

Is it possible to make a global submission?

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ABSTRACT

CDISC standards and guidance documents from authorities are created to help the sponsors preparing their submissions. Sometimes sponsors experience that the standards and guidance are not aligned. What do you do as a sponsor in these cases?

INTRODUCTION

Is it possible to make a global submission? That is an interesting question. Before we started to standardise our clinical development towards using CDISC, we often prepared our trials for global submissions. So the same submission package would be used for both FDA and PMDA. Today with CDISC standardisation you would think that to make a global submission would be even easier, but is that the case? Let's take a look at the different tasks within the submission and see what challenges we have today.

PREPARE FOR THE SUBMISSION

When preparing for a submission you need to look into which trials, you will include and which to submit in CDISC format. FDA and PMDA have stated different ways of deciding which trials to submit in CDISC format.

The two agencies also have different documents to fill in at different time points before the submission.

PLANNING YOUR TRIAL



When you start planning your trial, you need to have the future submission in mind. Already at that point you will need to look into which versions of standards to use for SDTM, ADaM and CTs using the Data Standards Catalog from each of the two agencies.

CHOOSING SDTM AND ADAM VERSIONS

Since we know, that a clinical development can take many years, we will like to use the latest version supported by both agencies. The CDISC organisation can have even newer standards released, but if it is not in the Data Standards Catalog, it is not supported.

CAN WE USE THE SAME DATA MODEL?

Both agencies accept submission data in CDISC format. They both accept the CDISC SDTM data model and the implementation guidelines.

TECHNICAL CONFORMANCE GUIDES AND FAQs



To help the sponsors with their implementation, both agencies have created Technical Conformance Guides. PMDA has also made a FAQ document with implementation guidance. The technical conformance guides and FAQs are not binding, but the agencies expect the sponsors to comply with them. And what do we do as sponsors, if these guides contradict each other, or when the technical conformance guides and SDTMIG are not aligned?

An example of contradicting guidelines.

Description of ARM for screening failure subjects SDTMIG 3.2:

- Data for screen failure subjects, if submitted, should be included in the Demographics dataset, with ARMCD = "SCRNFAIL" and ARM = "Screen Failure". Sponsors may include a record in the Disposition dataset indicating when the screen failure event occurred. DM/SE Example 6 shows an example of data submitted for a screen failure subject.

PhUSE EU Connect 2018

FDA Technical Conformance Guide v. 4.1:

DM Domain (Demographics)

In the DM domain, each subject should have only one single record per study.

Screen failures, when provided, should be included as a record in DM with the ARM field left blank. For subjects who are randomized in treatment group but not treated, the planned arm variables (ARM and ARMCD) should be populated, but actual treatment arm variables (ACTARM and ACTARMCD) should be left blank.²⁴

CONFORMANCE CHECKS – FINDING YOUR WAY

When you start validating the conformance of your datasets and define.xml, you will experience some differences between the agencies.



The submission deliverables also have some differences between the two agencies with respect to the naming of documents.

We as sponsors need to find our way through the different requirements and to find an order of priority, when the requirements are contradicting.

CONCLUSION

Back to the question. Can a global submission still be made? The answer must be 'No', since the differences in the regulatory requirements will require two different implementations and two packages to be made.

So if we as sponsors could be granted a wish, it will be for more alignment and standardisation. We should try to get rid of the agency specific technical conformance guides and FAQs and have the guidance implemented in the CDISC IGs instead.

CONTACT INFORMATION

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