I. Policy

It is the policy of the Department of Health (DOH) Institutional Review Board (IRB) to uphold its Assurance as filed with the Department of Health and Human Services (DHHS) Office for Human Research Protections (OHRP).

II. Authority

A. Chapter 381.86, Institutional Review Board, *Florida Statutes*

B. Rule 64H-2.001, Institutional Review Board, *Florida Administrative Code*

III. Supportive Data

A. *The Belmont Report*

B. 45 CFR 46, 160 and 164

C. 21 CFR 50 and 56, 312, 812

D. Health Insurance Portability and Accountability Act of 1996 (HIPAA)

E. Terms of Assurance, Office of Human Research Protections, Department of Health and Human Services (http://www.hhs.gov/ohrp/humansubjects/assurance/filasurt.htm)

IV. Definitions

See DOHP 400-11.1, “Definitions”.

V. Procedures

A. Institutional Commitments

DOH’s Assurance will be maintained in the office of the Director of Public Health Research, and will be available via the DOH IRB website. DOH’s Assurance is based on the following commitments:

1. Safeguarding the rights and welfare of human participants in research through the creation of an Institutional Review Board (IRB) is a general policy established in Florida Public Law 381.86. The State Surgeon General serves as the Institutional Official responsible for DOH’s Assurance. It is the State Surgeon General’s responsibility to exercise appropriate administrative oversight to assure that the Department of Health’s policies and procedures designed for protecting the rights and welfare of human participants are effectively applied in compliance with its Assurance. The State Surgeon General is responsible for ensuring the independence of the IRB and others responsible for the oversight of research. The State Surgeon General delegates responsibility for

administration of the program to the Human Research Protection Administrator designated in the Department's Assurance. This individual is an official with sufficient standing, authority, and independence to ensure implementation and maintenance of the program.

2. DOH employees, contractors, and anyone acting as an agent of the DOH and which comprise its bureaus, divisions, offices, county health departments, and facilities, are subject to the Assurance and this policy when they are engaged in research under the jurisdiction of the DOH IRB (See DOHP 400-1.2, "Activities Subject to IRB Jurisdiction").

3. DOH agrees to uphold the ethical principles of the Belmont Report and apply DHHS regulations (45 CFR 46, including Subparts A, B, C, & D) for federally-funded research, or equivalent protections to all proposed research in which the Department of Health is engaged or which involves DOH clients. The ethical principles set forth in the Belmont Report are:

   a. Respect for Persons: Recognition of the personal dignity and autonomy of individuals and special protection of those persons with diminished autonomy;

   b. Beneficence: Obligation to protect persons from harm by maximizing anticipated benefits and minimizing possible risk of harm; and

   c. Justice: Fairness in the distribution of research benefits and burdens.

4. DOH agrees to apply additional regulations such as the U.S. Food and Drug Administration Human Subject Regulations (21 CFR 50, 56, 312 and 812), U. S. Environmental Protection Agency Regulations (40 CFR 26), or the Health Insurance Portability and Accountability Act of 1996 (HIPAA), when applicable, to research involving human participants under review.

5. DOH further agrees to apply additional state laws, such as Florida Public Law 381.86 (Institutional Review Board) and any other relevant state law relating to conduct of research with human subjects.

6. No research in which the Department is engaged may be approved by DOH Officials or others that has not been previously approved by the DOH IRB.

B. Structure of the Institutional Review Board

1. The IRB Committees are appointed by the State Surgeon General. As such, the IRB serves the DOH as a whole, rather than a particular office, division, bureau, or county health department, and any institution for which the DOH IRB is designated as the IRB of record in an Assurance filed with OHRP with a corresponding Memorandum of Understanding.

2. The Department of Health's Assurance presently designates two OHRP-registered IRB Committees. Designation of additional IRB Committees under the Assurance requires prior notification of and approval by OHRP.

C. Responsibilities of the IRB to Provide Oversight for its Assurance Agreement

1. Approval of the IRB is required prior to the initiation of research involving human participants.

2. Through the review process, the IRB has the authority to approve, require modifications to secure approval or disapprove research.

3. The IRB has authority to suspend or terminate approval of research not being conducted in accordance with the IRB's requirements or that has been associated with unexpected serious harm to participants.

4. The IRB has the authority to observe, or have a third party observe, the consent process and the conduct of research.

5. Research reviewed and approved by the IRB may be subject to review and disapproval by officials of the DOH, or any institution for which the DOH IRB is designated as the IRB of record in accordance with an Assurance or a signed MOU with the DOH IRB.

D. Process to ensure that research does not commence until the research has obtained all required approvals. Researchers complete a worksheet, "Research Site and Program Support" to ensure that:

1. Researchers have created an application for review by the DOH IRB prior to submission of grant applications; IRB review is not required prior to submission of grant applications. (See DOHP-57.1 "Grant Application Review and Approval Process".)

2. Approval of Bureau Chiefs, Division Directors, or Office Directors is obtained by researchers prior to IRB review of research involving central office programs.

3. A data use agreement is obtained by the researcher prior to IRB review of research involving DOH registries.

4. Approval of the Administrator or Director is obtained by researchers prior to IRB review of research involving County Health Departments by completing the "Research Site and Program Support" worksheet.

5. Approval of the Medical Director or CEO is obtained by researchers prior to IRB review of research involving A.G. Holley State Tuberculosis Hospital.

6. Researchers provide a copy of the contract or funding agreement prior to IRB review.

E. Process to respond to attempts to influence the IRB or others responsible for the oversight of research

1. To ensure decisions of the IRB are impartial, DOH does not tolerate attempts to sway, pressure, manipulate, or otherwise influence the decisions of the IRB.

2. Persons aware of attempts to influence the IRB, or who have questions or concerns, may report this to an IRB Chair, IRB Administrator, the Human Research Protection Administrator designated in the Department's Assurance, the Director of the Office of Public Health Research, Deputy Secretary, or State Surgeon General.

3. Reports of undue influence will be investigated by the Human Research Protection Administrator designated in the Department's Assurance, in coordination with the program attorney and senior leadership. If the allegation involves the Human Research Protection Administrator, then the Director, Office of Public Health Research will be responsible for the investigation.

VI. History Notes

The Office of Public Health Research, Ethics and Human Research Protections Program is responsible for this policy.

Reviewed 8/28/2013

VII. Signature Block with Effective Date

Ana M. Viamonte Ros, M.D., M.P.H.
State Surgeon General
Florida Department of Health

Date

I. Policy

It is the policy of the Department of Health (DOH) Institutional Review Board (IRB) to have jurisdiction over all human subjects research subject to its Assurance.

II. Authority

A. Chapter 381.86, Institutional Review Board, *Florida Statutes*

B. Rule 64H-2.001, Institutional Review Board, *Florida Administrative Code*

III. Supportive Data

A. *The Belmont Report*

B. 45 CFR 46, 160 and 164

C. 21 CFR 50 and 56, 312, 812

D. Terms of Assurance, Office of Human Research Protections (OHRP), Department of Health and Human Services (DHHS) http://www.hhs.gov/ohrp/humansubjects/assurance/filasurt.htm

E. Guidelines for Defining Public Health Research and Public Health Non-Research, Centers for Disease Control and Prevention, October 4, 1999. http://www.cdc.gov/od/ads/opspoll1.htm

IV. Definitions

See DOHP 400-11.1, “Definitions”

V. Procedures

A. Review and Approval of Human Subjects Research.

1. All human subjects research, and all other non-exempt research activities, which in part involve human subject research, must be reviewed and approved by the DOH IRB whenever DOH is engaged in research. DOH is engaged in non-exempt research when DOH employees or agents for the purposes of research obtain data about participants in the research through intervention or interaction with them; or identifiable private information about participants in the research. Examples of when DOH is engaged in research include but are not limited to the following:

    a. DOH programs, agents or employees receive support directly from federal agencies for non-exempt human subjects research (for example DOH receives research funding from CDC), even where

all activities involving human subjects are carried out by agents or employees of another institution.

b. DOH employees or agents intervene or interact for research purposes with any human subjects of the research by performing invasive or noninvasive procedures.

c. DOH employees or agents intervene for research purposes with any human subject of the research by manipulating the environment.

d. DOH employees or agents obtain for research purposes identifiable private information or identifiable biological specimens from any source. Obtaining includes, but is not limited to: observing and/or recording private behavior and using, studying, or analyzing for research purposes identifiable private information or identifiable specimens already in the possession of the employees or agents of the institution.

e. DOH employees or agents are determined to be engaged in research by the Institutional Official, or the Human Research Protection Administrator designated in the Department's Assurance, or the Director, Office of Public Health Research, or the IRB Administrator.

2. When conducting research, an agent of DOH refers to anyone who obtains data about living individuals for research purposes through intervention or interaction with them, or anyone who obtains individually identifiable private information for research purposes, or anyone performing institutionally designated research activities and acting on behalf of the institution or exercising institutional authority or responsibility for the conduct of research. Examples include, but are not limited to, DOH employees, medical fellows and residents and others serving at DOH facilities through cooperative agreements, students and interns, and persons conducting research on under a contract or memorandum of understanding with DOH programs (not including where the sole activity of DOH is grant-letting).

3. No intervention or interaction with human subjects in research, including advertising, recruitment, and/or screening, may begin until the IRB has reviewed and approved the research.

4. It is the responsibility of the Institutional Official, Human Research Protection Administrator designated in DOH's Assurance, Director, Office of Public Health Research, or IRB Administrator to determine what activities constitute "human subjects research."

5. Activities where the sole involvement of DOH is grant letting does not require review by the DOH IRB, unless DOH employees or agents are

otherwise engaged in research. Examples of grant letting programs at DOH that do not require review by the DOH IRB include the James and Ester King Biomedical Research Program, the Bankhead-Coley Program and other similar programs where DOH's involvement is limited to grant-letting or funding.

B. Scope of Authority

The DOH Assurance with the Federal government defines its jurisdiction over the review of research involving human participants. The DOH IRB must review all human participant research if one or more of the following apply:

1. The research is sponsored (funded) in whole or in part from federal research appropriations to DOH, even where all activities involving human subjects research are carried out by agents or employees of another institution ("pass-through funding");

2. The research is conducted by or under the direction of any employee or agent of DOH in connection with his or her official responsibilities;

3. The research is conducted using any property or facility of the DOH;

4. The research involves DOH clients, including recruiting participants at county health departments or other DOH clients;

5. The research involves the use of non-public information maintained by the DOH when released outside DOH, except as otherwise required by law.

6. The research is conducted in accordance with an Assurance filed with the Office of Human Research Protections (OHRP) in which the DOH IRB is designated as the IRB of record through an established Memorandum of Understanding.

C. Review of Research Involving Data Collected for Non-Research Purposes

1. If after data are collected for non-research purposes, an Investigator wants to access the data with the intent of conducting research, IRB review and approval may be required prior to accessing the data for research purposes.

2. If an Investigator begins a non-research project and later finds that the data gathered could contribute to generalizable knowledge, the Investigator should contact the Ethics and Human Research Protection Program for a determination.

3. Because there are no universally accepted or completely specified criteria for determining when data collected for non-research purposes is being used for research, projects are reviewed on a case-by-case basis.

D. Failure to Submit a Project for IRB Review

1. The implications of engaging in activities that qualify as research that is subject to IRB review without obtaining such review are significant. In addition to disciplinary action or other action that the Institutional Official may take, the results from such research may not be published or presented unless IRB approval had been obtained prior to collecting the data.

2. Investigators who request approval to continue human subjects research that was not previously reviewed or to use research data that was collected without IRB approval face the possibility that the IRB will administratively withdraw or request the Investigator to administratively withdraw the application. The IRB will make a case by case determination of whether the study may proceed.

3. The IRB may not approve applications where the Investigator has attempted to circumvent IRB policies and procedures regarding human subjects research by collecting data as non-research and then applying to use them as existing data. It is therefore in the Investigator's best interest to consider carefully the likelihood that he or she will want to use the data for research purposes in the future, and to err on the side of inclusion and seek IRB approval prior to commencing the work.

VI. History Notes

The Office of Public Health Research, Ethics and Human Research Protections Program is responsible for this policy.

Reviewed 08/28/2013

VII. Signature Block with Effective Date

Ana M. Viamonte Ros, M.D., M.P.H.
State Surgeon General,
Florida Department of Health

Date

I. Policy

It is the policy of the Department of Health (DOH) Institutional Review Board (IRB) to review funding agreements to ensure with human subjects protections requirements are included.

II. Authority

A. Chapter 381.86, *Florida Statutes*, Institutional Review Board

B. Rule 64H-2.001, Institutional Review Board, *Florida Administrative Code*

III. Supportive Data

A. Association for Accreditation of Human Research Protection Programs Standard I-8

IV. Definitions

See DOHP 400-11.1, “Definitions”

V. Procedures

A. Staff responsibilities

1. Staff review funding agreements as part of Administrative Pre-Review using the Human Subject Protection Requirements for Funding Agreements Worksheet. Inclusion of human subject protections in funding agreements generally only applies to clinical research.

2. Staff determine whether the Sponsor is responsible for monitoring research; it is not necessary to require the Sponsor to include human participant protections in the funding agreement if the Sponsor does not monitor research.

3. Staff evaluate the risk of injury in the research conducted under its auspices and make determinations whether medical care for research-related injury might be needed.

4. Staff notify researchers when contracts and funding agreements do not contain required information. The notification and Human Subject Protection Requirements for Funding Agreements Worksheet are recorded in IRBWise as supplemental documents viewable by researchers.

5. Staff may send for review a research study when required human participant protection information is not included in the contract or funding

agreement. However, the study will not be approved until a draft contract exists that includes required human participant protections. For such research, the staff will verify, in addition, that the researcher has provided an attestation from the entity responsible for negotiating contracts that the required information will be included in the final contract.

6. When the contract is finalized, staff verify that the human subject protection language is present, and make an administrative comment documenting that. It is not necessary to have the IRB reviewer verify contracts.

B. Researcher responsibilities

1. Researchers are responsible for including human subject protection requirements in funding agreements. Funding agreements must specify human participant protections before research starts:

   a. who will provide medical care to participants in clinical research and who will be responsible to pay for it. DOH does not require any particular entity to be responsible for providing care, only that the funding agreement and informed consent process make it clear to participants who will provide medical care and who will be responsible to pay for it.

   b. that the Sponsor will promptly report to the researcher any findings that could affect the safety of participants or influence the conduct of the study, when Sponsors are responsible for monitoring the progress of the study. Researchers are responsible for promptly submitting copies of monitoring reports that contain findings that could affect the safety of participants or influence the conduct of the study to the IRB using the Problems Requiring Prompt Reporting to the IRB Form.

   c. that contracts or other funding agreements specify that data and safety monitoring plans are provided prior to IRB prior to approval of the research, and that contracts or other funding agreements specify the time frame for providing routine and urgent data and safety monitoring reports to the IRB.

   d. that Sponsors should follow DOH policies regarding dissemination of research findings, for programs at DOH that have such policies

   e. that Sponsors notify the researcher when participant safety could be directly affected by study results after the study has ended (normally for a period of two years). Researchers will notify the IRB using the Problems Requiring Prompt Reporting to the IRB Form. The IRB will determine whether the researcher should inform participants.

f. When the contract is finalized, the researcher emails the final contract to Staff

2. Researchers should review expectations for human participant protections in contracts and funding agreements, and verify the information is included, using the "Human participant Protections for Funding Agreements" worksheet.

3. Researchers are responsible for ensuring human participant protections are included in contracts. Failure to include this information will result in delays in approval of research.

B. IRB responsibilities

1. The IRB, or reviewer using the expedited procedure, may not approve research unless:

a. a draft contract includes required human participant protection language

b. provisions for medical care for research-related injury defined in the contract are substantively similar to those disclosed in the informed consent document.

VI. History Notes

The Office of Public Health Research, Ethics and Human Research Protections Program is responsible for this policy.

Reviewed 08/23/2013

VII. Signature Block with Effective Date

Ana M. Viamonte Ros, M.D., M.P.H. Date
State Surgeon General,

I. Policy

It is the policy of the Department of Health (DOH) Institutional Review Board (IRB) to have sole authority to determine when activities covered by the human research protection program constitute research involving human participants. Investigators do not have the authority to make an independent determination. Determinations may only be made by the human research protection program.

II. Authority

A. Chapter 381.86, *Florida Statutes*, Institutional Review Board

B. Rule 64H-2.001, Institutional Review Board, *Florida Administrative Code*

III. Supportive Data

A. 45 CFR 46

B. 21 CFR 50 and 56

C. OHRP Guidance on Research Involving Coded Private Information or Biological Specimens, August 10, 2004

D. Public Health Practice vs. Research: A Report for Public Health Practitioners Including Cases and Guidance for Making Distinctions. Hodge and Gostin, et al. 2004. http://www.cste.org/pdffiles/newpdffiles/CSTEPHResRptHodgeFinal.5.24.04.pdf

E. Lynn J, Baily MA, Jennings B et al. The Ethics of Using QI Methods to Improve Health Care Quality and Safety. Annals of Internal Medicine 2007; 146, 666-673

IV. Definitions

See DOHP 400-11.1, “Definitions”

V. Procedures

A. Criteria used to make determinations of whether activity involves research

1. The applicable regulations under which research determinations are made are 45 CFR 46 (DHHS regulations) and 21 CFR 56 (FDA regulations)

2. Research is defined at 45 CFR 46.102(d); to make the regulatory definition more precise, where applicable, DOH further specifies the following:

a. “Investigation” means an inquiry, examination, or search for facts, usually involving the formulation or testing of a hypothesis

b. "Systematic" means conducted according to a plan, organized method, or procedure for testing or formulating a question or hypothesis and interpreting results

c. "Designed" means planned, purposed, or conducted to apply to phenomena outside the observed data, or to contribute to generalizeable knowledge.

d. "Generalizable knowledge" means observations, findings, information, or results that have been demonstrated with enough confidence and significance to confirm or alter the consensus within the professional norms of a community or discipline.

