



Data and Safety Monitoring

Presenter: Trish Lindstrom

What is the purpose of monitoring a clinical trial?

Data and safety monitoring is one of the most complex and important aspects in the process of protecting human research subjects. A good plan will:

- Protect the safety of subjects
- Monitor the validity and integrity of the data
- Detect and promptly report Unanticipated Problems (UPs) and Adverse Events (AEs).

How is the level of monitoring determined?

It varies.....

- Regardless of study design, monitoring should be done on a regular basis.
- Consideration should be given to the spectrum of AEs that might occur
- The study should be evaluated for the expected level of severity of the AEs that may be caused by the intervention

Who is doing the monitoring?

You have some choices:

- *It may be you – Investigator monitor*
- *It may be someone outside of the research with the appropriate expertise– an Independent Monitor*
- *It may be a group of multidisciplinary folks composed of 3-6 experts that know the disease, the drug/device, procedures, outcomes and how trials work - Data Safety Monitoring Board (DSMB) or Data Monitoring Committee (DMC)*
- *It could be an entity that you work with here that already has needed expertise for the trial you are doing – Knight Cancer Institute*

So where does the IRB come in?

About now.....

- Depending on the risks of the research and the fact that it could involve risks that haven't been seen, the IRB is charged with making sure that the research includes adequate provisions for monitoring the data collected to ensure the safety of subjects.

So what does the IRB look for?

- The plan should be tailored to the expected risks, type of subjects, and the nature, size, and complexity of the research

Anything else?

Of course, it's the IRB:

- *The provisions must be sufficiently detailed for the IRB to determine whether they are appropriate for the research and*
- *The provisions / plan must be continuous in nature*

Nobody is off the hook.....

All research requires some level of monitoring and PIs are ultimately responsible for monitoring their studies. However, the IRB must approve the plan for monitoring data and safety for all research except minimal risk research where OHSU is the only site.

When do I include a Monitoring Plan?

- When the research is greater than minimal risk
- When it's a multi-site study and OHSU is the coordinating center
- When it's a study where there is an NIH requirement for one

The application must include provisions which include the designation of a monitoring entity.

- Trish – show them the decision tree!

So, I'm putting the plan together or I've been given one to be used, what are required provisions of a Data and Safety Monitoring Plan (DSMP)?

- The data and events that will be reviewed
- The monitoring entity(s) that will monitor the data collected, including UPs and AEs
- The role(s) of the entities
- The time frames for reporting AEs and UPs to the monitoring entity
- Schedule of reviews by each monitoring entity
- Specific triggers or stopping rules that will require action
- Procedures for communicating to the IRB, sponsor, investigators, and other appropriate officials, the outcome of the reviews. Check out the IRB website for reporting timelines...need to include these timelines in the plan
- The provisions should be tailored to the expected risks of the research; the type of subject population being studied, the nature, size (in terms of enrollment here and at all sites), and the complexity of the protocol

Haven't I Seen That List Before?

Yes, you have!

(Show them the template, Trish.....)

This IS a deal breaker folks.....

How do I determine the Monitoring Entity?

*You'll pick an **Investigator Monitor** if:*

- There is a small number of subjects
- The study is only conducted at one site
- The study involves low risk to subjects

Other choices?

An Independent Monitor may be appropriate if:

- You are conducting a trial that the interventions pose only moderate risks
- You are looking at short term treatments (days/months)
- Small # of subjects, the study is quick, and risks may be done through simple comparison

One more.....

Data Safety Monitoring Board (DSMB)/ Data Monitoring Committee(DMC) is a good choice if:*

- The trial is a large number of subjects where risks may be better assessed through comparisons of treatment groups
- If the trial has blinded study treatments
- If there are multiple sites – that means lots of AE reports submitted to a central group that has to review, report in a timely manner to the sites and IRBs
- High risk interventions where death or severe disability is a major risk
- If it's a controlled trial with mortality and morbidity as primary or secondary endpoints

**The NIH requires a DSMB for all multi-site trials or those involving high risk interventions. This includes in most cases phase III trials.*

Now it's time to submit the plan....

What do I do next?

- The plan needs to be submitted with your study*
- If the protocol contains all of the requirements, indicate where we can find it within the IRQ (Trish, show them what we DON'T want).*
- If you're using Knight Cancer's DSMP, download a copy from their website and upload with your study documents – questions about that? contact Mindy Roberts at 4-4684*
- If your protocol does NOT contain all of the requirements for monitoring provisions and there is not a DSMP in place, complete the template.*

Analyst Review:

The deal breakers:

- There is no plan and you meet the criteria for one – the study is coming back to you
- The info isn't where you say it is – the study is coming back to you
- The actual document is referenced in the protocol and you haven't submitted it – the study is coming back you
- You haven't provided the '8 provisions' or it isn't clear IF all are provided – the study is coming back to you to complete the template or provide further documentation

IRB Review:

The IRB will review the plan to ensure:

- It adequately aids in the protection of human subjects by detecting adverse events and unanticipated problems
- The design of the monitoring provisions and the monitoring entity is appropriate for your submission

The Great Wrap-Up

So, do I need one, a DSMP that is?

- Maybe not – some have too few subjects to support analysis done by a DSMB
- Maybe not- early phase non-randomized trials with limited safety concerns probably won't
- Maybe not – studies with rapid recruitment and short-term endpoints may not be long enough
- **BUT if your study poses more than minimal risk, yes, you should have a plan in place**

Ultimately all studies need some level of monitoring

If you have submitted a study and it's been approved as human subjects research, then it's our job to protect the humans. All protocols should have a certain level of a data and safety monitoring plan in place – even in minimal risk studies. The expectation is that whomever your subject population is, your protocol will outline your plan to protect them and protect their information.



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