to the Committee with further information on the following points:

1. **Details on the extent of the administrative backlog and the length of time taken to process individual requests**

As described during the Committee session, from mid-2016 to 2018 we experienced administrative resource issues and competing priorities which resulted in a backlog in bringing up-to-date the Competent Authority and Ethics Committee decision dates in the European database (EudraCT), which is what moves the entry from the secure EudraCT database to the public register. Despite best efforts, it was not possible to fully recruit to the vacant posts and at its peak, the administrative backlog constituted 2179 entries to the system. It is important to note that there is no question of this having adverse public health impacts as all of the information in the secure database was available for regulators to see and was publicly available on the HRA research summaries webpage. Further, trial sponsors also register studies via ClinicalTrials.gov which is an online database of privately and publicly funded clinical studies worldwide. It is ClinicalTrials.gov and the International Standard Randomised Controlled Trial Number registries (and not EudraCT) that feed the UK “Be Part of Research” website (formerly UK Clinical Trials Gateway).

This backlog was reduced to zero by July 2019 and therefore no longer exists. Our current process means that the final MHRA decision date is entered in EudraCT on the same day it is generated, wherever possible. Ethics committee opinions are received from the Health Research Authority (HRA) on a monthly basis and are entered on to the system on receipt. The reasons for not being able to upload to the system on the day of decision are due to issues with the technical validation of the “eXtensible markup language” (XML) file provided by trial sponsors or problems with the EudraCT database itself. In these cases we need to consult with the sponsor organisation and/or the European Medicines Agency (EMA) to manage upload into the EU system. Average time taken to upload MHRA decision into the EU system for October-November 2019 was 10.9 days (range of 0-34 days).

In terms of time taken to process individual requests, during the period of June 2016 to September 2019, we received 403 queries relating to sponsors contacting us about problems they experienced with their entries in the public register. Our timeline for addressing these was within an average of 8.24 days (ranging from 0 days to 86 days). The reason for delays to addressing some of these (approx. 17% outside of our target of 14 days) has been ongoing conversations with sponsors and in some cases the EMA service desk to fix technical issues with the file type provided, particularly when they related to older trials.

2. Further information on specific issues encountered (by sponsors and the MHRA) with the EudraCT system, to be resolved by the European Medicines Agency

These can be broadly grouped as follows:

- System support: our stakeholders have reported problems with the length of time for service desk responses, and often answers which direct them to contact their local competent authority when the problem lies with the EMA system.
- System usability: the interface for the system could be more user friendly and does not allow sponsors or their delegates to amend or update their own information in the register.
- System functionality: for example the inability of sponsors to provide a null response for abandoned trials or to report results from adaptive design trials (eg “basket” or “umbrella” trials). For competent authorities, there currently is no easy way for member states to monitor compliance with reporting expectations (and involves duplication of effort for multi-Member State trials as there is no centralised update to records).
- System stability: recently the number of incidences of ‘downtime’ with the system has increased making it difficult for competent authorities to enter data and sponsors to upload results information in a timely manner.

In the longer term, for the EMA, the Clinical Trials Information System (CTIS) being developed for the new Clinical Trials Regulation will address all of these problems.

3. How regulations regarding the reporting of results for trials of medical devices is expected to change, and who in the UK would be responsible for ensuring compliance

New regulations for medical devices came into force in May 2017 and will fully apply from 26 May 2020. These regulations include provisions for clinical investigations of medical devices and introduce a requirement for the sponsor of such studies to submit a clinical investigation report and a summary within one year of the end of the clinical investigation. The sponsor shall upload this report and summary onto the European Eudamed system and these reports will become publicly accessible through Eudamed within the following timescales:

- Immediately if the clinical investigation was terminated early or temporary halted.
- When the device is registered before being placed on the market.
- One year after the summary and report have been entered onto Eudamed if the device has not been registered by then.

With the delay of the development of the Eudamed database, expected to be operational by May 2022, the UK will look at practical options with a view to implementing this requirement domestically by May 2020

We will also ensure that reports are published within the required timescales by sponsors of clinical investigations being conducted in the UK.

I hope that you find these answers helpful. Please let me know if you require any more information

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