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Participant Flow Module

Rebecca J. Williams, Pharm.D., M.P.H., Assistant Director, ClinicalTrials.gov
National Library of Medicine

This presentation will be covering the first of the scientific modules within the results database and that is the participant flow module.

I will cover sort of an overview of what the participant flow module is as well as the required data elements. I will review criteria at ClinicalTrials.gov for assessing the appropriateness of the information to be posted as well as examples of common errors that we have seen in the entry of participant flow information.

The participant flow module is designed to provide information about the study design by documenting the flow of the participants through various stages of the study. The module should account for all of the enrolled participants and should really inform the interpretation of study outcomes by illustrating which participants were analyzed and which participants did not complete the study.

The design of the participant flow module is really driven by the requirements of FDAAA. What FDAAA required was a table of information and that table is supposed to include the number of patients who dropped out of the clinical trial as well as the number of patients who were excluded from the analysis if there were any.

The participant flow module in ClinicalTrials.gov is, therefore, a tabular presentation of the progress of the participants through each stage or period of that trial. Because a lot of the information regarding the arms and interventions is already provided in the protocol section of the module, of the record, that information is copied over to the result section, but it may be modified once initially created.

A table may consist of a single period or multiple periods that can represent different stages of the trial if there were different stages. If the study started with a double blind period and then progressed into an open label period, each of those periods could be demarcated with two different periods within the participant flow module. There are also options to include additional milestones, which would essentially be any additional information that was important within a period. At a minimum, each period must contain two milestones and that is the number of participants who started and the number of participants who completed each period.

You may be familiar with the Figure 1 format from a journal article, which is essentially a graphic presentation of how participants flowed through the study. The participant flow module within ClinicalTrials.gov is essentially a tabular adaptation of this flow diagram.

What I am showing here is actually the public view of the information on the ClinicalTrials.gov Web site where you include key information about recruitment, anything that happened before participants were assigned to a study group. You can provide detailed information about the groups in the study as well as the basics of the number of participants who started and the number completed.

In order to enter that data into ClinicalTrials.gov, it is important to understand what the data elements are, the specific requirements that complete a table and those are listed on this slide. There are both optional data elements and required data elements. On this slide, when you see a red asterisk, those are the data elements that are required to complete a table within the participant flow module. At a minimum, you have to have an arm and group title and description. That forms the columns of the participant flow module. If you have more than one period, it is necessary to provide a descriptive title for that period, but if you only have one period just defaulting to "overall study" is appropriate. Then, for each of the periods within the participant flow module, it is important to describe the number who started. It is the data. It is the actual number of participants who started the study per group, so looking at the arms and groups that you have identifying which participants started that particular group and the number that completed. It is also possible to provide additional informative information about things that happened to the participants through the course of the study and that can be included in the reasons for non-completion. If a certain number of participants did not complete the study, it is possible to provide additional explanations about those reasons for noncompletion.

This is just another view of the required data elements within ClinicalTrials.gov as well as the optional data elements. It is just a little easier to visualize on this slide how the data elements transform into a table within the ClinicalTrials.gov system.

I talked about both having optional and required data elements. It is important to also focus on not only what is required but what is considered a best practice in terms of completing the information within ClinicalTrials.gov. Essentially, if there is more than one period within a study it is important to actually use that feature within ClinicalTrials.gov to be able to explain any changes or different phases of the study as participants progressed. It is also important to use milestones to convey key events. A common example that is used is the number of participants who are randomized then having additional milestone that would explain the number of those randomized participants who actually received the intervention and that often informs that outcome measures module in being able to explain who it was that was analyzed for your outcome measures. It is also important to provide additional context about the reasons for noncompletion, the number of participants may drop out of a study, but it is useful to have additional information for understanding what those reasons were for noncompletion. The participant flow module makes it easy to provide all of this information.

Here I am just going to walk you through a few screen shots of how the information actually gets entered into ClinicalTrials.gov. It is a combination of free text fields as you see here for these optional data elements.

Here I am just highlighting that you can actually modify any arm or group that was copied over from the protocol section. These three arms were copied from the protocol and it is possible to click and change any descriptions as necessary.

This is just a shot of how the information is entered for the arm and group description.

This slide is just illustrating how the actual data then are entered after you have constructed essentially your arms and columns. The data make up the rows of the table.

When the information is submitted to ClinicalTrials.gov, there is both automated business rules that go into effect but then after that once it is released to ClinicalTrials.gov, we have staff assigned to actually reviewing the information before it is posted on the public site.

I am going to walk through what our general review criteria are for the participant flow module. This first slide really applies to all of the modules. A key point is that we ask that abbreviations be expanded the first time used because not all readers of the medical literature may be familiar with the abbreviations used within this particular study being reported. Check the record for any spelling errors. The arms and groups which form the columns of the table should be informative—meaning that the title itself should be informative, a brief description of what it was that was done to those participants in that group, and then ensuring that the arm/group description is also descriptive. There is additional information about the interventions administered as well as any additional information about the groups if there was not actual intervention provided. The information should be consistent with other sections of the record. This is really a key point that the information with any of the modules in the ClinicalTrials.gov database should be consistent with other sections of the record. If there are any discrepancies, those need to be explained in the available fields. Finally, Congress required that the basic results database essentially be just that. It is tables of information. It is basic information about the results. There shouldn't be any written results or conclusions. All of the results information should be available in the tabular format.