3. A "human subject" is defined at 45 CFR 46.102(f)

4. A "clinical investigation" is defined at 21 CFR 50.3(c) and 21 CFR 102(c)

5. An "experimental subject" is defined 21 CFR 50.3(e) and 21 CFR 102(e)

6. Criteria when DOH is engaged in research and the jurisdiction of the IRB are specified in DOHP 400-1.2, "Activities Subject to IRB Jurisdiction"

B. Common examples of activities requiring determination of research involving human participants

1. Public health practice

a. To make determinations, DOH relies upon criteria specified in "Public Health Practice vs. Research: A Report for Public Health Practitioners Including Cases and Guidance for Making Distinctions." Hodge and Gostin, et al. 2004. Available on the web at: http://www.cste.org/pdffiles/newpdffiles/CSTEPHResRptHodgeFinal.5.24.04.pdf

b. Criteria used to make determinations and examples are provided in the "Human Subject Research Determination" Worksheet

c. Public health investigations into acute or chronic infectious diseases, conditions, or environmental hazards, and activities explicitly required by statute, are generally not research involving human participants. However, a statute may require both public health reporting, and also authorize use of information for research (such as the Florida Cancer Registry).

2. Quality improvement and program evaluation activities

a. To make determinations, DOH relies upon criteria specified in Lynn J, Baily MA, Jennings B et al. The Ethics of Using QI Methods to Improve Health Care Quality and Safety. Annals of Internal Medicine 2007; 146, 666-673

b. Criteria used to make determinations and examples are provided in the Human Subject Determination Worksheet

c. Quality assurance activities conducted as an ongoing part of program operations using a standard framework such as Sterling, Plan-Do-Check-Act, Six-Sigma and similar framework are generally not research involving human participants.

C. Criteria used to make determinations of whether research involves human subjects

1. Activities do not involve human participants as defined by DHHS regulations if they do not involve the investigator gathering information about living individuals through intervention or interaction with individual participants and they do not involve the investigator gathering identifiable private information about living individuals.

2. Information is considered “not identifiable” if the identity of the participant is not or may not readily be ascertained by the investigator or associated with the information.

3. Activities do not involve humans as participants as defined by DHHS regulations if they involve specimens/data that are received by the Investigator as de-identified stripped of all HIPAA identifiers.

4. When the Investigator receives the private information or specimens with no code or link that would allow an Investigator to establish identity, this would not involve human subjects as defined by DHHS regulations. For example, a publicly available, unidentifiable, non-linked cell line qualifies as not involving human subjects.

5. The Investigator may receive coded private information or specimens and qualify for non-human subjects as defined by the DHHS regulations if the following conditions are met:

a. The code is not derived or related to the HIPAA identifiers that must be stripped from private health information (e.g. patient medical record number and the last 4 digits of individual’s Social Security Number);

b. The private information or specimens were not collected specifically for the currently proposed research project through an interaction or intervention with living individuals; and

c. The Investigator cannot readily ascertain the identity of the individuals to whom the coded private information or specimens pertain, because:

(1) The key to decipher the code is destroyed before the research begins;

(2) The Investigator and the holder of the key enter into an agreement prohibiting the release of the key to the Investigator under any circumstances, until the individuals are deceased;

(3) The private information is received from an IRB-approved repository or data management center that includes written operating procedures that prohibit the release of the key to the Investigator under any circumstances, until the individuals are deceased; or

(4) There are other legal requirements prohibiting the release of the key to the Investigator until the individuals are deceased.

D. Process for making determinations

1. The human research protection program has sole authority to determine whether an activity covered by the human research protection program represents “Human Subject Research.”

2. The person responsible for an activity may request a consultation about whether an activity is research involving human participants using the form on the HRPP web site, “Distinguishing Public Health Practice and Quality Improvement from Research.” Investigators do not have the authority to make an independent determination. Determinations may only be made by the human research protection program.

3. The applicant provides sufficient information for the HRPP to make a determination, either by requesting a consultation, or in IRBWise.

4. Determinations of whether activities covered by the human research protection program are research involving human participants are made by the Human Research Protection Administrator designated in the Department’s Assurance, or other HRPP Staff. If the Human Research Protection Administrator has direct involvement in the activity, then another person without direct involvement will make the determination. Normally, this is the Director, Office of Public Health Research, but an IRB Chair will make the determination when the Director, Office of Public Health Research also has direct involvement in the activity. Determinations are made using criteria in the “Human Subjects Research Determination Worksheet.”

5. Determinations are communicated to the applicant using IRBWise.

6. Determinations are normally made in less than one month.

E. Process for providing guidance about activities that sometimes are and sometimes are not research involving human participants

1. The program provides a consultation service, accessed through the "Distinguishing Public Health Practice and Quality Improvement from Research" form on the HRPP web site, to discuss specific projects.

2. The HRPP provides guidance through regular presentations tailored to specific public health programs

3. Guidance is available through the program web site

F. Amendments

Any change that might disqualify the activity from a "Non-Human Subject" or "Non-Research" status must be reported to the IRB for review and verification prior to implementation.

G. Additional Requirements

Activities that are not research involving human participants must meet the Florida Department of Health's ethical standards (e.g., acceptable risk-benefit relationship, equitable selection, informed consent where appropriate, protections of privacy interests of participants and the confidentiality of their data (under state law) where appropriate, transparency about the process, proportionality, and where applicable, community involvement in quality improvement and public health efforts.)

VI. History Notes

The Office of Public Health Research, Ethics and Human Research Protections Program is responsible for this policy.

Reviewed 08/23/2013

Replaces DOHP 400-4.6, "Human Subjects Research/Non Research Determination"

VII. Signature Block with Effective Date

Ana M. Viamonte Ros, M.D., M.P.H. Date
State Surgeon General

I. Policy

It is the policy of the Department of Health (DOH) Institutional Review Board (IRB) that all human subjects research activities under its jurisdiction be reviewed to determine whether the research meets one or more of the exemption categories described in the Federal regulations and complies with DOH's ethical standards.

II. Authority

A. Chapter 381.86, Institutional Review Board, *Florida Statutes*

B. Rule 64H-2.001, Institutional Review Board, *Florida Administrative Code*

III. Supportive Data

A. 45 CFR 46.101(b)(1-6)

B. 45 CFR §46.301(a)

C. OHRP Guidance at 45 CFR 46.101(b)(5): Exemption for Research and Demonstration Projects on Public Benefit and Service Programs, OHRP Guidance on the Involvement of Prisoners in Research, May 23, 2003, Federal Register, Vol. 48, pp. 9266-9270, March 4, 1983

D. 21 CFR §56.104(c)-(d)

E. DOHP 400-4.6, "Differentiating Research from Public Health Practice and Quality Improvement"

F. OHRP Compliance Activities: Common Findings and Guidance -7/10/2002 Item #30

G. OHRP Guidance: Coded Private Information - 8/10/2004

IV. Definitions

See DOHP 400-11.1, "Definitions"

V. Procedures

A. Exempt Eligibility

1. The IRB may not create new categories of exempt research. Only the DOH Human Research Protections Program may determine which activities qualify for an exempt review. Investigators do not have the authority to make an independent determination that research involving human subjects is exempt and must contact the HRPP concerning the status of proposed research or changes in ongoing research.

2. An Investigator may request a particular category of exemption, but the final determination of applicability will be made by DOH Staff . The IRB

Administrator or Assistant IRB Administrator has authorization to determine whether research meets regulatory criteria for exemption, and will consult the Human Research Protection Administrator designated in the Department's Assurance for an authoritative decision about whether research can be exempt from the regulations.

3 Researchers will complete an application in IRBWise.

4 Exemption determinations are communicated to researchers using IRBWise.

5. Research may be granted exempt status by Staff if all research activities involve procedures listed in one or more of the specific categories under 45 CFR 46.101(b). NOTE**:** Under federal regulations these categories do not apply to research involving prisoners. Under Florida DOH policies and procedures these categories do not apply to research involving deception. Also, categories 1-5 do not apply to FDA regulated research. Categories at 45 CFR 46.101(b) permitting exemptions are:

   a. 45 CFR 46.101(b)(1): Research conducted in established or commonly accepted educational settings, involving normal educational practices, such as:

      (1) Research on regular and special education instructional strategies; or

      (2) Research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.

      (3) The research does not involve prisoners as participants

      (4) The research is not FDA regulated

   b. 45 CFR 46.101(b)(2): Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior, unless:

      (1) Information obtained is recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects; and

      (2) Any disclosure of the human subjects' responses outside of the research could reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, or reputation.

      (3) If the research involves children as participants, the research must be limited to educational tests (cognitive,

diagnostic, aptitude, achievement), and observation of public behavior when the investigator(s) do not participate in the activities being observed. Research that uses survey procedures, interview procedures, or observation of public behavior when the investigator(s) participate in the activities being observed cannot be granted an exemption.

c. 45 CFR 46.101(b)(3): Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior that is not exempt under 45 CFR 46.101(b)(2) if:

(1) The human subjects are elected or appointed public officials or candidates for public office; or

(2) Federal statutes require without exception that the confidentiality of the personally identifiable information will be maintained throughout the research and thereafter.

d. 45 CFR 46.101(b)(4): Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or the information is recorded by the Investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects. To qualify for this exemption, normally data, documents, records, or specimens must have been collected before the research project begins. However, OHRP Guidance (08/10/05) specifies limited conditions whereby an Investigator may de-identify data prior to the initiation of research that would qualify for exempt review.

(1) Example: Investigator A wishes to screen blood samples at a rural hospital for incidence of HIV infection. She does not want to draw specimens specifically for this purpose; rather she proposes to use specimens that were drawn for some other purpose but which remain in the hospital laboratory. If Investigator A proposes to use specimens that had been drawn prior to the initiation of her research and are, for some reason, "on the shelf," the protocol may qualify as exempt, assuming the other requirements are met (i.e., the sources are either publicly available or the information is recorded by the Investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects).

(2) Under this exemption, an Investigator (with proper institutional authorization) may inspect private, identifiable records, but may only record information in a non-identifiable manner. The data must be permanently and completely de-linked at the time of extraction. A code may be used to organize data as it is collected. However, the

I. Policy

It is the policy of the Department of Health (DOH) Institutional Review Board (IRB) to assure that the privacy and confidentiality protections are adequate for all research participants, which may include requesting the Investigator to secure a Certificate of Confidentiality.

II. Authority

A. Chapter 381.86, Florida Statutes, Institutional Review Board

B. Florida Administrative Code Rule 64H-2.001 Institutional Review Board

III. Supportive Data

A. NIH Frequently Asked Questions on Certificates of Confidentiality, Web Posting: July 22, 2003

B. Public Health Service Act 301(d), 42 U.S.C.241(d)

C. OHRP Guidance Document, "Guidance on Certificates of Confidentiality," February 25, 2003

IV. Definitions

See DOHP 400-11.1, "Definitions"

V. Procedures

A. Circumstances When a Certificate of Confidentiality May be Indicated

Data collection about sensitive issues (such as illegal behavior, alcohol or drug use, or sexual practices or preferences) requires the protection of confidentiality beyond preventing accidental disclosures. Under Federal law, Investigators can obtain an advance grant of confidentiality, known as a Certificate of Confidentiality that will provide protection against compulsory disclosure, such as a subpoena, for research data. The Investigator should describe in the IRB application any conditions under which confidential information might be disclosed and create an informed consent document that accurately reflects those conditions, including any voluntary disclosure by the Investigator. The IRB is required to determine whether the risks to subjects are minimized, informed consent is appropriate, and privacy and confidentiality protections are adequate.

B. Eligibility for a Certificate of Confidentiality

Federal funding is not a prerequisite for requesting a Certificate of Confidentiality. Any research that collects personally identifiable, sensitive information and that has been approved by an IRB is eligible for a Certificate.

C. Protections Provided by a Certificate of Confidentiality

A Certificate of Confidentiality provides protection for the Investigator and the participants against compelled disclosure of identifying information about participants of biomedical, behavioral, clinical, and other research (Public Health Service Act '301(d), 42 U.S.C. '241(d)). Under this Act, the Secretary of Health and Human Services (HHS) may authorize persons engaged in research to protect the privacy of participants by withholding from all persons not connected with the conduct of the research the names or other identifying characteristics of the participant. This means that Investigators may not be compelled in any Federal, State or local civil, criminal, administrative, legislative, or other proceedings to identify their participants.

1. The protection is available only when the research is of a sensitive nature where the protection is judged necessary to achieve the research objectives.

2. Research can be considered sensitive if it involves the collection of information in the following categories:

    a. Research on HIV, AIDS, and other STDs;

    b. Information relating to sexual attitudes, preferences, or practices;

    c. Information relating to the use of alcohol, drugs or other addictive products;

    d. Information pertaining to illegal conduct;

    e. Information that if released could reasonably be damaging to an individual’s financial standing, employability, or reputation within the community;

    f. Information that might lead to social stigmatization or discrimination if it were disclosed;

    g. Information pertaining to an individual's psychological well being or mental health;

    h. Research on behavioral interventions and epidemiologic studies; and

    i. Genetic information.

3. Examples of studies that would not qualify for a certificate of confidentiality are:

    a. Projects that are not research based;

    b. Projects that are not approved by an IRB in accordance with the NIH guidelines governing Certificates of Confidentiality;

    c. Projects that do not collect sensitive information or information

that might harm the research participants; or

d. Projects that do not collect personally identifiable information.

D. Limitations of a Certificate of Confidentiality

The Certificate of Confidentiality does not govern the voluntary disclosure of identifying characteristics of research participants but only protects participants from compelled disclosure of identifying characteristics by the Investigator. Investigators, therefore, are not prevented from the voluntary disclosure of matters such as child abuse or a subject's threatened violence to self or others. However, if an Investigator intends to make such voluntary disclosures, the consent form should clearly indicate this.

E. Investigator's Responsibility for Assuring Confidentiality

Investigators are responsible for assuring confidentiality of research data. If the Investigator is conducting research involving sensitive information, the IRB may require the Investigator to obtain a Certificate of Confidentiality. The Investigator is responsible for submitting a request for the Certificate of Confidentiality from the National Institutes of Health (NIH). Additional information and submission instructions are located on the NIH website: http://grants.nih.gov/grants/policy/coc/contacts.htm.

VI. History Notes

The Office of Public Health Research, Ethics and Human Research Protections Program is responsible for this policy.

Reviewed 08/23/2013

Replaces DOHP-400-2.5-08

VII. Signature Block with Effective Date

Ana M. Viamonte Ros, M.D., M.P.H.. Date
State Surgeon General
Florida Department of Health

code may not be a means of re-linking the data set to the original data source.

(3) Example: Investigator B wishes to examine court records of involuntary commitments to psychological institutions. If he uses court records that were on file before the initiation of his research, the protocol may qualify as exempt.

e. 45 CFR 46.101(b)(5): Research and demonstration projects, which are conducted by or subject to the approval of Federal Department or Agency heads, and which are designed to study, evaluate, or otherwise examine:

(1) Public benefit or service programs; this exemption is for federally supported projects and is most appropriately invoked with authorization or concurrence by the funding agency. The following criteria must be satisfied to invoke the exemption for research and demonstration projects examining "public benefit or service programs:"

(a) The program under study must deliver a public benefit (e.g., financial or medical benefits as provided under the Social Security Act) or service (e.g., social, supportive, or nutrition services under the Older Americans Act);

(b) The research or demonstration project must be conducted pursuant to specific Federal statutory authority;

(c) There must be no statutory requirements that the project be reviewed by an IRB; or

(e) The project must not involve significant physical invasions or intrusions upon the privacy of participants.

(2) Procedures for obtaining benefits or services under those programs;

(3) Possible changes in or alternatives to those programs or procedures; or

(4) Possible changes in methods or levels of payment for benefits or services under those programs.

(5) This exemption is for projects conducted by or subject to approval of Federal agencies and requires authorization or concurrence by the funding agency.

f. 45 CFR 46.101(b)(6) and 21 CFR 56.104(d): Taste and food quality evaluation and consumer acceptance studies;

(1) If wholesome foods without additives are consumed; or

(2) If a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural chemical or environmental contaminant at or below the level found to be safe, by the Food and Drug Administration or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture.

B. Amendments

1. If there is a change in research such that it would change the exempt status, then regardless of the time period, the researcher must submit a new research determination.

C. Other Considerations Concerning Exempt Research

1. All research conducted under exempt review is subject to all applicable DOH institutional and IRB policies and procedures.

2. Exempt research activities are subject to the same subject protections and ethical standards as outlined in *The Belmont Report*.

VI. History Notes

The Office of Public Health Research, Ethics and Human Research Protections Program is responsible for this policy.

