

Clinical trial disclosure: Perspective from a medical writer for a contract research organisation

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Abstract

In this article, I summarise how, as a medical writer with over 20 years of experience in regulatory writing, all with a contract research organisation, I transitioned into the world of disclosure and how I now have my feet firmly in both camps: regulatory medical writing and clinical trial disclosure. I describe how disclosure captured my attention and the subsequent actions I have taken.

Background

Clinical trial transparency and clinical trial disclosure are terms that we are now all familiar with, and it is not just pharmaceutical companies that are under increasing pressure to make clinical trial data that has not traditionally been disclosed available to the public; any research group that registers a trial must comply with the same regulations.¹⁻⁴

As a medical writer working for a contract research organisation (CRO), these regulations have had a considerable but positive impact on my day-to-day activities. While our Global Regulatory Affairs group has been supporting our clients in their clinical transparency efforts since 2008 and the release of the Food and Drug Administration Amendments Act (FDAAA 801), requests to prepare clinical trial results

postings were intermittent and fluctuated in number. With the implementation of mandatory posting to the EMA's European Clinical Trials Database (EudraCT) of interventional clinical trials that ended on or after July 21, 2014, the impact was almost immediate: we saw a huge increase in the number of current and new clients reaching out to ask if we could support this activity.

The article is a summary of how, as a medical writer with over 20 years of experience, all with a CRO, I made the transition into the world of disclosure.

Clinical trial disclosure

EMWA played a big part in my leap into the world of disclosure, starting with the 2014 conference in Budapest, which attracted my attention with the 1-day symposium "Transparency of Clinical Trial Data – Where Does Medical Writing Fit In?". It was the start of a special relationship with a group of fellow EMWA members, some of whom I already knew through our years in the industry. I am talking about the Budapest Working Group (BWG) – the EMWA-AMWA developers of CORE (Clarity and Openness in Reporting: E3-based)



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Reference (www.core-reference.org). I returned from Budapest a member of the BWG and full of ideas and insights for how our medical writing group could provide support in the area of transparency to our clients, old and new. Medical writers are ideally suited to working in results disclosure; we already have the skills that enable us to summarise clinical trial data and present the results to address the objectives of a particular study. In addition, we are renowned for our attention to detail. I know I am not the only medical writer who cannot help but “edit” everything I read, from newspaper articles to printed works of fiction!

I spent many hours getting up to speed on the regulations for the USA and EU/EEA. By the end of 2014, we had established a clinical trial disclosure group in the UK along with the role of

“disclosure specialist”. The sole purpose of this group was to perform disclosure activities, and the first two members of this group (including me) were medical writers by trade. We worked hard to learn the relevant regulations, taking advantage of all the training resources that are freely available through ClinicalTrials.gov and EudraCT.^{5,6}

We continued to grow our dedicated disclosure group by enticing other medical writers who were perhaps looking for diversity or even part-time work/reduced hours per week. Our aim was to engage a couple of candidates who could prepare the postings while supporting each other on their out-of-office days. Preparing a clinical trial results posting takes much less time than, for example, preparing a clinical study report (CSR), and this effort can be moulded to

suit part-time employees. This worked in our favour and over the past 4 years this group has grown.

We also invested in our own software solution to facilitate the creation, review, and upload of clinical trial results postings to EudraCT and ClinicalTrials.gov. This has proved fruitful for dual postings, where the clinical trial results are required to be posted to both EudraCT and ClinicalTrials.gov, as the software tool avoids the need for duplicate data entry. In addition, for EudraCT postings where the sponsor does not have a primary results user, the EMA can take up to 25 calendar days to process a EudraCT access request, and sometimes impending registry deadlines do not afford the luxury of time. Our software tool allows us to initiate the results posting and to download drafts for sponsor review. We can then upload the entry to EudraCT as an XML file⁷ when we get access.

