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## 1.0 PURPOSE

The purpose of this policy is to provide guidance as to the requirements for the development of Informed Consent for Division of Acquired Immunodeficiency Syndrome (DAIDS) funded and/or sponsored human subjects clinical research.

This policy is intended to ensure consistent and acceptable standards for adherence to Title 45 Part 46 of the Code of Federal Regulations (45 CFR 46) in addition to all DAIDS/Department of Health and Human Services (DHHS) guidance or directives as well as other applicable local, federal, and international laws and regulations regarding the process and documentation of informed consent.

## 2.0 SCOPE

This policy applies to all human subjects clinical research requiring an informed consent and that is funded and/or sponsored by DAIDS.

## 3.0 BACKGROUND

All National Institute of Allergy and Infectious Diseases (NIAID) supported research involving human subjects must be consistent with and adhere to 45 CFR 46, any DAIDS/DHHS guidance or directives, as well as other applicable local, federal, and international laws and regulations regarding the content, process, and documentation for obtaining informed consent.

## 4.0 DEFINITIONS

**DAIDS funded** – DAIDS is providing financial support for the clinical trial.

**DAIDS sponsored** – DAIDS is responsible for the management (including submission of the Investigational New Drug Application (IND) to the FDA, and initiation of the study), and oversight for the clinical trial.

**Full Regulatory Review** – The final review of the protocol, including the sample informed consent(s), by the Regulatory Affairs Branch (RAB) prior to Medical Officer sign off and distribution to the sites.

**Informed Consent Form (ICF)** – A document that provides information to a prospective research subject regarding the purpose, procedure, and potential risks and benefits as outlined 45 CFR 46.

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**Institutional Review Board/Ethics Committee (IRB/EC)** – An independent committee of physicians, statisticians, researchers, community advocates, and others that ensures a clinical study is ethical, and the rights of clinical participants are protected.

**Scientific Review Committee (SRC)** – A reviewing body instituted by DAIDS to review the concepts and protocols developed by various programs within DAIDS.

For additional definitions see DAIDS Glossary.

## 5.0 RESPONSIBILITIES

It is the responsibility of the DAIDS Medical Officer/Program Officer (MO/PO) to provide a preliminary assessment of the accuracy and completeness of the informed consent document(s) prior to SRC review. For clinical studies not undergoing SRC review, the DAIDS MO/PO is responsible for providing oversight and review of IC documents submitted to DAIDS, and for ensuring that the IRB/IEC has reviewed and approved the ICF reflecting the most current version of the protocol.

It is the responsibility of the DAIDS Regulatory Affairs Branch (RAB) Human Subjects Protection (HSP) Team to provide oversight and review of the submitted IC document(s) at the time of SRC review and, if applicable, full regulatory review.

## 6.0 POLICY

6.1. ICFs must be written using lay terms in a language level understandable to all participants being consented. and must include all basic elements and additional elements as appropriate as described in 45 CFR 46 subsection 116 [see Appendix 1, Office for Human Research Protections (OHRP) Informed Consent Checklist], the DHHS Policy on HIV Testing and Counseling (see Appendix 2), as well as any DAIDS-specific guidance or requirements listed below.

6.1.1. Breast Feeding - Because there may be potential risk to the newborn, a statement about breast feeding must be included in the ICF for clinical trials that enroll women of child bearing potential. This statement must specify whether it is known or unknown if the study drug(s) pass through breast milk and whether this may produce adverse effects in the infant. If applicable, the ICF must also state whether it's known or unknown if taking study drugs will reduce the risk of passing HIV to the baby while breast feeding.

6.1.2. Reproductive Risks - There must be information regarding birth control in the ICF. DAIDS uses the following contraception information guidance for selecting the applicable use of contraception.

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- 6.1.2.1. **Category A - Controlled studies show no risk.** Adequate, well-controlled studies in pregnant women have failed to demonstrate a risk to the fetus in any trimester of pregnancy.
- 6.1.2.2. **Category B - No evidence of risk in humans.** Adequate, well-controlled studies in pregnant women have not shown increased risk of fetal abnormalities despite adverse findings in animals, or, in the absence of adequate human studies, animal studies show no fetal risk. The chance of fetal harm is remote, but remains a possibility.
- 6.1.2.3. **Category C - Risk cannot be ruled out.** Adequate, well-controlled human studies are lacking, and animal studies have shown a risk to the fetus or are lacking as well. There is a chance of fetal harm if the drug is administered during pregnancy; but the potential benefits may outweigh the potential risk.
- 6.1.2.4. **Category D - Positive evidence of risk.** Studies in humans, or investigational or post-marketing data, have demonstrated fetal risk. Nevertheless, potential benefits from the use of the drug may outweigh the potential risk. For example, the drug may be acceptable if needed in a life-threatening situation or serious disease for which safer drugs cannot be used or are ineffective.
- 6.1.2.5. **Category X - Contraindicated in pregnancy.** Studies in animals or humans, or investigational or post-marketing reports, have demonstrated positive evidence of fetal abnormalities or risk that clearly outweighs any possible benefit to the patient.