Reviewed 08/23/2013

Replaces DOHP 400-4.3-08, “Research Exempt from IRB Review”

VII. Signature Block with Effective Date

Ana M. Viamonte Ros, M.D., M.P.H.
State Surgeon General
Florida Department of Health

Date

I. Policy

It is the policy of the Department of Health (DOH) Institutional Review Board (IRB) that all Investigators meet the following requirements to conduct research involving human participants under the jurisdiction of the DOH IRB.

II. Authority

A. Chapter 381.86, Florida Statutes, Institutional Review Board

B. Florida Administrative Code Rule 64H-2.001 Institutional Review Board

III. Supportive Data

A. DOHP 400-1.1, “Institutional Oversight of Assurance”

B. DOHP 400-1.2, “Activities Subject to IRB Jurisdiction”

C. DOHP 400-2.3, “Investigator and Key Study Personnel Conflicts of Interest”

IV. Definitions

A. See DOHP 400-11.1, “Definitions”.

V. Procedures

A. As described in DOH IRB Policy 400-1.1 “Institutional Oversight of Assurance”, DOH’s Federalwide Assurance (FWA) with the Federal government specifies that all human subjects research that is conducted by or under the direction of any employee or agent of DOH or covered entity, in connection with his or her institutional responsibilities must be reviewed by the DOH IRB.

B. All DOH employees or agents of DOH engaged in research will have reviewed the ethical principles of *The Belmont Report*, Federal and State laws and regulations, institutional policies and procedures, DOH IRB policies and procedures, and if applicable, Good Clinical Practice standards when conducting human subjects research. Additionally, they will have completed the required training (initial and continuing education) for the ethical conduct of human subjects research (See DOHP-400-9.1, “Research Ethics Education and Training”).

C. Conflict of Interest. The protection of human research participants requires objectivity in communicating risks, selecting subjects, promoting informed consent, and gathering, analyzing and reporting data. Therefore, the IRB will consider conflict of interest issues in its deliberations of applications

D. All individuals conducting human subjects research must be adequately qualified

and, if necessary, licensed relevant to the scope and complexity of the research conducted.

VI. History Notes

The Office of Public Health Research, Ethics and Human Research Protections Program is responsible for this policy.

Reviewed 08/23/2013

Replaces DOHP-400-2.1-07

VII. Signature Block with Effective Date

Ana M. Viamonte Ros, M.D., M.P.H. Date
State Surgeon General,

I. Policy

It is the policy of the Department of Health (DOH) Institutional Review Board (IRB) that Investigators conduct human subjects research in accordance with Federal, State and institutional rules, regulations, and policies, and IRB policies and procedures.

II. Authority

A. Chapter 381.86, Institutional Review Board, *Florida Statutes*

B. Rule 64H-2.001, Institutional Review Board, *Florida Administrative Code*

III. Supportive Data

A. *The Belmont Report*

B. 45 CFR 46

IV. Definitions

See DOHP 400-11.1, “Definitions”

V. Procedures

A. Human Subjects Protection

1. The DOH IRB policies and procedures are designed to protect the rights and safety of human research participants based on the ethical principles of *The Belmont Report*.

2. It is the Investigator’s responsibility to disclose any interests specified in the IRBWise application and, if applicable, complete the researcher and research staff conflict of interest worksheet. See DOHP 400-2.3, "Identifying, Evaluating, and Managing Researcher and Research Staff Conflicts of Interests"

3. The Investigator assumes responsibility for compliance with all Federal, State, and local laws, institutional rules, regulations and policies, and DOH IRB policies and procedures related to research involving humans and, if applicable, to the Good Clinical Practice Guidelines as adopted by the Food and Drug Administration (FDA) available at http://www.fda.gov/oc/gcp/default.htm.

4. The Investigator is the ultimate protector of the participant’s rights and safety. Each Investigator is obligated to be personally certain that each participant is adequately informed and freely consents to participate in the research. The Investigator must personally assure that every reasonable precaution is taken to reduce risks to the participants.

5. The Investigator may not initiate any research involving humans without prior IRB review and approval. In addition, the Investigator may not amend or change an approved protocol without prior IRB review and approval, except where necessary to eliminate apparent immediate hazard to the participant.

6. The Investigator is responsible for designing research studies that are sound enough to demonstrate the research outcome, minimize risks, and ensure that risks are reasonable in relation to anticipated benefits, if any. The researcher shall demonstrate adequate resources to protect participants in the research. To this end researchers shall provide the IRB the following information to evaluate whether the researcher has minimized risks:

    a. The purposes of the research.

    b. The scientific or scholarly rationale.

    c. The procedures to be performed.

    d. A description of the procedures being performed already for diagnostic or treatment purposes.

    e. The risks and potential benefits of the research to participants, considering physical, psychological, social, economic, and legal risks.

    f. Description of the time for the researchers to conduct and complete the research.

    g. Description of the number and qualifications of staff

    h. Description of research facilities

    i. Whether the researcher has access to a population that will allow recruitment of the necessary number of participants.

    j. Description of the availability of medical or psychosocial resources that participants may need as a consequence of the research.

B. Investigator Training

1. It is the responsibility of each Investigator to complete research ethics training consistent with requirements in DOHP 400-9.1, “Research Ethics Education and Training”

2. It is the responsibility of each Investigator to assure that other Investigators and key study personnel who are responsible for the design

and conduct of the research are adequately trained in human research protections and assure completion of continuing education requirements.

C. Investigator and Key Study Personnel Conflicts of Interest

1. It is the Investigator's responsibility to disclose all actual or perceived conflicts of interest as defined by institutional policy to the DOH IRB for review to assure full disclosure to participants in human subjects research of the potential conflict.

2. It is the Investigator's responsibility to assure that all actual or perceived conflicts of interest as defined by institutional policy are reviewed and a determination rendered by an Ethics Committee and that the outcome of such review is submitted to the DOH IRB, prior to initiation of the research.

D. Congruence with Funding Proposals

1. It is the responsibility of the Investigator to assure that the IRB application is consistent with the proposal for funding for extramural or intramural support.

2. The Investigator should act as a liaison between the IRB and the research sponsor.

E. Supervision and Auditing of Research Process

1. It is the responsibility of each Investigator to assure that all procedures associated with the research are performed, with the appropriate level of supervision, only by individuals who are licensed or otherwise qualified to perform them under the laws of Florida and the polices of the Department of Health. The Investigator must assure adherence to the study protocol and monitor the informed consent process. The Investigator must also assure there are appropriate facilities and resources to conduct the research.

2. It is the responsibility of the Investigator to regularly review his or her research processes and address any deficiencies identified.

3. It is the responsibility of the Investigator to conduct and document auditing of research activities on a regular basis.

4. It is the responsibility of the Investigator to audit external performance sites routinely, assuring adequate staff, resources, and pharmacy practices.

F. Confidentiality

1. The conditions for maintaining confidentiality of the participants' research records are required for the life of the data.

2. Research conducted with Food and Drug Administration (FDA) regulated articles must be kept in accordance with current FDA regulations.

3. The Investigator must also assure participant privacy and confidentiality according to HIPAA guidelines, Institutional and IRB policies and procedures.

G. Additional Requirements for Activities Involving Vulnerable Populations

1. The IRB must review and approve the use of a vulnerable population in research activities. Special considerations are provided in the Federal regulations and the DOH IRB policies and procedures for the following populations:

a. Pregnant Women, Human Fetuses, Neonates, and Transplantation of Fetal Tissue. For research activities involving pregnant women, human fetuses, neonates and transplantation of fetal tissue, the Investigator must assure that all requirements are satisfied and adequate provisions have been made for monitoring the informed consent process. See DOHP 400-6.1, “Research Involving Pregnant Women”

b. Prisoners. If a participant becomes a prisoner after enrolling in a research study that the IRB did not approve for inclusion of prisoners, the Investigator is responsible for immediately reporting this situation using the IRBWise problems requiring prompt reporting application. The Investigator must cease all interactions or interventions with the prisoner-participant until approval has been received from the DOH IRB and the OHRP. If the investigator wants to enroll prisoners in research, then the investigator needs to request an amendment. All research activities conducted or supported by the federal Department of Health and Human Services involving the use of prisoners as participants require both DOH IRB approval and OHRP approval. See DOHP 400-6.2, "Research Involving Prisoners"

c. Children. For research activities involving children, the Investigator must assure that all requirements in Subpart D are satisfied, or equivalent protections. The Investigator is responsible for assuring parental consent, as well as child assent/dissent, in accordance with the determinations of the DOH IRB. See DOHP 400-6.3, "Research Involving Children"

d. Cognitively Impaired. Individuals who are or who may become decisionally impaired may have diminished autonomy that may limit their capacity to provide consent. Therefore, the Investigator is responsible for assuring that informed consent is conducted in accordance with the determinations of the DOH IRB. See DOHP 400-6.4, "Research involving Cognitively Impaired persons"

2. The IRB may also determine that other target populations identified in the research proposal are “vulnerable” in particular types of research; and may impose additional protections not outlined in the Federal regulations.

H. Amendments and Requests for Changes in IRB Application

It is the responsibility of the Investigator to not deviate from the IRB approved research activities until the Investigator has received written approval from the IRB except when necessary to eliminate apparent immediate hazards to the participant. Such changes must be reported promptly to the IRB.

I. Informed Consent

1. The Investigator must assure that the performance of the informed consent process is congruent with IRB policy and Federal regulations.

2. The Investigator may delegate obtaining informed consent to a member of his or her study team. However, the Investigator is responsible for monitoring the informed consent process and assuring copies of the consent documents have been provided to participants while keeping the original on file.

J. Unanticipated Problems Involving Risk to Participants or Others

The Investigator must report to the IRB, Data and Safety Monitoring Boards, sponsors and appropriate Federal agencies any problems requiring prompt reporting to the IRB. See DOHP 400-4.6, “Problems Requiring Prompt Reporting to the IRB”.

K. Continuing Reviews

1. All approved research proposals, with the exception of those which qualify for exemption in accordance to 45 CFR 46.101 and 21 CFR 56. 104(d) must receive continuing review at intervals appropriate to the degree of risk as determined by the IRB.

2. Continuing review must be conducted not less than once per year. The Investigator must assure that continuing review applications are submitted in a timely manner so that their review occurs prior to their expiration date. The Investigator acknowledges that the Federal regulations do not allow a grace period.

3. Continuing review must be substantive and meaningful. Therefore the Investigator must submit a comprehensive summary of the research activities and progress since the last continuing review, which would include a summary of adverse events and unanticipated problems, amendments, results of literature searches, publications, etc. The Investigator is responsible for being aware of the current literature in his/her field of study to assure participants are no longer placed at risk if additional risks have been identified or no benefit has been proven.

L. Research Records

1. At a minimum, Investigators must maintain research records for at least three (3) years from the date the research is closed with the DOH IRB.

2. All research records must be accessible for inspection and copying by authorized representatives of the IRB, Federal regulatory agency representatives, and the department or agency supporting the research.

3. Beyond three years, requirements for record retention vary with the type of research conducted and provisions of the Investigator's funding source. It is the Investigator's responsibility to have a clear understanding of the retention requirements of a sponsor.

4. All Health Insurance Portability and Accountability Act (HIPAA) related documentation must be maintained for at least six (6) years from the date of the last use or disclosure of the Protected Health Information (PHI).

5. If for any reason there is a change in PI on a protocol, then the DOH IRB must be notified. The Investigator may either have another Investigator assume Principal Investigator responsibilities, close any research studies with the IRB, or take the research studies to the new location. The Investigator must also notify in writing to the DOH IRB the plan for either destroying the data or transferring the data to another Principal Investigator.

M. Use of Investigational Drugs and/or Investigational Devices

The Investigator is responsible for obtaining the Investigational New Drug (IND) or Investigational Device Exemption (IDE) from the FDA in accordance with Federal regulations.

N. Additional Institutional Committee/Institution Approvals

1. It is the responsibility of the Investigator to seek review and approval from any other required DOH central office programs, or county health departments, or other Institutions (universities, hospitals, school districts) as required and provide documentation to the DOH IRB using the "Research Site and Program Support" worksheet, prior to the initiation of any research.

O. Federalwide Assurances (FWA), Memos of Understanding (MOU), Other IRB Approvals, and Letters of Cooperation

1. It is the Investigator's responsibility to assure that the proper approvals and agreements are in place prior to the commencement of research. This includes research at performance sites, "engaged" or "not engaged," that are not a legal entity of the DOH or covered entity.

2. The Investigator is responsible for submitting copies of all IRB approvals or letters of cooperation, whichever is applicable, for all performance sites

indicated in the IRB Application that are not a legal entity of the DOH or covered entity.

3. The Investigator must assure that each performance site indicated in the IRB Application as "engaged" in research, has a *current* FWA and IRB approval, not just initially but throughout the conduct of the research.

4. If the DOH IRB has agreed to serve as the IRB of Record for a performance site "engaged" in research as evidenced by an executed MOU, it is the Investigator's responsibility to assure that the MOU is current and that he/she upholds the terms and conditions defined within the MOU.

VI. History Notes

The Office of Public Health Research, Ethics and Human Research Protections Program is responsible for this policy.

Reviewed 08/23/2013

Replaces DOHP-400-2.2-07

VII. Signature Block with Effective Date

Ana M. Viamonte Ros, M.D., M.P.H.
State Surgeon General,

Date

I. Policy

It is the policy of the Department of Health (DOH) Institutional Review Board (IRB) that all financial interests are disclosed, evaluated, and managed or eliminated to prevent financial interests from adversely affecting the protection of participants or the credibility of the Human Research Protection Program at DOH..

II. Authority

A. Chapter 381.86, Florida Statutes, Institutional Review Board

B. Florida Administrative Code Rule 64H-2.001 Institutional Review Board

C. 42 CFR §50, 45 CFR §690

D. 21 CFR §54.2(a)-(d), 21 CFR §54.2(f), 21 CFR, §54.4(a)(3), 21 CFR §54.4(b)

III. Supportive Data

A. DOHP 400-1.1, "Institutional Oversight of Assurance"

B. DOHP 400-1.2, "Activities Subject to IRB Jurisdiction"

IV. Definitions

See DOHP 400-11.1, "Definitions"

V. Procedures

A. Investigators and all research personnel involved in the design, conduct, or reporting of research must complete a "Researcher and Research Staff Conflict of Interest Disclosure" worksheet in IRBWise at initial review, continuing review, and any time financial or circumstances change, and disclose whether the researcher or immediate family members (spouse or domestic partner and dependent children) have any of the following:

1. Ownership interest, stock options, or other financial interest related to the research of any value.

2 Compensation related to the research of any value.

3. Proprietary interest related to the research including, but not limited to, a patent, trademark, copyright or licensing agreement.

4. Board or executive relationship related to the research, regardless of compensation.

5. Any interest that could be affected by the outcome of the research

B. An investigator reporting any of the above will describe the financial interest and propose a plan to prevent the financial interest from interfering with the design, conduct, or reporting of the research, including interfering with the protection of participants and submit this information for review by the convened IRB using IRBWise. The convened IRB has final authority to determine whether the management plan is adequate.

C. When researchers come from organizations that use personnel and committees external to the IRB to evaluate and manage financial conflicts of interest, researchers are required to report these determinations as part of the IRB application. The convened IRB has final authority to determine whether the management plan is adequate. For example, if a researcher's university has a conflicts of interest committee, then the determinations of this committee must be submitted to the IRB as part of the application for review using IRBWise.

D. The convened IRB will evaluate disclosures using the "Researcher and Research Staff Conflict of Interest Disclosure" worksheet and determine if they represent a conflict that might adversely affect the protection of participants or the credibility of the HRPP, and will evaluate proposed management plans to determine if they are adequate. The criteria to evaluate conflicts do not vary by funding or regulatory oversight. The IRB will determine whether:

1. the financial interest will adversely affect the protection of participants in terms of the criteria for IRB approval

2. the financial interest will adversely affect the integrity of the research.

E. When the convened IRB determines a conflict exists, it will review a researcher's proposed management plan, or require specific actions to manage the conflict. Disclosure of conflicts to participants is not sufficient by itself to manage conflicts. Examples of actions the convened IRB may take to manage conflicts include requiring:

1. Partial or complete divestiture of financial or other interests (not just those related to a particular research study)

2 An independent researcher to obtain informed consent

3. Frequent continuing review

4. Disclosure of conflicts and their management to participants in research

5. Disapproval of research if the convened IRB determines the conflict cannot be managed

F. The convened IRB's determination will be communicated to the researcher using IRBWise.

VI. History Notes

The Office of Public Health Research, Ethics and Human Research Protections Program is responsible for this policy.

Reviewed 08/23/2013

Replaces DOHP 400-2.3-07, “"Investigator and Key Study Personnel Conflicting Interests”

VII. Signature Block with Effective Date

Ana M. Viamonte Ros, M.D., M.P.H.
State Surgeon General,

Date

I. Policy

It is the policy of the Department of Health (DOH) Institutional Review Board (IRB) that each research application, excluding "Exempt" research, submitted to the IRB for review include a plan to assure the safety and welfare of its participants.

II. Authority

A. Chapter 381.86, Institutional Review Board, *Florida Statutes*

B. Rule 64H-2.001, Institutional Review Board, *Florida Administrative Code*

III. Supportive Data

A. NIH/NIAMS "DSMB Charter"

B. *Data Monitoring Committees in Clinical Trials*. Ellenberg, Susan S., Thomas R. Fleming, and David L. DeMets; 2003 John Wiley and Sons, LTD

IV. Definitions

See DOHP 400-11.1, "Definitions"

V. Procedures

A. Investigator Responsibility for Data and Safety Monitoring

The Principal Investigator should develop a data monitoring plan, which may include a DSM or DSMB for his or her study as appropriate for the size, complexity, and level of risk involved in the research. This requirement does not apply to industry-sponsored research, where the sponsor is responsible for safety monitoring.

