

How to critically (and quickly) read a protocol

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One of the challenges of being a CCG member is learning how to critically review a protocol from a community perspective. These suggestions will help you focus on the most critical areas of the protocols you will be reading and save you time.

The cover sheet of the protocol tells by which RAC (Research Agenda Committee) the protocol is developed within and supervised. Next is a listing of all the members of the protocol team, and should always include the CCG representative. Then there is a list of the sub studies of the main study.

The first section to review to get a basic understanding of the protocol is the "Schema".

There, the basic protocol is outlined, including any randomizations, the number of subjects, the treatment arms, criteria for treatment response and/or failure, and secondary steps, etc. Spend some time reviewing the schema so you have a good idea of the general design of the study, and the target subjects, i.e. treatment naïve, single PI failure, heavily pretreated, etc.

Next review the primary and secondary objects of the study. Primarily focus on the primary objectives and ask if this is a reasonable question to answer, is it important, is it very feasible, etc?

I think the most important areas to review are the inclusion and exclusion criteria. It is here where very critical decisions are made concerning who can get into the study and who cannot. Ask if the criteria unreasonably exclude certain people, i.e. those between 13 and 18 years old, people with only minor liver function abnormalities, etc. Unless there is a good justification for it, most AACTG studies are open to all people, 13 years of age or older. The more people who are excluded from a study, the less generally applicable will be the results of the study. For example, many studies used to exclude people with liver function test 3 times above normal, which excluded many people co-infected with Hepatitis C. Now, many protocols only exclude people with liver function tests five times above normal.

Look at the table of evaluations, which will tell you how often someone has to come in for exams and blood tests. Are too many blood tests being done, are not enough viral loads being done, etc.? Also, ask whether the person in the study will get the result of the blood test in "real time", i.e. will it be done immediately, or will the test be "batched", i.e., run at a much later time, often with the result never being provided to the person in the study.

Lastly, review the informed consent. Now that you have a good idea about what the study is all about, does the informed consent explain it in simple, clear language? Is there too much "medicalese" in the consent? Are all the major risks and benefits explained? Keep in mind that the informed consent is only a "template", in that each individual institution's Institutional Review Board has their own requirements for the content and format for informed consents. Also, quickly review the number of sub studies, and ask if it is feasible to try to do so many studies under one main study?