Clinical trial results postings

Our daily tasks include the preparation of both EudraCT and ClinicalTrials.gov postings and, more recently, review of the study protocol, applicable protocol amendments, and the statistical analysis plan for any information requiring redaction before submission to ClinicalTrials.gov.³

As is typical in a CRO, levels of requests for our disclosure services can fluctuate. Following publication of the EU Trials Tracker⁸ (which lists, by sponsor, all interventional clinical trials in the EU Clinical Trials Register), we noticed a surge in requests from clients. Although not built or monitored by the EMA, the EMA have been using the tracker to reach out to sponsor companies directly, using the last known contact information from the EU Clinical Trials Register, to inform them that they either:

- a. Have results due, i.e., it has been more than 1 year since the “global end of trial date”; or
- b. Have inconsistent data, i.e., the sites where the trial was conducted have listed their status as “completed” but there is no accompanying “global end of trial date”; there is a “global end of trial date” but some sites are listed as “ongoing”; or the trial status is blank.



Where the EMA has been successful in reaching the appropriate sponsor contacts, there has been much surprise as to the number of sponsor studies currently without results in EudraCT.

The same group who put together the EU Trials Tracker (Evidence-Based Medicine Data Lab, University of Oxford) have also created the FDAAA Trials Tracker⁹ (which lists, by sponsor, all applicable clinical trials and probable clinical trials, where an applicable clinical trial is a trial that began after January 18, 2017, and a probable clinical trial is a trial that began before and ended after January 18, 2017). Note: the FDA itself is not publicly tracking compliance.

I predict that we will see the effect of these trackers for some time to come as increasing numbers of sponsor companies become aware of the trackers and can access them to see where they are non-compliant.

Clinical trial disclosure in a CRO

As is typical for a CRO, we are exposed to a wide variety of clinical trial results data, both in terms of phase and therapeutic area. No two studies are the same and, combined with the challenges of working in regulated databases with restrictions, character limits, and required verification steps, this means that preparation of clinical trial results postings is anything but routine. All this can keep even the most challenge-hungry individual satisfied.

This is a moving landscape and our group continually monitors industry and regulatory agency changes. We do this in several ways, including by signing up to notifications and blogs from the FDA (<https://www.clinicaltrials.gov/ct2/resources/rss>) and EMA (<https://eudract.ema.europa.eu/>), attending webinars hosted on their public sites, and using other online training resources provided by both agencies. We share lessons learned within our group and in the broader field of disclosure through forums such as the Drug Information Association (DIA).

Internally, our disclosure specialists have worked with our medical writers to make changes to the protocol and CSR templates to take account of data transparency. This not only helps our global medical writers ensure that they can provide sponsors with CSRs that

are disclosure-ready for any submission packages, but also ensures that – right from the outset with the protocol – medical writers are thinking about results disclosure.

For example:

- Both the protocol and CSR should contain only the necessary confidential information regarding the compound under investigation or the people involved in the trial (for example, avoid the inclusion of investigator or vendor names, centre IDs, subject-specific information, and proprietary information, where possible).
- Within the ClinicalTrials.gov Protocol Registration and Results System, there is a 600-character limit for the “official title” of the trial.
- Within EudraCT and ClinicalTrials.gov, there is a 255-character limit for an outcome measure title.
- Outcome measures should include the measure, units, and time points.

My role as head of clinical trial disclosure

To help me in my role leading this group, I am a member of DIA and associated medical writing and clinical trial transparency community groups. The BWG published CORE Reference in May 2016¹⁰ and we remain engaged in supporting the global medical writing community in fulfilment of reporting obligations that take full account of transparency and disclosure requirements.¹¹ I am an EMWA workshop leader on CORE Reference and was a panel member on this topic at the DIA 2017 Global Annual Meeting (Driving International Awareness and Use of Regulatory Writing Guidelines: Case Studies of the Clarity and Openness in Reporting:E3-based [CORE] Reference Guidelines).

Conclusion

I feel very lucky to have been able to play a pivotal role in the creation and subsequent growth of our in-house clinical trial disclosure group by engaging in activities such as hiring staff, establishing processes and standard operating procedures, and developing job descriptions and job grades. As well as our disclosure specialists, we also have an additional

bank of medical writers trained in the preparation of clinical trial results postings. It is clear that medical writers have the skills required to competently complete the tabulated data postings in EudraCT and ClinicalTrials.gov: We have the ability to understand the design of a study and why it was performed; to understand what the objectives were and what the resulting endpoint results show; to extract the data that should be included; and to appropriately summarise text within the character limits set by the database.

