Authorship of clinical trial documents

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Abstract

Authorship of publications has been the subject of much public debate; however, authorship of clinical trial documents such as clinical study protocols, clinical study reports, investigator's brochures and informed consent forms has not really been given much attention. This article looks at the common practices of authorship attribution and signing off on these documents and examines what the ICH guidelines, on which their contents are based, say about these issues. The implications of the EMA Policy 0070 on clinical trial disclosure are discussed.

Introduction

Clinical study protocols (CSPs), clinical study reports (CSRs), investigator's brochures (IBs) and informed consent forms (ICFs) are among the most common documents that regulatory medical writers author as professionals. Unlike publications where authorship has been under scrutiny in recent years, authorship of CSPs, CSRs, and other clinical trial documents has not really been a topic of discussion. This is probably because these documents have traditionally been hidden behind the shroud of confidentiality.

However, with increasing requirements for transparency having reached the realms of regulatory documents, it is about time that authorship attribution of these documents should be considered. As we move towards posting some of these documents in the public domain, it is also important to see the implications of disclosure on the authors and signatories of these documents.

Clinical Study Protocol (CSP)

The contents of a CSP are based on ICH E6 (Guidelines for Good Clinical Practice, 1996)[1] and the ICH E6 integrated addendum (2015)[2]. The protocol is frequently written by a regulatory medical writer who receives input from other functional groups. Contributors to the document will include, but are not limited to, a biostatistician and a medical expert. In some cases, investigators or clinical research scientists also draft a CSP with or without the support of a medical writer.

The ICH E6 guideline does not provide guidance with respect to authorship attribution of the CSP. However, it does indicate the individuals and institutions who should be signatories of the final protocol, namely, the '*investigator/institution and the sponsor*'. In signing off the protocol ('*or an alternative contract*'), these individuals and institutions thereby declare their commitment to follow the protocol and abide to the principles of Good Clinical Practice (GCP).

The CSP eventually ends up as part of appendix 16.1.1 of the CSR, which is

expected to be posted in the public domain under the EMA Policy 0070 Publication of Clinical Data for Medicinal Products for Human Use[3,4]. Only the names of investigators may be disclosed. If other names appear in the protocol, these may need to be redacted or the concerned individuals may need to sign a waiver to disclose their personal data. Moving forward, it might be advisable for the signatories to sign off on an *alternative contract* that is not part of the main document, an option that is provided for in ICH E6.

The CSR and CSP are the two most important clinical trial documents impacted by disclosure through the EMA Policy 0070. ICH E6 does not provide any guidance on authorship of CSPs. ICH E3 provides somewhat unclear recommendations for authorship of CSRs. The CORE Reference may provide much needed clarity.

Clinical Study Report (CSR)

CSRs are more often than not written by regulatory medical writers. The CSR has a dedicated ICH guideline (ICH E3 Structure and Content of Clinical Study Reports 1997[5] and Q and A update 2012[6]), thus belying its importance. It is also the centrepiece of the EMA Policy 0070[3] and its implementation.

Authorship is mentioned in two sections of ICH E3.

In Section 6 *Investigators and Study Administrative Structure*, the guideline recommends that a list of people 'whose participation materially affected the conduct of the study should also be provided in appendix 16.1.4.' This listing should include '…the author(s) of the report, including the responsible biostatistician(s).'

Authorship is also touched upon in appendix 16.1.5 *Signatures*. In the sample signature form provided in Annex II of ICH E3, the term *study author(s)* is used (Figure 1) but the authors are not necessarily the signatories of the CSR. The distinction between *report author* and *study author* (if any) is not clearly specified in ICH E3.

Assuming that these two terms of authorship are used interchangeably, in theory, the medical writer(s) who drafted the text sections of the CSR would qualify as author(s) of the report. The biostatistician(s) who provide the statistical outputs would qualify as well. Other roles that would be considered for authorship or contributorship are the site staff (investigators and subinvestigators) as well as the sponsor and the contract research organisation (CRO) staff (if used).

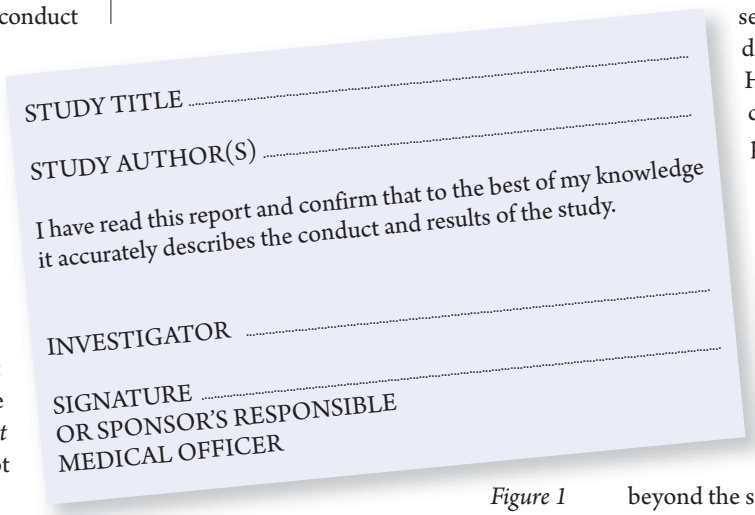
In practice, attribution of authorship is usually dependent on company policy. Below are a few scenarios that I have encountered over the years.