B. Research Activities that Should Include a DSM or DSMB

1. The study is intended to provide definitive information about the effectiveness and/or safety of a medical intervention;

2. Prior data suggest that the intervention under study has the potential to induce a potentially unacceptable toxicity;

3. The study is evaluating mortality or another major endpoint, such that inferiority of one treatment arm has safety as well as effectiveness implications; or

4. It would be ethically important for the study to stop early if the primary question addressed has been definitively answered, even if secondary questions or complete safety information were not yet fully addressed.

C. DSMB Composition

1. The DSMB should have multidisciplinary representation, including physicians from relevant medical specialties and biostatisticians. This may include other experts such as bioethicists, epidemiologists and basic scientists.

2. The DSMB should have membership limited to individuals free of apparent significant conflicts of interest, whether they are financial, intellectual, professional, or regulatory in nature.

3. The appropriate size depends on the type of study and types of expertise needed.

D. DSM or DSMB Responsibilities

1. The primary responsibility of the DSM or DSMB is to safeguard the interests of study participants. Therefore, the DSM or DSMB will approve the safety measures in the protocol:

   a. To preserve the study integrity and credibility; and

   b. To facilitate the availability of timely as well as reliable findings to the broader clinical community.

2. The DSM or DSMB should provide written documentation confirming that they have read the protocol and agree with the study design and the data safety monitoring plan (DSMP).

3. The DSM or DSMB will review the progress of the study carefully and diligently.

4. Each enrolled subject's research chart should be reviewed monthly for side effects and tolerability of the investigational drug.

5. The DSM or DSMB will assure that all problems requiring prompt reporting to the IRB (See DOHP 400-4.6, "Problems Requiring Prompt Reporting to the IRB"), are reported to the IRB according to policies and procedures.

6. The DSM or DSMB will be available to the Investigator for consultation concerning any untoward study events or any questions regarding consent issues.

7. The DSM or DSMB will provide a letter of predefined frequency to the IRB, through the Investigator, summarizing the oversight activities of the DSM or DSMB during the monitoring period which should include:

8. Results of the chart reviews;

a. Summary of consultations with the Investigator; and

b. Concerns, if any, regarding subject safety or study drug tolerability.

E. DSM or DSMB Charter

1. The DSM or DSMB Charter should include the following:

a. A detailed presentation of the membership composition, including qualifications and experience;

b. Roles and responsibilities of the DSM or DSMB and if relevant, of Steering Committee members;

c. The authority of the DSM/DSMB (e.g. advisory to the Sponsor, Principal Investigator).

d. The timing and purpose of DSMB meetings;

f. The procedures for maintaining confidentiality;

g. The format, content and frequency of DSM or DSMB reports;

h. Statistical procedures including monitoring guidelines, which will be used to monitor the identified primary, secondary, and safety outcome variables; and

i. Plans for changing frequency of interim analysis as well as procedures for recommending protocol changes.

2. A copy of this Charter should be maintained with the research study files.

G. DSM or DSMB Tasks

Tasks may include, but not be limited to, the following:

1. Conduct initial review of the proposed research to assure quality study conduct;

2. Review procedures to assure quality of study conduct including data management and quality control procedures;

3. Evaluate the quality of ongoing study conduct by evaluating the study accrual, compliance with eligibility, participant adherence to study requirements, and accuracy and completeness of data;

4. Consider factors external to the study when relevant information becomes available, such as scientific or therapeutic developments that may have an impact on the safety of the participants or the ethics of the study;

5. Recommend early termination based on efficacy results;

6. Recommend termination due to unfavorable benefit-to-risk or inability to answer study questions;

7. Recommend continuation of ongoing studies;

8. Consideration of overall picture; primary and secondary analysis;

9. Modify sample sizes based on ongoing assessment of event rates; and

10. Review final results.

H. Data Safety Monitoring Plan

A detailed plan is required for all research that is not “Exempt” under Federal regulations. The level of detail in the plan should be based on the degree of risk entailed by the research participants. Low risk studies may have simple plans but the plan must contain at a minimum the following:

1. Identification of a DSM or DSMB;

2. A description of the general data safety monitoring plan;

3. A description of the plan to monitor progress and safety;

   a. This may include a plan for safety review either by an assigned board, committee or monitor at predetermined intervals relevant to the complexity of the research;

   b. Depending on the complexity of the research, the plan may include assessments of data quality, timeliness, participant recruitment, accrual and retention.

4. A description of the plan to assure compliance FDA regulations and reporting of adverse events, and DHHS regulations concerning problems that may represent unanticipated problems involving risk to participants or others. This may include:

   a. A description of the process for detecting and reporting adverse events that require reporting according to the data and safety monitoring plan and reporting problems that may represent unanticipated problems involving risk to participants or others;

   b. A description of who will be monitoring and collecting problems

requiring prompt reporting (e.g., Principal Investigator, Research Nurse, etc.);

c. Specification of who will be notified of problems requiring prompt reporting (e.g., IRB, NIH, FDA, Principal Investigator, etc.)

d. A reporting plan indicating the timing of reports;

e. A plan for annual reporting of problems requiring prompt reporting if study longer than one year;

f. A description of the plan to assure suspensions of funded trials are reported to the grants program director; and

g. A description of the plan to assure data accuracy and protocol compliance.

VI. History Notes

The Office of Public Health Research, Ethics and Human Research Protections Program is responsible for this policy.

Reviewed 08/23/2013

VII. Signature Block with Effective Date

Ana M. Viamonte Ros, M.D., M.P.H.
State Surgeon General
Florida Department of Health

Date

I. Policy

It is the policy of the Department of Health (DOH) Institutional Review Board (IRB) to assure that the privacy and confidentiality protections are adequate for all research participants, which may include requesting the Investigator to secure a Certificate of Confidentiality.

II. Authority

A. Chapter 381.86, Florida Statutes, Institutional Review Board

B. Florida Administrative Code Rule 64H-2.001 Institutional Review Board

III. Supportive Data

A. NIH Frequently Asked Questions on Certificates of Confidentiality, Web Posting: July 22, 2003

B. Public Health Service Act 301(d), 42 U.S.C.241(d)

C. OHRP Guidance Document, "Guidance on Certificates of Confidentiality," February 25, 2003

IV. Definitions

See DOHP 400-11.1, "Definitions"

V. Procedures

A. Circumstances When a Certificate of Confidentiality May be Indicated

Data collection about sensitive issues (such as illegal behavior, alcohol or drug use, or sexual practices or preferences) requires the protection of confidentiality beyond preventing accidental disclosures. Under Federal law, Investigators can obtain an advance grant of confidentiality, known as a Certificate of Confidentiality that will provide protection against compulsory disclosure, such as a subpoena, for research data. The Investigator should describe in the IRB application any conditions under which confidential information might be disclosed and create an informed consent document that accurately reflects those conditions, including any voluntary disclosure by the Investigator. The IRB is required to determine whether the risks to subjects are minimized, informed consent is appropriate, and privacy and confidentiality protections are adequate.

B. Eligibility for a Certificate of Confidentiality

Federal funding is not a prerequisite for requesting a Certificate of Confidentiality. Any research that collects personally identifiable, sensitive information and that has been approved by an IRB is eligible for a Certificate.

C. Protections Provided by a Certificate of Confidentiality

A Certificate of Confidentiality provides protection for the Investigator and the participants against compelled disclosure of identifying information about participants of biomedical, behavioral, clinical, and other research (Public Health Service Act '301(d), 42 U.S.C. '241(d)). Under this Act, the Secretary of Health and Human Services (HHS) may authorize persons engaged in research to protect the privacy of participants by withholding from all persons not connected with the conduct of the research the names or other identifying characteristics of the participant. This means that Investigators may not be compelled in any Federal, State or local civil, criminal, administrative, legislative, or other proceedings to identify their participants.

1. The protection is available only when the research is of a sensitive nature where the protection is judged necessary to achieve the research objectives.

2. Research can be considered sensitive if it involves the collection of information in the following categories:

    a. Research on HIV, AIDS, and other STDs;

    b. Information relating to sexual attitudes, preferences, or practices;

    c. Information relating to the use of alcohol, drugs or other addictive products;

    d. Information pertaining to illegal conduct;

    e. Information that if released could reasonably be damaging to an individual’s financial standing, employability, or reputation within the community;

    f. Information that might lead to social stigmatization or discrimination if it were disclosed;

    g. Information pertaining to an individual's psychological well being or mental health;

    h. Research on behavioral interventions and epidemiologic studies; and

    i. Genetic information.

3. Examples of studies that would not qualify for a certificate of confidentiality are:

    a. Projects that are not research based;

    b. Projects that are not approved by an IRB in accordance with the NIH guidelines governing Certificates of Confidentiality;

    c. Projects that do not collect sensitive information or information

that might harm the research participants; or

d. Projects that do not collect personally identifiable information.

D. Limitations of a Certificate of Confidentiality

The Certificate of Confidentiality does not govern the voluntary disclosure of identifying characteristics of research participants but only protects participants from compelled disclosure of identifying characteristics by the Investigator. Investigators, therefore, are not prevented from the voluntary disclosure of matters such as child abuse or a subject's threatened violence to self or others. However, if an Investigator intends to make such voluntary disclosures, the consent form should clearly indicate this.

E. Investigator's Responsibility for Assuring Confidentiality

Investigators are responsible for assuring confidentiality of research data. If the Investigator is conducting research involving sensitive information, the IRB may require the Investigator to obtain a Certificate of Confidentiality. The Investigator is responsible for submitting a request for the Certificate of Confidentiality from the National Institutes of Health (NIH). Additional information and submission instructions are located on the NIH website: http://grants.nih.gov/grants/policy/coc/contacts.htm.

VI. History Notes

The Office of Public Health Research, Ethics and Human Research Protections Program is responsible for this policy.

Reviewed 08/23/2013

Replaces DOHP-400-2.5-08

VII. Signature Block with Effective Date

Ana M. Viamonte Ros, M.D., M.P.H.. Date
State Surgeon General
Florida Department of Health

I. Policy

It is the policy of the Department of Health (DOH) Institutional Review Board (IRB) that the composition of IRB Committees be in accordance with Federal regulations.

II. Authority

A. Chapter 381.86, *Florida Statutes*, Institutional Review Board

B. Rule 64H-2.001, Institutional Review Board, *Florida Administrative Code*

III. Supportive Data

A. 45 CFR 46.107

B. 34 CFR 350 and 356

C. OHRP IRB Guidebook

IV. Definitions

See DOHP 400-11.1, "Definitions"

V. Procedures

A. Composition of Institutional Review Boards

Each IRB must include at least one member whose primary interests are in a scientific area, one member whose primary interests are in a non-scientific area and one member who is not affiliated with DOH (i.e. not an employee, not recently retired, not a contractor or vendor providing goods or services, or a family member or spouse of an employee). The non-scientist and non-affiliated member may be the same individual. The IRB must include at least one member who represents the perspective of research participants, such as a former or current research participant or a research participant advocate.

1. Ex Officio and Administrative Members

a. Ex officio members, administrative members, invited guests or expert consultants do not have voting privileges.

b. Ex officio and administrative members on the IRB may include the following:

(1) Persons who are automatically members by virtue of the position held; and

(2) Persons necessary to the Committee by virtue of special knowledge or area of expertise (e.g., expert consultant).

B. Membership Selection

Selections for IRB member voting positions and Chairpersons for the IRBs are made by the State Surgeon General based upon the specific needs of the IRB Committee, e.g. medical specialty, diversity, non-scientist, non-affiliated, etc.

1. The Human Research Protection Administrator designated in the Department's Assurance in collaboration with the Director for the Office of Public Health Research recruits volunteers as needed, seeking advice from IRB Committee Chairpersons, IRB Members, Division Directors, Bureau Chiefs, and others in making recommendations to the State Surgeon General.

2. Decisions for selecting board members are made to assure that the membership on IRBs have appropriate qualifications and expertise and retain diversity while maintaining regulations for required individuals to serve on the Committee.

3. IRB Chairs and Vice Chairs are selected as highly respected individuals from within or outside the institution, fully capable of managing the IRB and matters brought before it with fairness and impartiality.

C. Number of Members

IRBs must have a minimum of five members each, with varying backgrounds and expertise to provide complete and thorough review of research activities commonly conducted by the DOH or involving DOH resources or clients.

D. Alternates

Alternate IRB members, if appointed, are designated for a specific member or members. Alternate members, if not already appointed as IRB committee members, are appointed by the State Surgeon General.

1. Meeting minutes must document when an alternate member replaces a voting member. If both the alternate IRB member and the primary IRB member attend a meeting, only one of these two may vote.

2. The IRB roster identifies the primary members or class of primary members for whom each alternate member can substitute.

3. Alternate members receive and review the same material that the primary members receive.

E. Qualifications of IRB Members

1. The IRB membership must be:

    a. The IRB must have appropriate expertise and be sufficiently qualified through the diversity of the members, including consideration of race, gender, and cultural backgrounds and sensitivity to such issues as community attitudes, to promote respect for its advice and counsel; and

    b. Able to ascertain the acceptability of proposed research in terms of institutional commitments, regulations, applicable law, and standards of professional conduct and practice;

2. Additionally IRB Members and Chairpersons must:

    a. Be committed to the workload;

    b. Understand the required time commitment;

    c. Come to meetings prepared for discussion;

    c. Be committed to the institution's goals for human research protections;

    d. Possess good communication skills;

    e. Be able to act as a facilitator;

    f. Be willing to contact Investigators to discuss issues and initiate solutions prior to the meeting; and

    g. When applicable have,

        (1) Strong clinical expertise; and/or

        (2) Research experience

F. Annual Review of Membership Needs

Composition of the membership of the IRB should be adequate in light of the anticipated scope and complexity of research activities, the types of subject populations likely to be involved, and the size and available resources of the DOH. The Human Research Protection Administrator designated in the Department's Assurance conducts an annual review of IRB membership to meet regulatory and organizational requirements.

G. Term of Service

1. IRB Members

a. IRB members are requested to serve a minimum of two years.

b. IRB members are requested to serve as an alternate member at the completion of their term.

2. IRB Chairs

a. IRB Chairpersons are respected, active members of the Department who are well-informed in regulations relevant to the use of human subjects in research. IRB Chairpersons normally include individuals from central office programs and county health departments.

b. Candidates for IRB Chairs are selected by the Human Research Protection Administrator designated in the Department's Assurance and the Director, Office of Public Health Research based on their experience in human research protections, professional discipline(s) and achievements, educational background, and their availability to commit the appropriate amount of time and effort to the DOH IRB program.

c. The State Surgeon General appoints the Chair(s) based on their experience in human research protections, professional discipline(s) and achievements, educational background, and their availability to commit the appropriate amount of time and effort to the DOH IRB program.

d. Chairs are normally requested to serve one year as an IRB member prior to assuming the role of Chair.

e. Chairs are requested to serve a minimum of three years including a minimum of one year as Chair.

f. Chairs are requested to serve an additional year as an IRB member at the completion of their term to serve as a mentor for the newly selected Chair to promote consistency and continuity. In addition, this will provide a resource for the newly selected Chair and IRB members on historical perspectives, rationale for decisions made regarding policy, and meeting facilitation skills.

g. Chairs are requested to serve as a regular or alternate member at the completion of their term.

H. Required Expertise for Review of Research Involving Vulnerable Populations

1. Research Involving Children

The IRB considering a protocol involving children as participants should:

a. Assess its needs for pediatric expertise among the IRB voting membership to assure that it possesses the professional competence necessary to review the specific research activities; and

b. Include one or more individuals who are knowledgeable about and experienced in working with children, or requests review by an expert with such knowledge or experience. To fulfill this requirement, the IRB may invite nonvoting individuals to assist in the review of issues which require expertise beyond, or in addition to, that available among voting IRB members.

c. When reviewing proposed research on handicapped children or mentally disabled persons sponsored by the US Department of Education, the DOH IRB must also include a member with the expertise in the area of this population as described in the US Department of Education's regulations at 34 CFR 350 and 356.

2. Research Involving Prisoners

Federal regulations require that the IRB membership be modified if it is to review research involving prisoners. Therefore, if any IRB will review research involving prisoners, at least one voting member of the IRB present at the meeting shall be a prisoner, or a prisoner representative with appropriate background and experience to serve in that capacity.

3. Research Involving Pregnant Women and Neonates Representative

The IRB considers all applicable Federal regulations regarding research with this population, requires at least one member present at the meeting to be knowledgeable or experienced in working with this population, requests review by an expert with such knowledge or experience.

4. Research Involving Cognitively Impaired Participants

The IRB includes at least one member with expertise in the area of the cognitively impaired population when reviewing studies with this population or studies in which the participants may become cognitively impaired throughout the course of the research, or requests review by an expert with such knowledge or experience.

I. Additional Appropriate Expert Consultants

On a case-by-case basis, the IRB or staff may request review by an individual with competence in an area not represented by the IRB membership. The Human Research Protection Administrator designated in the Department's Assurance is responsible for identifying a consultant.

