Monday Morning Practice Pearls #23

What should the Research Coordinator do if there is an ineligible subject who was enrolled on a clinical research study?

Enrollment of subjects who are ineligible is a rare event in clinical research, yet it does happen. Regardless of the reason why this has occurred, this is still a compliance issue as the team did not follow the currently approved investigational plan (i.e., the protocol), GCP guidance, federal regulations, and if applicable, the Statement of the Investigator (e.g., FDA Form 1572).

The NIH Human Research Protection Program's (HRPP) Policy 801 identifies this as a major deviation reportable to the IRB via the Reportable New Information (RNI) form in PROTECT within 7 days of the team becoming aware. For IND/IDE sponsored studies, you also need to let your sponsor know.

Remember that when you notify the IRB, you will need to include the Corrective Action Plan (CAP). Consider the following:

- Develop or review/revise current team QA practices as relates to eligibility review.
- If specific eligibility criteria are negatively impacting recruitment and enrollment of participants, b*ut do not impact safety*, the research team should evaluate the possibility of amending the protocol to allow for more flexible eligibility criteria.
- For subject safety you may still need to:
    - Complete any clinical and laboratory assessments required by the protocol.
    - Collect any remaining study drug.
    - Discuss treatment alternatives with the subject.
    - Follow the subject as required by the protocol.
- Data analysis and data used in publications may need to be annotated to reflect the ineligibility. Follow specific IRB guidance as appropriate (e.g., IRB may tell you that you can't use the data as part of analysis or publication).

Should the subject be taken off study?

The IRB or sponsor will let you know if the subject should be taken off study. If they don't; ask. Often for oncology trials, they will let the subject continue if they are doing "well" (few toxicities) and/or possibly benefiting from the study intervention. If the subject is allowed to stay "on study", then all protocol specific interventions and activities must be followed.

What if the subject becomes eligible?

Once enrolled, there is not the concept of the subject "becoming eligible" – the subject is either eligible or not at the time of enrollment.

Can the subject be re-enrolled?

No, each subject can only be enrolled once on a study unless the protocol states a patient may be re-enrolled.

In rare instances, the subject may initially be deemed eligible, but does not start on the study intervention. As part of your QA process, someone on the team realizes that they aren't eligible since not all the screening was completed (e.g., maybe you forgot to do a blood test). What should you do?

What typically happens is you delay the treatment, complete the screening/eligibility assessment, and if eligible, you then begin treatment. However, if the missing criteria, then makes the subject ineligible for the study, you will need to remove them from the study.

What if we could amend the study, specifically the eligibility criteria since safety won't be impacted and then the subject would be eligible?

Amend the protocol and consent and keep the study intervention "on hold" until the protocol amendment is approved. The subject is then re-consented with the amendment IRB approved consent and treatment can begin. **DO NOT** re-enroll the subject. However, if any other eligibility screening tests fall outside of the study parameters, those tests would need to be reassessed before deeming the subject eligible.

Does the ineligible subject count towards total sample size?

Yes. The total sample size may need to be amended. In a rare instance this scenario and what to do may be included in the protocol. Seek IRB guidance on what to do about replacing the subject if not already addressed in the protocol.