1. Authorship of CSRs is, by default, attributed to sponsor personnel. If CSR writing is outsourced, the medical writing company, consultant or CRO will be listed in appendix 16.1.4 as being responsible for writing the CSR. However, the title page of the report would only list the name(s) of the sponsor's responsible person(s) and one, some or all of these people will be the CSR signatories.
2. There is no authorship attribution to any individual. In many CSRs I have written for clients, an institutional author (company name) is provided on the title page and the synopsis. A responsible medical officer on the sponsor side will sign off on the report. Appendix 16.1.4 may or may not list individuals or institutions responsible for CSR development.
3. A CSR is a shared endeavour and responsibility is across the functional groups. I have had clients who insisted on naming the medical writer, the biostatistician and the medical officer as authors of the document. Furthermore, they usually expected these authors to be signatories in appendix 16.1.5.

It is important to clarify that the authors and the signatories of a CSR are not necessarily the same people, as in scenarios #1 and #2. For the signature page in appendix 16.1.5, the minimum requirement is for the sponsor's responsible medical officer to sign off on the document. In European studies, the signature of the coordinating investigator is also required.[7]

Scenario #3 is especially controversial as some medical writers do not feel comfortable in signing off on such an important document. With the requirement to disclose CSRs in the public domain, the reluctance to sign has increased. It should be noted that, based on the EMA policy 0070[3,4] on CSR disclosure, sections 16.1.4 and 16.1.5 will not be posted publicly. Hence, based on the current disclosure policy, attribution of authorship to individuals in these sections does not amount to disclosing their personal data. However, even this argument cannot allay concerns of possible legal implications.

If we argue that the terms *report author(s)* and *study authors(s)* are not synonymous, we might have to go down the road of defining metrics for an individual's level of involvement and contribution to a clinical study. This, however, would be a discussion that is beyond the scope of this article.


STUDY TITLE .....

STUDY AUTHOR(S) .....

I have read this report and confirm that to the best of my knowledge it accurately describes the conduct and results of the study.

INVESTIGATOR .....

SIGNATURE .....
OR SPONSOR'S RESPONSIBLE
MEDICAL OFFICER

Figure 1

In my search for further clarification on authorship of and signing off on a CSR, I reached out to Sam Hamilton (personal communication), chair of the Budapest Working Group (BWG). This group is developing the CORE (**C**larity and **O**penness in **R**eporting: **E**3 based) Reference as an open access user manual for CSR authors, with planned release in May 2016.

CORE Reference will recommend inclusion of a list of roles and responsibilities in Section 6 detailing investigators (principal or coordinating), data monitoring and evaluation committees, and laboratories. The BWG also recommends specifying study responsibilities clearly and study activities of the institutions involved, including report authoring and biostatistics with details provided in CSR appendix 16.1.4.

What about the reference to study authorship in appendix 16.1.5 (Figure 1)? CORE Reference will advocate the consistent use of *report authorship* and *CSR authorship* throughout the document. CORE Reference will not suggest the medical writer as an appropriate co-signatory for a CSR, because it is not mandated by existing regulatory guidelines. In reality, CSR signatories over and above those required according to ICH (or the relevant country or regional guidelines) remain a matter for individual sponsor consideration or policy.

Investigator's Brochure (IB) and Informed Consent Form (ICF)

ICH E6 also covers the contents of the IB and the ICF. As in the case of the CSP, no authorship attribution for these documents is specified in the guideline. But, unlike the CSR and CSP, these documents will not be posted publicly but will remain filed in the Trial Master File. Hence, the authorship attribution of these documents is less likely to become an important issue in the future.

Summary

In summary, regulatory medical writers continue to create key regulatory documents for clinical trials. The CSR and CSP are the two most important clinical trial documents impacted by disclosure through the EMA Policy 0070. ICH E6 does not provide any guidance on authorship of the CSP, IB and ICF. ICH E3 provides somewhat unclear recommendations for authorship of CSRs; CORE Reference may provide the much needed clarity. If handled appropriately, authorship attribution of and signing off on CSRs need not be impacted by public disclosure.

References

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Disclaimer

The views and opinions in this article are solely those of the author and do not reflect those of Clinipace Worldwide.

Author Information

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