J. IRB Member, Chair, and Staff Performance Evaluations

1. IRB members and Chairs complete a self-evaluation annually which includes the following:

   a. Knowledge and application of the Federal regulations;

   b. Knowledge and application of IRB policies and procedures;

   c. Participation in Committee meeting discussions;

   d. Interaction with Investigators and study contacts; and

   e. Completion of educational requirements.

2. The Human Research Protection Administrator designated in the Department's Assurance and other staff shall perform an ongoing assessment of IRB members and Chairs based on observations made during the IRB meetings, and provide feedback individually to the member to enhance and promote growth in their performance as an IRB member.

3. Staff are evaluated at least annually. The IRB Administrator and Assistant Administrator are evaluated by the Human Research Protection Administrator designated in the Department's Assurance, who in turn is evaluated by the Director, Office of Public Health Research.

K. Reporting Changes in IRB Membership

HRPP Staff is responsible for reporting any amendments or changes to the IRB roster to OHRP within 90 days of the initiation of such changes.

VI. History Notes

The Office of Public Health Research, Ethics and Human Research Protections Program is responsible for this policy.

Reviewed 08/23/2013

VII. Signature Block with Effective Date

Ana M. Viamonte Ros, M.D., M.P.H.
State Surgeon General, Department of Health

Date

I. Policy

It is the policy of the Department of Health (DOH) Institutional Review Board (IRB) that IRB chairs, board members, consultants, and IRB staff declare any conflicts of interest before review of any research under IRB jurisdiction. IRB members, consultants, and IRB Administrators with a conflict of interest may not participate in any portion of the review of research activities except to provide information requested by the IRBs and must leave the meeting room for discussion and voting.

II. Authority

A. Chapter 381.86, Institutional Review Board, *Florida Statutes*

B. Rule 64H-2.001, Institutional Review Board, *Florida Administrative Code*

III. Supportive Data

A. OHRP Guidance, “Conflict of Interest”

IV. Definitions

See DOHP 400-11.1, “Definitions.”

V. Procedures

A. Individuals involved in promotion of DOH’s research enterprise shall not serve as members of the IRB and shall not carry out the day-to-day operations of the review process.

B. IRB members sign a “IRB Member and Staff Conflict of Interest Disclosure” annually.

C. IRB members, consultants, or staff with a conflict of interest do not participate in the review of or vote on protocols in which they have a conflict, except to provide information as requested by the IRB. Staff do not conduct administrative review of research when they have a conflict.

D. IRB members, consultants, or staff with a conflict of interest must leave the meeting room for discussion and voting.

E. IRB members, consultants, or staff with a conflict of interest are documented in the minutes as being absent from the room with an indication that a conflict of interest was the reason for the absence. Members reporting a conflict of interest are not counted in the quorum for that particular study only.

F. IRB members, consultants and staff must report any conflict of interests when they are assigned a study for review in IRBWise, or at the beginning of each IRB meeting. A conflict of interest exists when IRB members, consultants, staff and their immediately family members (spouse or domestic partner, and dependent children):

1. Is a member of the research team.
2. Has a financial interest in the research with value that cannot be readily determined.
3. Ownership interest, stock options, or other financial interest related to the research of any value.
4. Has received or will receive compensation related to the research of any value.
5. Has a proprietary interest related to the research including, but not limited to, a patent, trademark, copyright or licensing agreement.
6. Has received any payments from the sponsor in the past year.
7. Is an executive or director of the agency or company sponsoring the research, regardless of compensation.
8. Has an interest that the IRB member believes conflict with his or her ability to objectively review a protocol.
9. Has any interest that could be affected by the outcome of the research.

G. This policy applies to all reviews including:

1. Administrative pre-review by Staff
2. Review by a convened IRB.
3. Review using the expedited procedure.
4. Initial review, continuing review, and review of modifications.
5. Review of unanticipated problems involving risks to participants or others.
6. Review of non-compliance with the regulations or the requirements of the IRBs.

H. Questions about whether a conflict of interest exists will be determined by the IRB Chair, or Human Research Protection Administrator designated in the Department's Assurance, or by consulting legal counsel, who may seek an opinion from the Department's Ethics Officer.

VI. History Notes

The Office of Public Health Research, Ethics and Human Research Protections Program is responsible for this policy.

Reviewed 8/23/2013

Replaced DOHP 400-3.2-08

VII. Signature Block with Effective Date

Ana M. Viamonte Ros, M.D., M.P.H.
State Surgeon General
Florida Department of Health

Date

I. Policy

It is the policy of the Department of Health (DOH) Institutional Review Board (IRB) that members will review all research involving human participants under the Department of Health's jurisdiction.

II. Authority

A. Chapter 381.86, *Florida Statutes*, Institutional Review Board

B. Rule 64H-2.001, Institutional Review Board, *Florida Administrative Code*

III. Supportive Data

A. 45 CFR 46

B. 21 CFR 50, 56

IV. Definitions

See DOHP-400-11.1, "Definitions"

V. Procedures

A. Committee Members

The mission of the DOH IRB is to protect the rights and welfare of human research subjects recruited to participate in research activities conducted under its jurisdiction (*See*: policy DOHP-400-1.2, "Activities Subject to IRB Jurisdiction") through ethically responsible and scientifically valid research, continuous education of the research community, monitoring of research activities, and compliance with the federal regulations and institutional policies and procedures.

1. Committee members have an understanding of basic ethical principles, the regulatory requirements, and the mechanics of serving on the IRB.

2. Committee members conduct prospective and continuing review of proposed research activities according to Department of Health and Human Services (DHHS) regulations 45 CFR 46, Food and Drug Administration (FDA) regulations 21 CFR 50 and 56 and when applicable, other Federal, State and local laws, and institutional policies and procedures including the IRB policies and procedures.

3. Committee members evaluate the research proposal for both scientific and scholarly merit to determine if it is sound enough to justify human subjects participation. This includes consideration of research design, statistical power, equitable subject selection process, etc.

4. Committee members identify any conflicts of interest prior to the review of

research activities and bring this to the attention of the Staff for reassignment.

5. Committee members obtain guidance or additional information in order to conduct an adequate study evaluation. This may include the request of an additional reviewer or consultant with expertise in the area of research under review (e.g., a Psychiatrist consultant may be asked to review a study that requires a "wash-out" period followed by intervention with investigational or novel agents in a population that has a high likelihood of enrollment of subjects that are or may become cognitively impaired).

B. Consultants and Ad Hoc Reviewers

1. Consultants and ad hoc reviewers are held to the same standards as those described above.

2. A consultant may serve as an ad hoc reviewer when expertise in a specific area is needed. The consultant may not be able to attend the meeting, but is expected to provide a written review of the research. This could be a narrative or could be captured on the reviewer's comment form.

3. The consultant may attend the meeting to participate in the review and discussion, however; the consultant may not count toward quorum or vote.

4. A Committee member or Administrative Staff may request a written review from an expert consultant and may also request they attend the meeting for participation in the discussion.

B. Review of scientific and scholarly validity. Reviewers at the convened IRB and reviewers using the expedited procedure verify that all regulatory criteria for approval are met, including review of scientific or scholarly validity. Reviewers must determine the science is sound enough to accomplish the research outcomes. When making this determination, reviewers should based determinations based on scientific and scholarly norms in the field of research of the study being reviewed.

VI. History Notes

The Office of Public Health Research, Ethics and Human Research Protections Program is responsible for this policy.

Reviewed 08/23/2013

Replaces DOHP-400-4.1-07

VII. Signature Block with Effective Date

Ana M. Viamonte Ros, M.D., M.P.H.
State Surgeon General,

Date

I. Policy

It is the policy of the Department of Health (DOH) Institutional Review Board (IRB) to conduct regularly scheduled meetings based on the volume of research to be reviewed in order to allow adequate time for discussion and for effective and consistent review according to applicable laws, regulations, codes, and guidance and DOH's policies and procedures.

II. Authority

A. Chapter 381.86, *Florida Statutes*, Institutional Review Board

B. Rule 64H-2.001, Institutional Review Board, *Florida Administrative Code*

III. Supportive Data

A. 45 CFR 46.108(b)

B. OHRP Guidance on Written Institutional Review Board (IRB) Procedures

C. 21 CFR 56.108

IV. Definitions

See DOHP 400-11.1, "Definitions"

V. Procedures

A. Development of the Agenda

1. IRB staff creates an agenda using the Department's electronic system for managing IRB review (IRBWise). Protocols are added to an agenda once staff determines the application for review of research is complete.

2. IRB staff limit the number of protocols for review at a convened meeting to allow for adequate time for discussion of all items on the agenda. The limit for items on the convened agenda is not more than 15 items for a two hour meeting, but is normally not more than approximately 10 items for a two hour meeting.

3. IRB staff prioritize the inclusion of items on agendas in the following order:

   a. Unanticipated problems involving risks to participants or others, and non-compliance.

   b. Amendments and continuing reviews of existing studies

   c. New applications for review of research

4. HRPP Staff consults with the IRB Chair when there are questions about whether an item should be on the agenda for a particular meeting.

5. HRPP Staff assigns primary reviewers using authority delegated by the IRB Chairs. Staff ensure that at least one person with appropriate scientific or scholarly expertise conduct an in-depth review of the research.

6. HRPP Staff, in consultation with an IRB Chair when necessary, evaluate each study and determine whether there is sufficient expertise or knowledge to review the research. In such an event, Staff may re-assign a study to a later meeting, or obtain a consultant. IRB Chairs or members may also request a consultant. Reviews are not conducted when members do not have sufficient expertise or knowledge.

    a. If HRPP Staff determine a consultant is needed, they identify persons with relevant qualifications and expertise by seeking suggestions from persons including, but not limited to, IRB members and Chairs, relevant DOH subject matter experts, DOH Bureau Chiefs and Division Directors, federal partners such as the Centers for Disease Control and Prevention, university partners, or through a literature search.

    b. The IRB Administrator or Assistant Administrator has the consultant complete the IRB Member and Staff Conflict of Interest Disclosure Worksheet. If there are no conflicts, the consultant is assigned to the study. Consultants provide information to the IRB by completing a reviewer comment worksheet in IRBWise. In addition, consultants may also present information to the convened IRB by attending a meeting. However, when a consultant attends a meeting, the consultant does not vote.

7. HRPP Staff sends an email informing IRB members that the agenda is complete approximately 10 days in advance of convened meetings, but no less than 5 days in advance of each committee's monthly meeting.

8. The Department anticipates that in exceptional circumstances, such as a declared public health emergency, the IRB may need to meet on an emergency basis for review of a specific study. The agenda would be provided to reviewers as soon as practical prior to the meeting, but not less than 24 hours in advance.

9. The IRB agenda is used to inform IRB members of research protocols approved using the expedited procedure, and applications that qualify for exemption or applications that are not research involving human participants, such as public health practice and quality improvement

10. The IRB agenda may be used to distribute information for continuing education of IRB members.

B. Quorum Required for Convened IRB Review

1. The IRB may only review proposed research at a convened meeting at which a quorum is present. A majority of the voting members of the IRB Committee must be present, including at least one member whose primary interests are in nonscientific areas, at least one member who is not affiliated with DOH, and at least one member who represents the general perspective of research participants. Chairs are voting members. A voice vote is taken for each action being reviewed by the IRB; votes are recorded by staff for inclusion in meeting minutes.

2. IRB meetings are not convened if a non-scientist, non-affiliated member, or member who represents the general perspective of research participants are not present

3. No official actions take place at a meeting where a majority of the voting members are not present.

4. Should the IRB meeting lose quorum (e.g., those with conflicts being excused, early departures, loss of all non-scientists), the meeting is terminated from further votes until the quorum is restored.

5. Wherever possible, IRB meetings take place with all participating IRB members physically present. When members participate via conference call, each participating IRB member:

   a. Has received all pertinent material prior to the meeting to allow adequate time for review and the request of additional information, if needed; and

   b. Can actively and equally participate in the discussion of all protocols (i.e., each member can hear and be heard by all other participating members).

   c. The minutes of such meetings clearly document that these two conditions have been satisfied in addition to the usual regulatory requirements (e.g., attendance; initial and continued presence of a majority of members, including at least one nonscientist member; actions taken by the IRB; the vote on such actions; discussion and resolution of controverted issues).

6. When the IRB reviews research involving prisoners, a prisoner representative is present.

7. If the IRB reviews research that involves categories of participants vulnerable to coercion or undue influence, one or more individuals who

are knowledgeable about or experienced in working with such participants are present.

8. No IRB Committee member may participate in any review by the IRB, including review of a project's initial submission, amendments, continuing review, reports of unanticipated problems involving risks to participants or others, or reports of non-compliance in which the member has conflict of interest. If a conflict exists, the Committee member can provide information requested by the IRB Committee but cannot be present for the discussion and the vote.

9. HRPP Staff are responsible for determining quorum is established and maintained during the meeting. Staff use a worksheet to document quorum during the meeting, and this information is recorded in the minutes for each meeting.

10. IRB members are encouraged to print out the reviewer comment worksheets and bring them to convened meetings. Members are provided access to laminate sheets containing the criteria for approval. The meeting room has posters on the wall listing criteria for approval. Video projections may also be used to view specific parts of an application during the discussion of a study, such as the informed consent document, and projection may be used to project the criteria for approval.

11. Chairs review the agenda prior to each meeting, and the assignment of reviewers. IRB staff provide notes to Chairs prior to meetings. Chair notes may include protocol-specific information, such as the fact that a reviewer was not able to approve a study using the expedited procedure, or requested a consultant. Staff distribute minutes to all committee members to allow members to comment. The Chair reviews and approves the minutes within 48 hours after staff draft the minutes. Chairs are responsible for ensuring that the IRBs discussion of the study provides opportunities for members to ask questions, seek more information, and generally facilitate discussion among all members.

C. Voting

1. Members must vote either in favor (affirmative) or against (negative) regarding a protocol. Under Florida law (Ch. 119), a vote of "abstention" can only be recorded if there is a conflict of interest. Under federal regulations IRB members with a conflicting interest may not participate in the IRBs' review of any protocol, except to provide information requested by the IRBs. Therefore, DOH IRB members with a conflict of interest should absent themselves from the meeting room during the IRBs' deliberative discussion and vote on the affected research and the remaining members must vote either in favor or against the protocol.

2. Votes are taken by voice vote. An affirmative vote represents the decision of the majority of members present. Chairs are voting members.

3. HRPP Staff take votes during the meeting, and record them in IRBWise as part of the minutes of the meeting.

4. HRPP Staff are responsible for assuring that consultants do not have conflicts of interest at the time they are retained.

D. Motions

1. Approval with no changes

   An approval is granted if the research activity meets the criteria for approval as defined in federal regulations no changes to the research application are recommended.

2. Approved Pending Verification of Changes by the Chairperson or His/Her Designee

   The convened IRB grants approval pending verification of the changes, provided the IRB provides specific changes required to secure approval, such that the Chair can verify whether or not they have been made. If any modifications have not been made, or additional modifications have been made that were not requested, the Chairperson or his/her designee refers the study to full Committee, including when the Committee specifically asked for clarification of factual errors.

3. Deferred

   A deferral is granted if the study does not meet the criteria for approval as defined in federal regulations or the IRB Committee recommends substantial revisions to the IRB Application, Sponsor's Protocol, informed consent document(s), or other pertinent documents rendering it unable to assess the risk/benefit ratio without the completed revisions.

   Studies are also deferred when the information provided in the application or protocol is insufficient for the convened IRB to conduct an adequate review, or where the convened IRB requires additional expertise, or where the IRB does not have adequate time to conduct an appropriate review.

4. Suspension

   A currently approved study is suspended for cause when evidence of a possible increase in risk to participants or non-compliance by the Investigator has been determined by the IRB. Suspensions for cause are made under full Committee review procedures.

5. Termination

A currently approved study may be terminated if the study is not being conducted in accordance with the IRB policies, is not in compliance with Federal regulations, and/or has been associated with unexpected serious harm to participants. Terminations for cause are made under full Committee review procedures.

6. Disapproval

Disapproval of new protocols is granted if the convened IRB determines the protocol does not meet the criteria for approval, or if the Investigator is unable to revise the protocol to meet the criteria for approval as defined in federal regulation.

VI. History Notes

The Office of Public Health Research, Ethics and Human Research Protections Program is responsible for this policy.

Reviewed 08/23/2013

Incorporates DOHP 400-4.2, "IRB Determinations and Motions"

VII. Signature Block with Effective Date

Ana M. Viamonte Ros, M.D., M.P.H. Date
State Surgeon General,

I. Policy

It is the policy of the Department of Health (DOH) Institutional Review Board (IRB) that all research involving human participants under its jurisdiction be reviewed according to criteria for approval in federal regulations (45 CFR 46.111 and 21 CFR 56.111).

II. Authority

A. Chapter 381.86, Institutional Review Board, *Florida Statutes*

B. Rule 64H-2.001, Institutional Review Board, *Florida Administrative Code*

C. Rule 64H-2.002, Institutional Review Board Applications, *Florida Administrative Code*

III. Supportive Data

A. 45 CFR 46.109(e)

B. 45 CFR 46.110

C. 21 CFR 56.109

IV. Definitions

See DOHP 400-11.1, “Definitions”

V. Procedures

A. Process for administrative screening by Staff and assigning reviewers

1. Staff checks applications for completeness using the Administrative Processing Checklist in IRBWise. Incomplete applications are returned with comments so the researcher can revise and submit a complete application.

