# Regulatory Questions and Answers: The Investigator's Brochure

**by Douglas Fiebig**

*Dear TWS Experts*

*I work for Novo Nordisk and I'm responsible for our IB SOP. I've been asked if I know about any official guidelines for the format of AE tabulations for IBs. I have not been able to find any, so our AE tabulations are based on the tabulations we use for our clinical trial reports. Do you know if there are official guidelines? And then I have another question. Does your department ever receive comments such as, "No comments on the content, BUT, I have a general comment that I have raised many times, must our IB's be such boring documents, not at all inviting the investigators to read them? I think they should be written much more like our product monographs, using colours, figures, graphs, and even pictures, etc. I mean this very seriously!"*

The first part of the question is quickly answered. The only official guidance for preparing an IB is given in the ICH E6 guideline on GCP (e.g. CPMP/ICH/135/95). However, this guideline provides only general recommendations for the structure and content of an IB, and the style of presentation is left to the discretion of the sponsor. Thus the most pragmatic approach to generating AE tabulations in IBs is to use the format chosen by the sponsor for other documentation, such as study reports or registration summaries. In this way, data programmers don't have to establish a specific format for IBs, and often it will probably be possible to use tabulations in the IB that were originally generated for other documentation.

Regarding whether IBs could be made less "boring", as most of us know from personal experience, boring literature tends not to be read in any detail, if at all, and so a boring IB is unlikely to be regarded by an investigator as an essential resource from which relevant information can be gleaned about the product being tested. The issue of what exactly constitutes a boring document (IB or otherwise) is undoubtedly subjective, but in general terms I would consider a document as inherently boring when its style of presentation, for whatever reason, tends to deter the intended audience from reading it.

***Medical writers can and should aim to influence the ease with which investigators can access the material presented.***

The style of presentation in any document has two basic components: the organisation of the material to be included and the formatting of the content (the colour, figures, pictures, etc. referred to in the question). As medical writers, we generally have little influence on the scope of the material to be included in an IB, and no influence on whether an investigator is predisposed to consult an IB, but what we certainly can and should aim to influence is the ease with which investigators can access the material presented should they turn to the IB for information.

So the question is: what is an appropriate style of presentation to achieve this aim? Personally I see no need for flashy colours, input from graphic artists, luxury quality

papers, etc. We have to remember that a common problem confronted by medical writers when preparing an IB is a shortage of time and information. The realities of deadlines being brought forward, reports often existing only as drafts, if at all, (particularly the case with preclinical studies in early-stage IBs), "final" tables of data needing further cycles of revision, etc, mean that preparing an IB often becomes the classic dilemma of doing the best job with the information available, in the time available. Under these conditions, the scope for artistic input to an IB is obviously limited, especially for early editions in view of the high attrition rate of compounds in Phase I of clinical development. The time involved for any such artistic input would not be justified under the generally tight timelines involved when preparing an IB, where the emphasis clearly has to be placed on ensuring the accuracy and completeness of the material presented (i.e. the quality of the content). Perhaps we also shouldn't underestimate the potential for glossy literature produced by the pharmaceutical industry to arouse suspicion.

Apart from the general lack of time for artistic input, while it might be tempting to think that the use of colours and pictures might make an IB inherently more interesting, in fact a user-friendly layout, the intelligent use of in-text tables and graphs, and a clear and concise text are undoubtedly the medical writer's most potent weapons for reducing boredom in any documentation. The basic principle behind a well-prepared IB that captures the reader's attention is much the same as in all medical writing, which is to highlight the important features of the development programme to date in a competent fashion, with the medical writer providing the competence. In essence, given the often extensive amount of research that has to be reported, the readability of the IB really needs to be ensured by having the main body of the text provide a series of take-home messages for the investigator. Further details are then provided in a hierarchical manner, with the text supported by in-text tables and graphs, which in turn are supported by the tables of all studies, which themselves are supported by the original reports archived by the sponsor. Realistically, the items most likely to be read, at least in the first instance, are the high-level summaries (one to two pages for each major section) and perhaps selected in-text tables and graphs, so special attention has to be paid to ensuring that these summaries really do convey the required messages.

***My take-home messages in response to the original questions are therefore:***

- ***There are no official guidelines on AE tabulations for IBs. Use the format your company uses for other documentation.***
- ***Elaborate artwork is generally not justified or necessary to make IBs less "boring".***
- ***The use of clear and concise text together with intelligently planned in-text tables and figures ensures that an IB is not only a document that fulfills a legal obligation, but also a useful resource for investigators who need to be informed about the product they are testing.***

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