Source: FDA *Use-In-Pregnancy* Drug Categories [21CFR § 201.57 (f)(6)(i)(a)-(e)]

- 6.2. Study Product Risk List - DAIDS maintains a pharmaceutical manufacturer approved list of expected risks associated with some agents that are used in DAIDS sponsored clinical trials. DAIDS requires the available risk list be included in the ICF, and given to subjects before signing the ICF. These lists can be found at <http://rcc.tech-res-intl.com/drugrisklist.htm>
- 6.3. Study Related Test Results - The subject must be informed if and/or when the results of any required study testing will be made available to them.
- 6.4. Study of Biological Specimens - There must be a description in the ICF concerning the storage of biological specimens. It must reflect if and how these specimens may be used in future study-related and/or unspecified future research. Subjects should also be

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informed if the storage of biological specimens for future research is a requirement for study participation. If not, subjects are to be given the option to refuse to allow or to withdraw their consent regarding any storage of biological specimens. Furthermore, the ICF should clarify if these biological specimens will be shipped and/or stored outside of the country where they were collected.

- 6.5. Compensation for Study Related Injury - The ICF must state that the U.S. National Institutes of Health (NIH) does not have a mechanism to provide direct compensation for research related injury. (If a mechanism to compensate for study related injury is available, this must be explained in the ICF.)
- 6.6. All documents to be used in the informed consent process must be in a language and at reading level that is understandable for intended study population and must be IRB/EC approved. An IRB/EC-approved short form informed consent process is to be used for any potential subject who does not read in the language of the consent document or who is illiterate. This process must be consistent with applicable U.S. federal regulations as well as with local/national laws.
- 6.7. Waivers of informed consent and waivers of documentation of informed consent - Investigators must seek guidance from the local IRB/EC (and local/national regulatory authorities as appropriate) for approval to waive informed consent, or waive documentation of informed consent consistent with applicable U.S. federal regulations as well as with local/national laws
- 6.8. Vulnerable populations - The informed consent process for vulnerable populations and those populations addressed in Subparts B, C, and D of the regulations at 45 CFR 46 must be consistent with applicable U.S. federal regulations as well as with local/national laws.

## 7.0 REFERENCE

U.S. Code of Federal Regulations, Title 45, Part 46, Subparts B, C, and D  
<http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm>

U.S. Code of Federal Regulations, Title 21, Part 201  
<http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/cfrsearch.cfm>

International Conference on Harmonisation, Guidance for Industry, E6 Good Clinical Practice: Consolidated Guidelines  
<http://www.fda.gov/oc/gcp/guidance.html>

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Office for Human Research Protections Guidance

<http://www.hhs.gov/ohrp/policy/>

## 8.0 INQUIRIES

Questions and comments regarding this policy may be directed to the OPCRO Policy Group at: [NIAIDOPCROPOLICYGROUP@mail.nih.gov](mailto:NIAIDOPCROPOLICYGROUP@mail.nih.gov)

## 9.0 AVAILABILITY

This policy is available electronically at the following URL:

<http://www3.niaid.nih.gov/research/resources/DAIDSClinRsrch/Default.htm>

The signed original is maintained in the OPCRO policy office.

## 10.0 CHANGE SUMMARY

Version #	Date	Replaces	Date of Revision	Rationale for Revision/Retirement
2.0	20 DEC 06	V 1.0	20 DEC 06	DAIDS Final Review
1.0	14 JULY 06	N/A	N/A	N/A

## 11.0 APPENDICES

Appendix 1- OHRP Informed Consent Checklist

<http://www.hhs.gov/ohrp/humansubjects/assurance/consentckls.htm>

Appendix 2 - DHHS Policy on HIV Testing and Counseling

<http://www.hhs.gov/ohrp/humansubjects/guidance/hcdc88jun.htm>

## 12.0 APPROVAL

Signature	Program/Branch	Date
Authorized By: <u><i>Richard Hafner</i></u> Richard Hafner, MD Director	Office for Policy in Clinical Research Operations (OPCRO)	<u>December 20, 2006</u>