2. Certain organizational entities of the Department may require investigators to obtain further approval of research, where applicable. Examples include divisions and bureaus in central office, public health laboratories, county health Departments, and A. G. Holley State Tuberculosis Hospital. These organizational entities may not approve research that has not been approved by the IRB, but may require further approval, such as formal permission to conduct research. When permission to conduct research contingent upon IRB approval is not present, Staff return applications to investigators to provide documentation of permission to conduct research.

3. When applications are complete, Staff assign reviewers using authority delegated from the IRB Chair to assign reviewers based on the qualifications and expertise listed in the IRB membership roster, and to ensure that at least one member with appropriate expertise and knowledge reviews the research. When a study involves vulnerable populations, Staff assign a reviewer with appropriate expertise in the specific vulnerable population. If Staff are unsure, they consult with an IRB Chair.

4. Applications are added to the agenda of the next available committee that has reviewers possessing necessary qualifications and expertise. Applications are normally assigned to the next agenda, unless that committee of the IRB does not have relevant qualifications and expertise. For example, if the application involves a vulnerable population such as prisoners, the application is assigned to the next meeting that a prisoner representative is in attendance.

5. If the Reviewer has a conflict of interest, the Reviewer will contact the IRB Administrator or Assistant IRB Administrator and recuse themselves from the review. (See DOHP 400-3.2, “Committee Member, Consultant, and Staff Conflicting Interests)

B. Process for review of applications for initial review by the convened IRB

1. The IRB uses a primary reviewer system for all review of research by the convened IRB. The electronic system provides members access to all materials. One or more primary reviewers are expected to conduct an in-depth review of all materials, including the IRBWise application for initial review of research, the complete protocol (DHHS-approved protocol when one exists), the proposed consent document (and DHHS-approved sample consent when one exists), recruitment materials, and any relevant grant applications or contracts. At least one member reviews the investigator brochure, when one exists.

2. All other members of the IRB (including alternate members) are provided access to all materials, but are expected to review the IRBWise application for initial review of research, which provides the relevant information to determine whether the proposed research fulfills the criteria for approval. In addition to the IRBWise application for initial review, all members read the proposed consent document (and DHHS-approved sample consent when one exists), and recruitment materials.

3. Reviewers use a worksheet to provide comments and to ensure all regulatory requirements are met. One or more primary reviewers use the worksheet to present the study to other board members, and to ensure there is sufficient discussion by the convened IRB to ensure the regulatory criteria for approval are met.

4. IRB members may request a consultant to supplement the IRB's review. (See DOHP 400-3.1, "Composition of the IRB")

5. IRB members determine whether continuing review should occur at an interval less than one year, based on information about anticipated risks posed by the research. Absent other compelling reasons, the convened IRB will require review more often than annually whenever the research involves one or more of:

    a. Phase I research

    b. Involvement of recombinant DNA or other types of gene transfer protocols;

    c. Classified research;

    d. Research for which participants would be exposed to additional risks, e.g. breach of confidentiality, phase I studies, disproportionate number or severity of adverse events;

    e. Previous Administrative Holds or Suspensions of the research due to compliance, record-keeping or other concerns; and/or

    f. Recommendations from other DOH committees

6. When the convened IRB requests substantive clarifications or modifications that are directly relevant to the determinations required by the IRB, the clarifications or modifications must be reviewed by the convened IRB, and may not be verified by the Chair or designee. Examples of substantive clarifications or modifications include "Explain why participants younger than 18 years of age will be allowed to participate", "Provide additional justification for the use of placebo", and "Clarify whether participants will be offered counseling services at the end of the study".

7. Requests by the IRB for the investigator to make a minor change may be verified by the Chair or designee. A minor change is one where the Chair or designee simply verifies the change was made as specified by the IRB. If the change is not made as specified, the application is returned to the convened IRB for review. For example, "Delete the duplicate contact information for the IRB (last page, bottom paragraph)", "Drop the placebo controlled arm of this study", and "Participants must be 18 years or older".

8. The range of possible actions that the IRB is allowed to take is described in policy (See DOHP 400-4.2, "Conduct of Meetings by the Convened IRB").

C. Process for review of applications for initial review using the expedited procedure

1. Applications for initial review that are eligible for review using the expedited procedure are assigned to one or more experienced reviewers from the designated IRB for review and approval. An experienced IRB member normally means a voting member or alternate voting member with appropriate qualifications and expertise who has received training relative to the expedited review categories, and possesses the expertise needed to review the proposed research.

2. The Reviewer assigned will have expertise in the area of the research adequate to the scope and complexity of the research. The Reviewer may request a second reviewer, request review by an expert consultant to the IRB, or refer the study to the convened IRB for determination. In the case of multiple reviewers, decisions are made by consensus of the review. In the absence of consensus, the application is submitted to the convened IRB. However, the determination of disapproval can only be made by the convened IRB.

3. The reviewer using the expedited procedure is provided and reviews the same materials as primary reviewers for the convened IRB.

4. The criteria for approval using the expedited procedure are the same as those for review by a convened IRB.

5. Reviewers use a reviewer comment worksheet to ensure all regulatory requirements are met. The criteria for eligibility for initial review using the expedited procedure are listed on the "Expedited Procedure Eligibility – Initial Review" checklist that is used by the review to determine whether research meets one or more expedited categories and other requirements to undergo continuing review using the expedited procedure.

9. If a reviewer using the expedited procedure determines that the continuing review period for a study would be less than one year, the study should be referred to the convened IRB for review.

10. The reviewer using the expedited procedure may approve research or require changes. However, the reviewer may not disapprove the research; if the reviewer is unable to approve research, it is referred to the full committee.

D. Process for notifying researchers and organization officials

1. The convened IRB is notified of the findings and actions of research applications that have been approved through the expedited procedure with the IRB agenda through the IRBWise system.

2. The Human Research Protection Administrator designated in the Department's Assurance, and the Director, Office of Public Health Research, are the organization officials notified of the findings of the IRB.

Staff include these officials when distributing draft minutes of meetings of the convened IRB to members of the IRB committee.

3. Researchers are notified of the IRB's decision to approve, disapprove, or require modifications to secure approval through the IRBWise system.

   a. The communication from IRBWise includes modifications or clarifications required as a condition for IRB approval.

   b. If the IRB disapproves a proposed research study, researchers are informed through IRBWise of the IRB's reasons for the decision, and how the researcher may respond in person or in writing.

4. Researchers are notified of the approval period for research through IRBWise. If the study is reviewed at the convened IRB meeting, and approved with minor changes to be reviewed and verified by the chair, then once the chair verifies that the changes required by the convened IRB have been made, the approval period begins with the date of the convened meeting. If the study is reviewed at the convened IRB meeting, and the convened IRB requires substantial changes and defers the study, it is returned to the investigator. When the investigator re-submits the application, the study is reviewed again by the convened IRB (normally the same committee). If the convened IRB approves, the approval date is the date of the meeting where the changes were reviewed and approved. The expiration date is the last date that the protocol is approved. For example, if a study is approved through June 10, authorization to conduct research expires at midnight on June 10.

E. Process for managing expiration of IRB Approval

1. There is no grace period extending authorization to conduct research beyond the expiration date of IRB approval. If the IRB does not re-approve the research by the specified expiration date, all study activities must cease including recruitment, enrollment, interventions, and interactions, and collection of private identifiable data, and analysis of identifiable information, pending re-approval of the research by the IRB. If the IRB requires changes to the research at continuing review, this does not extend the expiration period. Expiration of authorization to conduct research is automatic and requires no decision, determination, or action by an IRB. Such expirations of approval are not suspensions of IRB approval, terminations of IRB approval, or administrative holds. Allowing a protocol to expire is considered non-compliance, and is also reviewed for non-compliance. (See DOHP 400-10.1, "Investigating any Noncompliance, Serious or Continuing Noncompliance").

2. The researcher must immediately provide documentation to Staff that all research has stopped.

3. Once notified of the expiration, the Investigator must immediately submit to the IRB Chair, a list of research subjects for whom expiration of the research would cause harm.

    a. An IRB Chair reviews this list and allows individual participants to continue participating in the research interventions or interactions only when the IRB finds an over-riding safety concern or ethical issue involved such that it is in the best interests of individual participants to continue participating. The convened IRB is informed

4. Enrollment of new subjects shall not occur on or after the expiration of IRB approval.

VI. History Notes

The Office of Public Health Research, Ethics and Human Research Protections Program is responsible for this policy.

Reviewed 08/23/2013

VII. Signature Block with Effective Date

Ana M. Viamonte Ros, M.D., M.P.H.
State Surgeon General
Florida Department of Health

Date

I. Policy

It is the policy of the Department of Health (DOH) Institutional Review Board (IRB) that research activities receive regularly scheduled complete reappraisals at intervals appropriate to the degree of risk, but not less than once per year. Continuing review is substantive and meaningful. To approve research, the convened IRB or reviewer using the expedited procedure must find that the DHHS or FDA criteria for approval (45 CFR 46.111 and 21 CFR 56.111) are met. Continuing review occurs as long as research remains active for long-term follow-up of participants, even when the research is permanently closed to the enrollment of new participants and participants have completed research-related interventions, and as long as the remaining research activities include collection or analysis of identifiable private information or where the researcher can readily ascertain the identities of participants from the data.

II. Authority

A. Chapter 381.86, Institutional Review Board, *Florida Statutes*

B. Rule 64H-2.001, Institutional Review Board, *Florida Administrative Code*

C. Rule 64H-2.002, Institutional Review Board Applications, *Florida Administrative Code*

III. Supportive Data

A. 45 CFR 46.109(e)

B. 45 CFR 46.110

C. OHRP Guidance on Continuing Review

D. 21 CFR 56.109

IV. Definitions

See DOHP 400-11.1, “Definitions”

V. Procedures

A. Researchers must submit all materials listed in the IRBWise application for continuing review at least 60 days prior to the expiration of the IRB’s authorization to conduct research. The expiration date is the last date that the protocol is approved

B. Staff conduct pre-review and assign reviewers based on authority designated by the IRB Chairs

1. Staff conducts pre-review of applications for completeness using the Administrative Review worksheet in IRBWise. Incomplete applications are returned with instructions for the researcher to revise and submit a complete application.

2. Staff verify that researchers have obtained permission to conduct research and return applications to investigators to provide documentation of permission when organizational entities of the Department require Researchers to obtain further approval of research. Examples include divisions and bureaus in central office, public health laboratories, county health departments, and A. G. Holley State Tuberculosis Hospital. These organizational entities may not approve research that has not been approved by the IRB, but may require further approval, where applicable, such as formal permission to conduct research.

3. When applications are complete, staff assign reviewers using authority delegated from the IRB Chairs to assign reviewers based on the qualifications and expertise listed in the IRB membership roster. When a study involves vulnerable populations, staff assign a reviewer with appropriate expertise in the specific vulnerable population. If staff are unsure, they consult an IRB Chair.

4. HRPP Staff, in consultation with an IRB Chair when necessary, evaluate each study and determine there is sufficient expertise or knowledge to review the research. Applications are added to the agenda of the next available committee that has reviewers possessing necessary qualifications and expertise. Applications are normally assigned to the next agenda, unless that committee of the IRB does not have relevant qualifications and expertise. For example, if the application involves a vulnerable population such as prisoners, the application is assigned to the next meeting that a prisoner representative is in attendance.

    a. If HRPP Staff determine a consultant is needed, they identify persons with relevant qualifications and expertise by seeking suggestions from persons including, but not limited to, IRB members and Chairs, relevant DOH subject matter experts, DOH Bureau Chiefs and Division Directors, federal partners such as the Centers for Disease Control and Prevention, university partners, or through a literature search.

    b. Consultants provide information to the IRB by completing a reviewer comment worksheet in IRBWise. In addition, consultants may also present information to the convened IRB by attending a meeting. However, when a consultant attends a meeting, the consultant does not vote.

5. If the Reviewer has a conflict of interest, the Reviewer will contact the IRB Administrator or Assistant IRB Administrator and recuse themselves from the review. (See DOHP 400-3.2, “Committee Member, Consultant, and Staff Conflicting Interests)

C. Continuing Review by the Convened IRB

1. The Department uses a primary reviewer system for all review of research by the convened IRB. The electronic system provides members access to all materials. Reviewers are provided and review information necessary to determine whether the proposed research continues to fulfill the criteria for approval. One or more primary reviewers are expected to conduct an in-depth review of all materials, including:

   a. the IRBWise application for continuing review of research, which includes a status report

   b. the complete full protocol (including the DHHS-approved protocol when one exists),

   c. all study documents approved by the IRB during the previous approval period

   d. any protocol modifications previously approved by the IRB

   e. the investigator brochure

   f. the current consent document (including the DHHS-approved consent, when one exists)

   g. any newly proposed consent document (including the DHHS-approved revisions to the consent document, when they exist)

   h. any findings from conflict of interest committees (for example, when a University conflict of interest committee determines a Researcher has a conflict with the research, so the IRB can determine whether a management plan is appropriate.)

2. All other members of the IRB (including alternate members) are provided access to all materials, but are expected to review the IRBWise application for continuing review of research, which includes a status report and provides the relevant information to determine whether the proposed research fulfills the criteria for approval. In addition, all members read the current consent document, and review any newly proposed consent document.

3. Reviewers complete or discuss in detail at the convened IRB meeting a worksheet to ensure all regulatory requirements are met. One or more primary reviewers use the worksheet to present the study to other board members, and to ensure there is sufficient discussion by the convened IRB to ensure the regulatory criteria for approval are met.

4. IRB members may request a consultant to supplement the IRB's review. (See DOHP 400-3.1, "Composition of the IRB")

5. Review of the currently approved informed consent document must ensure that the information is still accurate and complete.

6. Any significant new findings that may relate to the participant's willingness to continue participation should be provided to the participant in an updated informed consent document. Review of currently approved or proposed informed consent document occurs during the scheduled continuing review of research by the IRB, but may be done more frequently if new information becomes available.

7. IRB members determine whether protocols need verification from sources other than the IRB on a case-by-case basis and according to the following criteria:

    a. Protocols randomly selected by the IRB Office

    b. Complex protocols involving unusual levels or types of risks to participants;

    c. Protocols conducted by Investigators who previously have failed to comply with Federal regulations or the requirements or determinations of the IRB; and/or

    d. Protocols where concern about possible material changes occurring without IRB approval have been raised based on information provided in continuing review reports or from other sources.

8. IRB members determine whether continuing review should occur at an interval less than one year, based on information about anticipated risks posed by the research, and any new information including reports of non-compliance, and complaints or other unanticipated problems. Absent other compelling reasons, the convened IRB will require review more often than annually whenever the research involves one or more of:

    a. Phase I research

    b. Involvement of recombinant DNA or other types of gene transfer protocols;

c. Classified research;

d. Research for which participants would be exposed to additional risks, e.g. breach of confidentiality, phase I studies, disproportionate number or severity of adverse events;

e. Previous Administrative Holds or Suspensions of the research due to compliance, record-keeping or other concerns; and/or

f. Recommendations from other DOH committees

9. When the convened IRB requests substantive clarifications or modifications that are directly relevant to the determinations required by the IRB, the clarifications or modifications must be reviewed by the convened IRB, and may not be verified by the Chair or designee. Examples of substantive clarifications or modifications include “Explain why participants younger than 18 years of age will be allowed to participate”, “Provide additional justification for the use of placebo”, and “Clarify whether participants will be offered counseling services at the end of the study”.

10. Requests by the IRB for the investigator to make a minor change may be verified by the Chair or designee. A minor change is one where the Chair or designee verifies the change was made as specified by the IRB. If the change is not made as specified, the application is returned to the convened IRB for review. For example, “Delete the duplicate contact information for the IRB (last page, bottom paragraph)”, “Drop the placebo controlled arm of this study”, and “Participants must be 18 years or older”.

11. The range of possible actions that the IRB is allowed to take is described in policy (See DOHP 400-4.2, “Conduct of Meetings by the Convened IRB”).

D. Process for review of applications for continuing review using the expedited procedure

1. Applications for continuing review that are eligible for review using the expedited procedure are assigned to one or more experienced reviewers from the designated IRB for review and approval. Only experienced IRB members may conduct reviews using the expedited procedure. An experienced IRB member means a voting member or alternate voting member with appropriate qualifications and expertise who has received training in the expedited review categories, and possesses the expertise needed to review the proposed research. Normally reviewers serve on the IRB at least 3 months before being designated as experienced reviewers.

2. The Reviewer assigned will have expertise in the area of the research adequate to the scope and complexity of the research. The Reviewer may request a second reviewer, request review by an expert consultant to the IRB, or refer the study to full IRB Committee for determination. In the case of multiple reviewers, decisions are made by consensus of the review. In the absence of consensus, the application is submitted to the convened IRB. However, the determination of disapproval can only be made by the convened IRB.

3. The reviewer using the expedited procedure is provided and reviews the same materials as the primary reviewers for the convened IRB.

4. The criteria for approval using the expedited procedure are the same as those for review by a convened IRB.

5. Reviewers use a worksheet to ensure all regulatory requirements are met. The criteria for eligibility for continuing review using the expedited procedure are listed on the Expedited Procedure Eligibility – Continuing Review worksheet used by the Reviewer to determine whether research meets one or more expedited categories and other requirements to undergo continuing review using the expedited procedure.

6. Review of the currently approved informed consent document must ensure that the information is still accurate and complete.