Clinical trial disclosure offers the opportunity to operate in an evolving environment and to become an expert in the evolving requirements and regulations. You get to use your practical experience in working with clinical trial data to help your customers understand and meet their obligations.

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Disclaimers

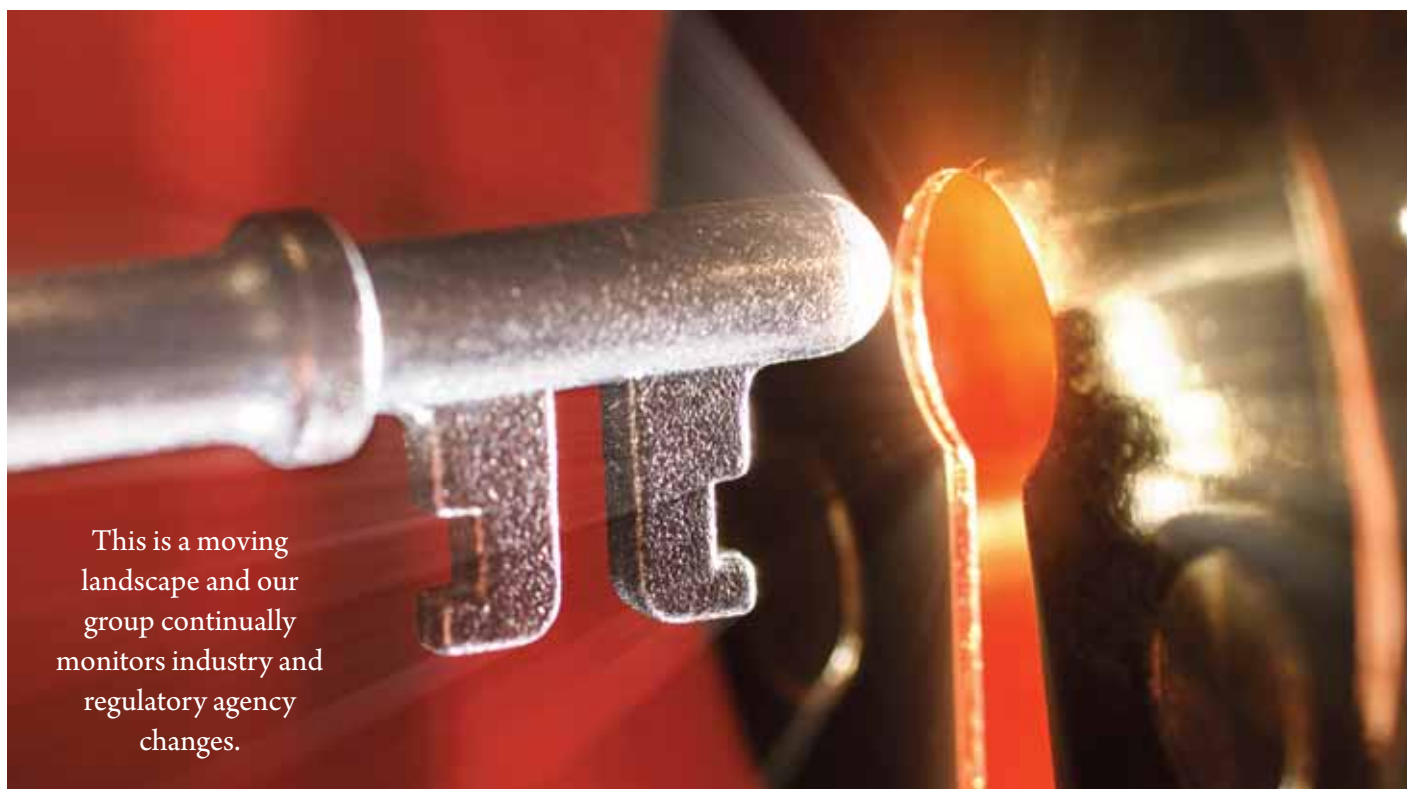
The opinions expressed in this article are the author's own and not necessarily shared by her employer, EMWA, or other members of the BWG.

Conflicts of interest

The author declares no conflicts of interest.

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