For the participant flow module, there are some very specific review criteria. Most importantly, the overall structure of the table itself should make sense. We should be able to follow the flow of the participants through the study and the numbers within the participant flow module in terms of the number of participants should make sense. We should be able to understand the general study design by looking at the participant flow module. That information should also be consistent with the protocol section. The protocol section describes key information about the study, whether it is parallel design or crossover. You already included in the protocol section the number of arms and information about the interventions, so that information in the participant flow module should be consistent with the protocol. Another key data element from the protocol is enrollment. At the time the study is completed, the actual enrollment for the study should be provided and in general, that number should be the same as the number started in the participant flow module. In addition, looking at the preassignment and recruitment details, those optional data elements, that content should be meaningful and that content should be relevant to that actual data element.

I have included here an example study and in looking at and applying the review criteria that we just went through, you can look at the recruitment details. The information is consistent with the data element. The reporting groups have meaningful titles for the arm titles as well as some informative descriptions about what actually happened to the participants who are within that particular arm.

Looking at the consistency of the information with the protocol section, I have just cut out a couple key elements from the protocol section, primarily the study design—this was a parallel assignment study—as well as the actual enrollment and some of the study's start date information. The enrollment in the protocol section is indicated as 146 participants, but if you add up the number who started in the participant flow module, that total is 143. That would trigger a flag by our review team to question what the reason is for the discrepancy or if perhaps one of the numbers in either of the sections is an error. The sponsor would actually have to make a determination about if it is an error or whether further explanation is required.

Another key review criterion that was evaluated here was that you can actually see the review comments from our ClinicalTrials.gov review team. They noted the enrollment number. The sponsor had also chosen to provide some additional comments about the number who started the participant flow module. Based on the information that they provided there, the reviewer had actually asked for some additional explanation about the footnote. If you look at footnote number 3, it is describing that 48 subjects were randomized, but 49 subjects were treated. It is not really clear how if only 48 were randomized how 49 were treated. Some additional explanation or clarification is necessary to make those numbers make sense.

Some additional review criteria for the participant flow module relate to milestones. Milestones are the number started, the number completed and any other important time period between starting and completion. In general, the number starting the study should always be greater than the number who completed the study. If there is more than one milestone, then the number for any subsequent milestone should generally not be greater than the number for the previous milestone.

We can look at an example to illustrate this a little bit better. This was another parallel design study. They provided the number who started. They provided an intermediate milestone indicating the number of participants who were treated and then finally, the number of participants who were completed. Looking at this example, you can see that the numbers flow logically on the vertical. One hundred and sixty started, a fewer number were treated, and a fewer number were completed, so that makes sense and that would be consistent with the review criteria I previously mentioned.

Some additional review criteria relate to the titles of a period. If there is more than one period, an informative title should be used. Finally, if there is more than one period, the number started a second period should generally be the same as the number who completed the previous period. If not, there should be an explanation.

We can look at an example of that here where we have a two period study. They are describing the periods as being different points in time. Apparently, that was important for this particular study. You can see that the number completed is the same for the placebo group. There were 291 completed and 291 started period two. When you look at the number who completed the first period for drug X, it is greater than the number who started the period for period two. We don't necessarily know why just looking at the record.

We would ask for additional explanation to be there or ask for an evaluation of whether or not that information is indeed correct. In this example, the sponsor chose to instead provide a comment explaining that five of the participants who completed that first period were not able to continue to the second period and provided some additional explanation of why.

Finally, all the examples that we have been looking at are a simple parallel design example, but crossover studies are also a common study design used in clinical trials and it is a little bit different when reporting in a tabular format the flow of participants in a crossover design. In this design essentially all the participants receive all of the interventions at some point in time during this study. Really the key here is to be able to explain which participants received which intervention at which point in time.

Ideally, you want to follow a single group of participants through the entire study. Here we have two different groups and it describes what is going to happen to each of these groups through this study. I will just use the first column as an example, where this group was going to first receive placebo and then after some period of time was going to then receive drug A. Those participants are all followed through the same column. You can see here 65 received the first intervention, which was placebo, and they all completed the study.

There is a wash out period of 2 weeks. During that washout period, we actually lost two participants during that period of time. In the second intervention phase of the study, you can see that 63 participants then received drug A in that first column. You can follow then who started and completed that final period. It is easy to follow that single group of participants through the different interventions that they received over time in that same singular column.

In this presentation, I covered parallel design studies and crossover design studies; however, there are many other study designs that you will likely need to enter into the results database. We have additional information about 2 by 2 diagnostic study design examples or factorial design on our Web site. If you need specific assistance with a particular study, please email register@clinicaltrials.gov and we'd be more than happy to provide some additional help in entering any more complicated study designs.