7. The reviewer considers any significant new findings that may relate to the participant's willingness to continue participation and whether they should be provided to the participant in an updated informed consent document. Review of currently approved or proposed informed consent document occur during the scheduled continuing review of research by the IRB, but may be done more frequently if new information becomes available. If a reviewer using the expedited procedure identifies significant new findings, the application should normally be sent for review by the convened IRB.

8. IRB members determine whether continuing review should occur at an interval less than one year, based on information about anticipated risks posed by the research, and any new information including reports of non-compliance, and complaints or other unanticipated problems. If a reviewer using the expedited procedure determines a shortened continuing review interval would be indicated, the application should normally be sent for review by the convened IRB.

9. The reviewer using the expedited procedure may approve research or require changes. However, the reviewer may not disapprove; if the reviewer is unable to approve research, it is referred to the convened IRB.

E. Process used by Staff to notify the IRB, researchers, and organization officials of the results of reviews

1. The convened IRB is notified of the findings and actions of research applications that have been approved through the expedited procedure with the IRB agenda.

2. The Human Research Protection Administrator designated in the Department's FWA, and the Director, Office of Public Health Research, are the organization officials notified of the findings of the IRB. Staff include these officials when distributing draft minutes of meetings of the convened IRB to members of the IRB committee.

3. Researchers are notified of the IRB's decision to approve, disapprove, or require modifications to secure approval through the IRBWise system.

    a. The communication from IRBWise includes modifications or clarifications required as a condition for IRB approval.

    b. If the IRB disapproves a proposed research study, researchers are informed through IRBWise of the IRB's reasons for the decision, and how the researcher may respond in person or in writing.

    c. The communication from IRBWise includes modifications or clarifications required as a condition for IRB approval.

4. Researchers are notified of the approval period for research through IRBWise. If the study is reviewed at the convened IRB meeting, and approved with minor changes to be reviewed and verified by the chair, then once the chair verifies that the changes required by the convened IRB have been made, the approval period begins with the date of the convened meeting. If the study is reviewed at the convened IRB meeting, and the convened IRB requires substantial changes and defers the study, it is returned to the investigator. When the investigator re-submits the application, the study is reviewed again by the convened IRB (normally the same committee). If the convened IRB approves, the approval date is the date of the meeting where the changes were reviewed and approved. The expiration date is the last date that the protocol is approved. For example, if a study is approved through June 10, authorization to conduct research expires at midnight on June 10.

F. Process for managing expiration of IRB Approval

1. There is no grace period extending authorization to conduct research beyond the expiration date of IRB approval. If the researcher has not provided continuing review information to the IRB or the IRB not approved the research by the specified expiration date, all interactions and interventions on current participants must stop, unless the IRB Chair finds an over-riding safety concern or ethical issue involved such that it is in the best interests of study participants to continue. If the IRB requires

changes to the research at continuing review, this does not extend the expiration period. Expiration of authorization to conduct research is automatic and requires no decision, determination, or action by an IRB. Such expirations of approval are not suspensions of IRB approval, terminations of IRB approval, or administrative holds. Allowing a protocol to expire is considered non-compliance, and is also reviewed for non-compliance. (See DOHP 400-10.1, “Investigating any Noncompliance, Serious or Continuing Noncompliance”).

2. The researcher must immediately provide documentation to IRB staff that all research has stopped.

3. Once notified of the expiration, the Investigator must immediately submit to the IRB Chair, a list of research subjects for whom expiration of the research would cause harm, where applicable

    a. An IRB Chair reviews this list and allows individual participants to continue participating in the research interventions or interactions only when the IRB finds an over-riding safety concern or ethical issue involved such that it is in the best interests of individual participants to continue participating. The convened IRB is informed.

4. Enrollment of new subjects cannot occur on or after the expiration of IRB approval.

VI. History Notes

The Office of Public Health Research, Ethics and Human Research Protections Program is responsible for this policy.

Reviewed 08/23/2013

Replaces DOHP 400-4.8, "Review of Human Subjects: Continuing Review"

VII. Signature Block with Effective Date

Ana M. Viamonte Ros, M.D., M.P.H. Date
State Surgeon General
Florida Department of Health

I. Policy

It is the policy of the Department of Health (DOH) Institutional Review Board (IRB) that changes in approved research are not implemented without prior IRB approval, except to eliminate immediate hazards to participant.

II. Authority

A. Chapter 381.86, Institutional Review Board, *Florida Statutes*

B. Rule 64H-2.001, Institutional Review Board, *Florida Administrative Code*

C. Rule 64H-2.002, Institutional Review Board Applications, *Florida Administrative Code*

III. Supportive Data

A. 45 CFR 46.109

B. 21 CFR 56.108(a), 21 CFR 46.109

C. OHRP Guidance on Written Institutional Review Board (IRB) Procedures

IV. Definitions

See DOHP 400-11.1, “Definitions”.

V. Procedures

A. Researchers submit applications in IRBWise to request approval to modify or amend an approved research study

1. Investigators must submit the exact text of an amendment or other revision to the protocol and any proposed changes to the consent document to the IRB, and a summary of the changes. Revised documents must be submitted with the changes highlighted, and clean versions.

2. Modifications to the informed consent document must take into account both prospective research subjects and, if applicable, research subjects already enrolled in the study.

3. The Investigator may make a modification to research activities to avoid an immediate hazard to the participant but must report this to the IRB as soon as possible, but within 5 business days; see policy, DOHP-400-4.6, “Problems Requiring Prompt Reporting to the IRB”.

4. Any changes made to research without prior IRB approval, except to

avoid an immediate hazard, will be evaluated using the policy, DOHP 400-10.1, “Investigating any Non-Compliance, Serious or Continuing NonCompliance.

B. Staff conduct pre-review and assign reviewers based on authority designated by the IRB Chairs

1. Staff conducts pre-review of applications for completeness using the Administrative Review worksheet in IRBWise. Incomplete applications are returned with instructions for the researcher to revise and submit a complete application.

2. When applications are complete, staff assign reviewers using authority delegated from the IRB Chairs to assign reviewers based on the qualifications and expertise listed in the IRB membership roster. When a study involves vulnerable populations, staff assign a reviewer with appropriate expertise in the specific vulnerable population. If staff are unsure, they consult an IRB Chair.

3. HRPP Staff, in consultation with an IRB Chair when necessary, evaluate each study and determine there is sufficient expertise or knowledge to review the research. Applications are added to the agenda of the next available committee that has reviewers possessing necessary qualifications and expertise. Applications are normally assigned to the next agenda, unless that committee of the IRB does not have relevant qualifications and expertise. For example, if the application involves a vulnerable population such as prisoners, the application is assigned to the next meeting that a prisoner representative is in attendance.

   a. If HRPP Staff determine a consultant is needed, they identify persons with relevant qualifications and expertise by seeking suggestions from persons including, but not limited to, IRB members and Chairs, relevant DOH subject matter experts, DOH Bureau Chiefs and Division Directors, federal partners such as the Centers for Disease Control and Prevention, university partners, or through a literature search.

   b. Consultants provide information to the IRB by completing a reviewer comment worksheet in IRBWise. In addition, consultants may also present information to the convened IRB by attending a meeting. However, when a consultant attends a meeting, the consultant does not vote.

4. If the Reviewer has a conflict of interest, the Reviewer will contact the IRB Administrator or Assistant IRB Administrator and recuse themselves from the review. (See DOHP 400-3.2, “Committee Member, Consultant, and Staff Conflicting Interests)

C. Review of Amendments by the Convened IRB

1. The Department uses a primary reviewer system for all review of research by the convened IRB. The electronic system provides members access to all materials. Reviewers are provided and review all modified documents.

3. Reviewers complete or discuss in detail at the convened IRB meeting a worksheet to ensure all regulatory requirements are met, when the modifications affect one or more criteria. One or more primary reviewers use the worksheet to present the study to other board members, and to ensure there is sufficient discussion by the convened IRB to ensure the regulatory criteria for approval are met.

4. IRB members may request a consultant to supplement the IRB's review. (See DOHP 400-3.1, "Composition of the IRB")

5. Reviewers determine whether any significant new findings that may relate to the participant's willingness to continue participation should be provided to the participant in an updated informed consent document.

6. Major changes in research shall be reviewed by the convened IRB. The convened IRB may also review minor changes.

D. Review of Amendments by a Reviewer Using the Expedited Procedure

1. Applications involving requests to make minor changes to the research that are eligible for review using the expedited procedure are assigned to one or more experienced reviewers from the designated IRB for review and approval. Only experienced IRB members may conduct reviews using the expedited procedure. An experienced IRB member means a voting member or alternate voting member with appropriate qualifications and expertise who has received training in the expedited review categories, and possesses the expertise needed to review the proposed research. Normally reviewers serve on the IRB at least 3 months before being designated as experienced reviewers.

2. The Reviewer assigned will have expertise in the area of the research adequate to the scope and complexity of the research. The Reviewer may request a second reviewer, request review by an expert consultant to the IRB, or refer the study to full IRB Committee for determination. In the case of multiple reviewers, decisions are made by consensus of the review. In the absence of consensus, the application is submitted to the convened IRB. However, the determination of disapproval can only be made by the convened IRB.

3. The reviewer using the expedited procedure is provided and reviews the same materials as the primary reviewers for the convened IRB.

4. The criteria for approval using the expedited procedure are the same as those for review by a convened IRB.

5. Reviewers use a worksheet to ensure all regulatory requirements are met. The criteria for eligibility for continuing review using the expedited procedure are listed on the Expedited Procedure Eligibility – Amendments worksheet used by the Reviewer to determine whether research meets one or more expedited categories and other requirements to undergo review using the expedited procedure.

6. The reviewer using the expedited procedure may approve research or require changes. However, the reviewer may not disapprove; if the reviewer is unable to approve research, it is referred to the convened IRB.

E. Minor Amendments

1. Minor changes are changes that pose no more than minimal risk. Proposed minor changes to previously approved research may be reviewed in an expedited manner. Examples of minor modifications may include, but are not limited to, the following:

   a. The addition of research activities that would be considered exempt or expedited if considered independent from the main research protocol

   b. Narrowing the range of the inclusion criteria;

   c. Broadening the range of the exclusion criteria

   d. Decreasing the number or volume of biological sample collections, provided that such a change does not affect the collection of information related to safety evaluations

   e. An increase in the length of confinement or number of study visits for the purpose of increased safety monitoring

   f. A decrease in the length of confinement or number of study visits, provided that such a decrease does not affect the collection of information related to safety evaluations

   g. Alterations in human research participant payment or liberalization of the payment schedule with proper justification

   h. Changes to improve the clarity of statements or to correct

typographical errors, provided that such a change does not alter the content or intent of the statement

i. The addition or deletion of qualified Investigators

j. A change in funding source

2. Minor changes must meet one or more of the categories eligible for expedited review listed in the Expedited Procedure Eligibility – Amendments worksheet

F. Major Amendments

1. If the study was approved using the expedited procedure, and the change is not minor, it may be reviewed using the expedited procedure if it continues to meet one or more expedite categories.

2. When a proposed change in a research study is not minor, then the convened IRB must review and approve changes at a convened meeting before changes can be implemented. Examples of major modifications may include, but are not limited to, the following:

a. Broadening the range of inclusion criteria

b. Narrowing the range of exclusion criteria

c. Alterations in the dosage or route of administration of an administered drug

d. Extending substantially the duration of exposure to the test material or intervention

e. Alterations in the dosage form (e.g., tablet to capsule or oral liquid) of an administered drug, provided the dose and route of administration remain constant

f. The deletion of laboratory tests, monitoring procedures, or study visits directed at the collection of information for safety evaluations

g. The addition of serious unexpected adverse events or other significant risks to the Informed Consent Document

h. Changes, which, in the opinion of the IRB chairperson or his/her designee, do not meet the criteria or intent of a minor modification

VI. History Notes

The Office of Public Health Research, Ethics and Human Research Protections Program is responsible for this policy.

Reviewed 08/23/2013

Replaces DOHP 400-4.7, "Amendments to Approved or Exempt Research"

VII. Signature Block with Effective Date

Ana M. Viamonte Ros, M.D., M.P.H.. Date
State Surgeon General
Florida Department of Health

I. Policy

It is the policy of the Department of Health (DOH) Institutional Review Board (IRB) that Investigators will report to the IRB as soon as possible all problems defined in this policy.

II. Authority

A. Chapter 381.86, Institutional Review Board, *Florida Statutes*

B. Rule 64H-2.001, Institutional Review Board, *Florida Administrative Code*

III. Supportive Data

A. 45 CFR §46.103(b)(5)(i)

B. 45 CFR §46.116(b)(5)

C. 21 CFR §50.25(b)(5)

D. 21 CFR §56.108(b)(1)

E. 21 CFR §812.150(a)(1)

F. OHRP Guidance on Reviewing and Reporting Unanticipated Problems Involving Risks to Subjects or Others and Adverse Events

G. OHRP Guidance on Reporting Incidents to OHRP

H. FDA Information Sheets: Continuing Review After Study Approval

IV. Definitions

See DOHP 400-11.1, “Definitions”

V. Procedures

A. Requirements for Reporting

Investigators must report the following problems to the IRB as soon as possible, but in all cases within five business days of any of the following:

Adverse event (regardless of whether the event was internal (on-site) or external (off-site) and regardless of whether the event meets the FDA definition of "serious adverse event"), which in the opinion of the principal investigator are both unexpected and related. “Adverse events” not meeting these criteria do not need to be reported.

Information that changes the risks, or potential benefits of the research. For example:

i. Any interim analysis or safety monitoring report indicating the frequency or magnitude of harms or benefits may be different than initially presented to the IRB.

ii. Any paper published from another study that shows that the risks or potential benefits of the research may be different than initially presented to the IRB.

Any breach of confidentiality.

Any change in FDA labeling or withdrawal from marketing of a drug, device, or biologic used in a research protocol.

Any change to the protocol taken without prior IRB review to eliminate an apparent immediate hazard to a research participant.

Any incarceration of a participant in a protocol not approved to enrol prisoners.

Any event that requires prompt reporting to the sponsor.

Any sponsor imposed suspension for risk.

Any complaint of a participant when the complaint indicates unexpected risks or cannot be resolved by the research team.

Any protocol violation (meaning an accidental or unintentional change to the IRB approved protocol) that harmed participants or others or that indicates participants or others may be at increased risk of harm or has the potential to recur.

Any unanticipated adverse device effect (Any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.)

Any non-compliance identified by Department of Health audit or monitoring

Any investigation by FDA or OHRP or other federal agency of

research (not just including this study) by any researcher on the study

Any loss of license or hospital privileges by any researcher on the study

Problems must be reported using IRBWise, the Department's electronic IRB application management system.

Researchers are required to report to all IRBs with jurisdiction over the research, and provide documentation of their determinations to the Department.

Reportable problems should be reported regardless of whether they occur during the study, after study completion, or after participant withdrawal or completion. For example, if the investigator learns during data analysis of a breech in confidentiality that occurred during the recruitment phase, this information should still be reported to the IRB.

B. Criteria used for reviewing unanticipated problems involving risks to participants or others

1. Reviewers determine whether the report meets the definition of "unanticipated problem involving risks to participants or others" by evaluating whether the problem is

a. unexpected (in terms of nature, severity or frequency) given (a) the research procedures, and (b) the characteristics of the participant population being studied.

b. related or possible related to participation in the research (possible related means there is a reasonable possibility that the incident, experience, or outcome may have been cause by participation in the research); and

c. suggests that the research places subjects or others at a greater risks of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

2. These criteria will be applied to evaluate each item of information reported by researchers.

C. Process for administrative screening of each reported problem:

1. The IRB staff, when necessary in coordination with the IRB Chair or an IRB member with relevant subject matter expertise, conducts an administrative pre-review to screen all reports and assess if the problem

involves unanticipated problems involving risks to participants or others. If IRB staff determines the event is not unexpected, not related, and does not suggest that participants or others are placed at greater risk of harm, then the problem is documented in IRBWise as "no further action" with justification. No further action is taken, unless the problem involves non-compliance. See DOH Policy 400-10.1, "Investigating any Non-compliance, Serious and Continuing Non-Compliance."

2. If staff are unable to make a determination, or are unsure, the report is forwarded to an IRB Chair.

D. Process for review of unanticipated problems by the Chair

1. The Chair reviews the report to determine if the problem is an unanticipated problem involving risk to participants or others. If the chair determines the event is not unexpected, not related, and does not suggests that participants or others at greater risk of harm, then the problem is documented in IRBWise as "no further action" with justification. No further action is taken, unless the problem involves non-compliance. See DOH Policy 400-10.3, "Investigating any Non-compliance, Serious and Continuing Non-Compliance."

2. If the chair determines the event is an unanticipated problem involving risks to participants or others, and the problem is not greater than minimal risks to participants or others, then the Chair may review and notify the IRB and report per policy 10.4

2. If the Chair or subject matter expert are unable to make a determination, the report is forwarded for review by the convened IRB. The convened IRB reviews all problem reports where the IRB staff or chair or subject matter expert are unable to determine that the problem report is not an unanticipated problem involving risks to participants or others or not noncompliance. See DOHP 400-10.1, "Investigating any Non-Compliance, Serious or Continuing Non-Compliance".

