Unit 11

# Generic Outline of an HVTN Protocol

**A standard protocol contains the following sections. This sheet provides a summary of the information contained in each section.**

1. **Ethical Considerations** describes how the HVTN addresses ethical issues that have been identified in major ethics guidance documents and international guidelines.
2. **IRB/EC review consideration** is provided for IRB and Ethics Committees reviewers, alerting them to how the HVTN handles key required elements for ethical conduct of research.
3. **Overview** provides a quick summary of the study objectives, schema, the products used, the study population, and key players in the conduct of the study. It also includes a list of members of the protocol team.
4. **Background** provides a rationale for doing the trial, background information about the study products including data from previous studies using the same or related product(s), and a table of potential risks of the study products.
5. **Objectives and endpoints:** The objectives are the research questions that this study will try to answer. They are grouped into primary, secondary, and exploratory questions. The endpoints are the specific pieces of study data that will be used to answer the questions. Exploratory objectives are typically questions that this study is too small to fully answer, but the data collected will inform the researchers’ understanding of these questions and may inform future research.

For example, if the objective is to evaluate the safety and tolerability of the vaccine, the endpoints might include:

Assessment after each injection and for 12 months after the first injection:

Local reactogenicity signs and symptoms (side effects at the injection site)

Systemic reactogenicity signs and symptoms (side effects throughout the body, like headache and fever)

Laboratory measures of safety (lab tests that measure kidney function, liver function, etc.)

Adverse events (all of the events that are reported, including things that might not be caused by the vaccine)

1. **Statistical considerations** provides a full description of how the study data will be analyzed in order to answer the research questions. It also provides information on how the size of the trial was determined (number of participants), how the participants will be assigned to the different groups (randomization), how the blinding of the study groups will be handled, and how any missing data will be handled.
2. **Selection and withdrawal of participants** includes the full list of criteria that participants must meet in order to be eligible to join the study (inclusion criteria), as well as a full list of criteria that a participant cannot have if they wish to participate (exclusion criteria). The section also describes reasons why a participant might be removed from the study, and why vaccinations may be stopped for an individual participant.

**Key issues** for community members to consider when reviewing this section:

 Is anyone excluded unnecessarily?

 - Do the gender and age descriptions seem appropriate?

 - If any particular gender is excluded from the study, look for the reason.

 - Would transgender people be eligible?

 Do any of the inclusion or exclusion criteria create barriers to enrollment?

1. **Study product and administration** provides details as to how the products are labeled, how they should be stored, and how they should be prepared to give to the participants. This section is primarily for the pharmacists at each site.
2. **Clinical procedures** describes the process for obtaining informed consent and how understanding will be assessed. It also explains the methods for screening people to see if they are eligible to join the study. The section includes information about all clinic procedures, HIV counseling and testing, and assessing reactions after vaccination. More specific details about which clinic procedures happen at each study visit can be found in Appendix F.

 **Key issues** for community members to consider when reviewing this section:

  Will it be a problem for people to comply with the study requirements?

  Are there issues with the procedures that might be a barrier to enrollment?

  Is the frequency of study visits too demanding, making it hard for someone to participate? Or are visits too long, making it hard to fit study participation into a person’s schedule?

1. **Laboratory** describes the procedures that will be followed by the local laboratory at each site. In addition, it describes the tests (assays) that will done by the HVTN Lab Program to analyze the samples that are collected from study participants. The section also describes what will be done with additional samples that remain in storage at the end of the study.
2. **Safety monitoring and safety review** provides a detailed description of the various groups that provide oversight and monitoring of the study, and lists the members of these groups. It also describes how safety reviews occur and when, and the types of safety concerns that must be reported promptly. A table is included to show what kinds of safety events can cause the study to be paused or halted completely.
3. **Protocol conduct** summarizes that the HVTN will conduct the study as directed, following all of the regulations and policies that are in place, and using all of the correct procedures. It also notes that HVTN will document any social impacts that occur and help participants to resolve them as needed. Finally, it tells the IRB/ethics committee that if we need to reach participants quickly, such as to share important safety information, we will do so and inform the IRB/ethics committee afterward.
4. **Version history** lists any modifications to the protocol that may take place over time.
5. **Document references** (other than literature citations) is a list of all of the other documents that are mentioned throughout the protocol, and where they can be found.
6. **Acronyms and abbreviations** is an alphabetical list of all of the “shorthand” that is used throughout the protocol.
7. **Literature cited** lists the other research that is cited in the protocol, giving credit to the work of others that has informed the current study.

**Key issues** **for community members to consider when reviewing**

**participant-facing appendices:**

  Is the language understandable?

  Are all the details and technical terms clearly explained?

  For a local CAB, are there local considerations that should be addressed? For example, when describing randomization, would using different metaphors be more familiar to people instead of talking about rolling dice?

  For a local CAB, are there any additional materials needed when conducting an informed consent discussion? For example, a local CAB might wish to consider use of videos, flip charts, slides, or other visual aids.

**APPENDIX A:** **Sample Informed Consent Form** – This sample contains instructions for sites to follow. Sites are allowed to make changes to the format and language according to their local needs, but they cannot leave out any of this information. Sites may also add additional information as required by their institution. This is also sometimes broken into separate consent forms for Part A and Part B of the study (if applicable).

**APPENDIX B: Approved Birth Control Methods** – This can be used as a handout for participants, or sites may choose to incorporate the list into their consent form.

**APPENDIX C: Sample consent form for use of samples and information in other studies** – this section describes what the HVTN would like to do with any samples that remain in storage at the end of this study. It describes the other kinds of research that might be done, and the information that could be shared. Participants can agree or disagree, and their choice does not have any impact on them being in the main study. Some sites’s IRBs/Ethics Committees prefer to include this information in the main consent form (blue-highlighted section in Appendix A), while others prefer to cover it in a separate document, in which case the highlighted section in Appendix A is omitted.

**APPENDIX D: Table of procedures** – This is a simplified version of the table of procedures that can be given to participants, and it matches the table found in the Appendix for Procedures performed at the site. It is intended to show participants what kinds of procedures will happen at their study visits, and how often. Some sites choose to incorporate this into their consent form, or it can be used as a separate handout.

**APPENDIX E: Table of Laboratory Procedures** – This appendix lists all of the different lab tests that will be done, and how much blood is taken at each study visit for use in doing the test. Take note of the lines in the middle of the page labeled Visit Total and 56-day total in bold print. These show the amount of blood in milliliters collected at each visit, and within a 2-month period. The total amount of blood that is allowed to be collected within 2 months is 500 ml. This total is the same for research as it is for blood donation centers.

**APPENDIX F:** **Study Procedures performed at HVTN CRS** – This appendix provides a detailed list of all the study procedures that are done at the site during each study visit. It should match the simplified version provided in Appendix D. For example, Appendix D shows that interviews or questionnaires are done at every study visit; Appendix F shows which specific questionnaires are used at which visits.

**APPENDIX G: Adverse Events of Special Interest (AESI)** – This appendix contains a list of medical conditions that are tracked by DAIDS. If a study vaccine was associated with causing these illnesses, it might be considered a safety problem.

**Appendix H: HVTN Low Risk Guidelines for the US and Africa** – This appendix contains the criteria used by the HVTN to evaluate whether a person in the US or Africa is at low risk for HIV and is appropriate to be enrolled in a Phase I study.

**Appendix I: Protocol Signature Page** – The Investigator of Record signs this page to indicate their commitment to following the study in compliance with all the applicable laws and ethical principles.