E. Process for IRB review of reported problems by the convened IRB

1. The convened IRB reviews problem reports using a primary and secondary reviewer system to determine if the problem involves unanticipated problems involving risks to participants.

a. Reviewers are assigned by the IRB staff, where necessary in consultation with the IRB Chair. Where possible, the report will be reviewed by the primary and secondary reviewers who conducted the most recent review of the protocol. Reviewers will have relevant subject matter expertise, and may request additional expertise.

b. All committee members have access to the report and supporting documents submitted with the report (including but not limited to safety monitoring board reports and sponsor reports). In addition, all committee members have access to all documents reflecting the current IRB-approved state of the protocol, including but not limited to the protocol, consent document, and supplemental information.

c. One or more primary reviewers will review the report, all supporting documents, and all the documents reflecting the current IRB-approved state of the protocol.

d. All other committee members will review the report, the initial IRB application updated with any changes, any supporting documents, and the consent document.

2. The IRB will determine whether the report meets the definition of "unanticipated problem involving risks to participants or others" using the criteria specified at V.B above.

3. If the IRB determines the problem is not an unanticipated problem involving risks to participants, no further action will be taken if the problem does not involve noncompliance.

4. If the IRB determines the problem is an unanticipated problem involving risks to participants, then the IRB will determine which of the following actions are appropriate regarding the protocol.

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a. Modification of the protocol.

b. Modification of the information disclosed during the consent process.

c. Providing additional information to past participants.

d. Notification of current participants when such information might relate to participants' willingness to continue to take part in the research.

e. Requirement that current participants re-consent to participation.

f. Modification of the continuing review schedule.

g. Monitoring of the research.

h. Monitoring of the consent.

i. Suspension of the research.

j. Termination of the research.

k. Referral to other organizational entities (legal counsel, county health department director, division director, Deputy Secretary. and State Surgeon General in the role of Institutional Official.

5. The IRBs discussion is documented in minutes, including discussion of controverted issues, if any, and their resolution.

6. The investigator is informed of the IRB's determination using IRBWise.

F. Any unanticipated problems involving risks to participants or others will be reported to regulatory agencies and institutional officials or others following the Department's reporting policy. See DOHP 400-10.3, "Reporting to Institutional Officials, Department or Agency Heads."

VI. History Notes

The Office of Public Health Research, Ethics and Human Research Protections Program is responsible for this policy.

Reviewed 08/23/2013

Replaces DOHP 400-4.9-07

VII. Signature Block with Effective Date

Ana M. Viamonte Ros, M.D., M.P.H.
State Surgeon General
Florida Department of Health

Date

I. Policy

It is the policy of the Department of Health (DOH) Institutional Review Board (IRB) to review and approve all recruitment materials for participants in research conducted under its jurisdiction.

II. Authority

A. Chapter 381.86, Institutional Review Board, *Florida Statutes*

B. Rule 64H-2.001, Institutional Review Board, *Florida Administrative Code*

III. Supportive Data

A. 21 CFR 56.107(a)

B. 21 CFR 56.111(a)(3)

C. 21 CFR 56.111(b)

D. 21 CFR 50.20

E. 21 CFR 50.25

F. 21 CFR 812.20(b)(11)

G. U.S. Food and Drug Administration Information Sheets: “Recruiting Study Subjects,” 1998 Update Clarification of Ethics Opinion 6.03, 65. Finder”s Fees: Payment for the Referral of Patients to Clinical Research Studies

H. 42 U.S.C. ‘1320a-7b(b)

IV. Definitions

See DOHP 400-11.1, “Definitions”

V. Procedures

A. All recruiting and advertising materials must be approved by the IRB. The IRB must assure that appropriate safeguards exist to protect the rights and welfare of research participants and prospective research participants. In fulfilling these responsibilities, the IRB must review all of the research documents and activities that bear directly on the rights and welfare of the participants of proposed research, including the methods and materials that Investigators propose to use to recruit participants.

1. The Investigator must obtain IRB approval for all television, radio, videotape or print advertisements, e-mail solicitations, Internet websites, and other recruitment methods and materials intended for the recruitment of prospective research participants. All methods of advertisement utilized require prior written approval from the facility where research is conducted (for example, the County Health Department Director or Administrator, if research is conducted at a county health department) or a Deputy Secretary, or the Secretary. All methods of advertisement require approval from the IRB prior to their use. All methods of advertisement require approval from the IRB prior to their use.

2. The following examples do not qualify as an advertisement:

    a. Communications intended only to be seen or heard by health professionals, such as “dear doctor” letters and doctor-to-doctor letters;

    b. News stories, so long as they are not intended for recruitment purposes (e.g. a news story would not include a phone number at the end to contact for more information to participate in a particular study, full details of inclusion/exclusion criteria of a particular study, etc.); and

    c. Publicity intended for other audiences (e.g., media releases regarding types of services available or offered by a particular clinic, institute, or physician).

3. The IRB considers advertising or soliciting for study participants to be the start of the informed consent process and subject selection process. Advertisements must be reviewed and approved by the IRB as part of the application package submitted for initial review. When the Investigator decides after the initial approval to advertise for participants or to change the advertisement, the new advertising or changes to approved advertising is considered an amendment to the ongoing study. The IRB reviews the advertising to assure that it is not unduly coercive and does not promise a certainty of cure beyond what is outlined in the consent and the protocol. This is especially critical when a study may involve participants who are likely to be vulnerable to undue influence.

4. When advertising is to be used, the IRB must review the information contained in the advertisement and the mode of its communication, to determine that

    a. the procedure for recruiting participants is not coercive and does not state or imply a certainty of favorable outcome or other benefits beyond what is outlined in the consent document and the protocol.

    b. advertising materials do not include exculpatory language.

c. advertising materials do not emphasize the payment or the amount to be paid, by such means as larger or bold type.

5. The IRB must review the final printer-ready draft copy of printed advertisements before they are sent to a printer to evaluate the relative size of type used and other visual effects. When advertisements are to be taped for broadcast, the IRB must review the final audio or video tape. The IRB may review and approve the wording of the advertisement prior to taping to preclude re-taping because of inappropriate wording. The review of the final taped message prepared from IRB approved text may be accomplished through expedited procedures.

B. Any advertisement to recruit participants should be limited to the information the prospective participants need to determine their eligibility and interest. When appropriately worded, the following items may be included in advertisements:

1. The name, address, and facility or institution of the Investigator or study coordinator (e.g. Florida Department of Health);

2. If applicable, include “investigational, meaning non-FDA approved”;

3. The condition under study and the purpose of the research;

4. In summary form, the criteria that will be used to determine eligibility for the study;

5. A brief list of participation benefits, if any (e.g., a no cost health examination);

6. The time or other commitment required of the participants; and

7. The location of the research and the person or office to contact for further information.

C. Advertising materials should not include the following:

1. Claims, either explicitly or implicitly, that the drug, biologic, device or other type of intervention is safe or effective for the purposes under investigation;

2. Claims, either explicitly or implicitly, that the test article is known to be equivalent or superior to any other drug, biologic, device or intervention;

3. Terms such as "new treatment," "new medication" or "new drug" without explaining that the test article is investigational, meaning non FDA-approved; or

4. Promises of "free medical treatment," when the intent is only to say that participants will not be charged for taking part in the investigation.

5. Compensation for participation in a trial offered by a sponsor to include a coupon good for a discount on the purchase price of the product once it has been approved for marketing.

D. IRB must review payments to determine that:

1. The amount of payment and the proposed method and timing of disbursement neither is coercive nor presents undue influence.

2. Credit for payment accrues as the study progresses and not be contingent upon the participant completing the entire study.

3. Any amount paid as a bonus for completion is reasonable and not so large as to unduly induce participants to stay in the study when they would otherwise have withdrawn.

4. All information concerning payment, including the amount and schedule of payments, is set forth in the consent document.

E. Receptionist Scripts. The first contact prospective study participants make is often with a receptionist who follows a script to determine basic eligibility for the specific study. The IRB must review the script and procedures to assure that they adequately protect the rights and welfare of the prospective participants. The IRB must have assurance that any information collected about prospective participants will be appropriately handled.

F. Internet Recruitment. All advertisements and recruitment methods must be reviewed and approved by the IRB prior to implementation except for two specific clinical trial listing services which do not require prospective IRB approval as determined by the Food and Drug Administration. These include the National Cancer Institute's cancer clinical trial listing (PDQ) and the government sponsored AIDS Clinical Trials Information Service (ACTIS). For other Internet recruitment sites, IRB review and approval is required to assure that the information does not promise or imply a certainty of cure or other benefit beyond what is contained in the protocol and the informed consent document. In addition, the Investigator must assure that the information shared for Internet recruitment is in accordance with their signed clinical trial agreement or grant.

G. Department of Health Mass Communication E-mail. Advertising submitted through mass email solicitation at DOH should be simple, readable, and understandable. It should meaningfully and respectfully convey a message to a broad spectrum of the DOH community. It should be text-based and written in paragraphs. The following format is recommended when utilizing this method of recruitment or advertisement:

1. A headline that describes the study and volunteers needed;
2. Use sentences and paragraphs;
3. Paragraph 1 – include enough information to help readers self-select;
4. Paragraph 2 – purpose of the study;
5. Paragraph 3 – requirements of participation;
6. Paragraph 4 – benefit to the participant or a statement there is no benefit; and
7. Paragraph 5 – a contact person "for more information".

H. Students as Participants. The IRB should exercise oversight with the use of students as participants in research.

I. Data Base/Primary Care Physician Recruitment. Often times Investigators request to use search methods of particular databases looking for potential participants that may be eligible for their research projects (e.g., disease, age, sex, etc.), or they request to contact primary care providers (PCP) for access to potential participants from the PCP's patient population. These recruitment methods require IRB approval prior to initiation.

J. Inclusion of Women, Children and Minorities. The inclusion of women, men, and minorities in research is important, both to ensure that they receive an appropriate share of the benefits of research and that they do not bear a disproportionate burden. To the extent that participation in research offers direct benefits to the participants, under-representation of men, women or minorities denies them the opportunity to benefit. Moreover, for purposes of generalizing research results, Investigators must include the widest possible range of population groups.

K. Involvement of Humans in Research. NIH-supported Investigators must provide to the IRB details of the proposed involvement of humans in their research protocols, including the characteristics of the subject population, anticipated numbers, age ranges, and health statuses. The proposed research should specify the gender and racial/ethnic composition of the subject population, as well as criteria for inclusion or exclusion of any subpopulation. If ethnic, racial, and gender estimates and continuing review numbers are not included in the background data for a protocol, the Investigators must provide a clear rationale for exclusion of this information.

L. Finder's Fees and Bonus Payments. Research sponsors may offer to pay Investigators or study personnel an additional fee to encourage participant recruitment efforts and the timely or accelerated opening of research studies. In some situations, these payments are prohibited. Each situation should be reviewed to be sure that it complies with Federal and state regulations, ethical opinions, DOH IRB, and other department policy.

M. Legal Implications

1. The Council on Ethical and Judicial Affairs of the American Medical Association denounced the practice of finder's fees in December 1994;

2. The Federal anti-kickback statute can also be implicated by this practice; and

3. For physicians, Florida Statutes may prohibit certain recruitment incentives and may be subject to disciplinary action. See for example, Chapters 456.045 and 458.311, Florida Statutes.

N. During the process of recruiting DOH clients or using a DOH facility to recruit participants, the Investigator must provide information on how a prospective research participant can contact the DOH Human Research Protection Program, including the toll-free telephone number, or if applicable the County Health Department Medical Director to voice concerns or ask questions.

VI. History Notes

The Office of Public Health Research, Ethics and Human Research Protections Program is responsible for this policy.

Reviewed 08/23/2013

Replaces DOHP 400-5.6-07

VII. Signature Block with Effective Date

Ana M. Viamonte Ros, M.D., MPH.
State Surgeon General
Florida Department of Health

Date

I. Policy

It is the policy of the Department of Health (DOH) Institutional Review Board (IRB) to determine if a specific research project requires the additional safeguard of a monitor to observe the consent process or serve as an advocate for the research participants to ensure the protection of the health and safety of participants.

II. Authority

A. Chapter 381.86, Institutional Review Board, *Florida Statutes*

B. Rule 64H-2.001, Institutional Review Board, *Florida Administrative Code*

C. 45 CFR 46.109(e)

D. 45 CFR 46.111(b)

E. 21 CFR 109(f)

F. 21 CFR 56.111(b)

III. Supportive Data

A. Office for Human Research *Protections' Protecting Human Research Subjects Guidebook (1993).* http://www.hhs.gov/ohrp/irb/irb_chapter3.htm

IV. Definitions

See DOHP 400-11.1, “Definitions”

V. Procedures

A. The convened IRB will determine if a specific research project requires the additional safeguard of a monitor to observe the consent process or serve as an advocate for the research subjects to ensure the protection of the rights and welfare of the subjects. This may include, but is not limited to the following:

1. Situations where participation in research is the only available medical option and no standard of care is available or proven effective.

2. Subjects who may, due to their illness or their hope at the prospect of receiving relief or “treatment” through research, be too willing to participate (not make a voluntary decision) or give due consideration to the range of options, some of which may not include research.

3. Research where the risk is such that a second party (i.e. consent monitor) functions as a subject advocate to enhance the informed consent process

4. Potential subjects may include vulnerable populations. Examples include but are not limited to the following:

    a. Subjects with limited or no resources;

    b. Subject population (e.g., runaway minors, refugees) where sensitive surveys, interviews, interactions and/or interventions may pose more than minimal risk;

    c. Subjects with diminished decision-making capabilities.

5. Situations where the IRB is concerned about the conduct of the study or the process of obtaining informed consent. Examples include but are not limited to the following.

    a. Complaints from subjects or others regarding the conduct of the study;

    b. Complaints from subjects or others regarding the consent process with the investigators;

    c. Audit report to the IRB identifying problems with the execution of the consent process and document;

    d. Audit report to the IRB identifying problems with the execution of the consent process and document;

    e. Audit review of violations or events of non-compliance identifying problems with the consent process or conduct of the study;

6. Situations where the convened IRB requires the additional safeguard of a consent monitor are distinct from quality improvement monitoring activities (See DOHP-400-10.1, “IRB Compliance Activities”)

B. The convened IRB may determine at any stage of the research review process the need for a consent monitor and may require the researcher to provide resources for monitoring.

C. The determination to remove the requirement of a consent monitor for specified research will be made by the convened IRB.

1. Reports from the consent monitor of the observations made during the consent process and/or “Summary of Consent Monitoring for Research” documents will be provided to the IRB.

D. Formal correspondence to the principal investigator will describe the IRB determination of the need and reasons for the requirement to use a consent monitor for the respective research project.

1. Correspondence will indicate the IRB's determination of whether the principal investigator or the IRB will identify a consent monitor. The IRB may seek the researcher's involvement in identifying a consent monitor; however, the selection of the consent monitor is ultimately the IRBs decision.

2. Correspondence will indicate the time frame for the response from the principal investigator and must approve the suggested consent monitor candidate.

3. With the approval of the Director, Office of Public Health Research, selected trained DOH Office of Public Health Research staff may serve as a consent monitor.

4. Approval letters will include language specifying that research may only be conducted under the terms of the IRB's specified monitoring requirements.

E. All potential consent monitor candidates will receive training from the Ethics and Human Research Protection Program. Training will include a review of the following.

1. Roles and responsibilities of the consent monitor.

2. Evaluation to Sign a Consent Form for Research.

3. Reporting Consent Monitoring for Research to the IRB.

F. Consent Monitoring Process

1. The principal investigator or designee will contact the consent monitor in advance of a consent session with a potential subject.

2. The principal investigator or designee will provide (in advance) to the consent monitor a copy of the current approved informed consent document.

3. The consent monitor has five principal duties:

a. Listen: The consent monitor should listen to the consent process and exchange between the investigator and the subject and the subject's family;

b. Observe: The consent monitor should closely observe the communication between the investigator and the subject. The monitor

should use her/his knowledge of the consent document and be prepared to ask questions of the investigator or the subject if it appears that things are not clear.

c. Ask Questions: The consent monitor should be prepared to ask questions in order to facilitate comprehension on the part of the subject. In order to understand whether the subject fully comprehends the research and is making a knowledgeable decision about participation, questions should elicit a response from the subject that requires some deliberation and thought about the research rather than yes/no questions;

d. Document: Document the interactions, questions, answers, and the decision making process.

e. Decide: Decide with the investigator and the subject whether the subject should be enrolled in the research, provided additional time to consider participation in the research, or should not be enrolled. The consent monitor may determine that a subject does not understand the consent process or the research and request that the investigator re-review the materials with the subject. If the monitor does not think the subject understands the research or all items of the consent document, then the subject should not be enrolled in the research;

4. The investigator will introduce the consent monitor to the potential subject and provide an explanation for the consent monitor's presence.

5. The consent monitor will utilize a copy of the approved informed consent document during the consent process to assure that all elements of the consent document are addressed by the investigator.

   a. At any time during the consent session, the consent monitor may request that the investigator review or clarify information for the potential subject and/or seek clarification of comprehension from the potential subject;

6. At the end of the consent session, the consent monitor will utilize a checklist to assess the potential subject's comprehension of the consent process.

   a. The potential subject will be asked the questions on the evaluation form by the consent monitor;

   b. The consent monitor may ask additional questions, as necessary;

7. The consent monitor will utilize a copy of the approved informed consent document during the consent process to assure that all elements of the consent document are addressed by the investigator.

8. The consent monitor will prepare a summary for IRB review.

    a. The summary will be maintained in the specific IRB research protocol file in IRBWise;

9. The summary will be reviewed by the convened IRB at an identified interval (e.g., every five subjects) as determined by the convened IRB.

VI. History Notes

The Office of Public Health Research, Ethics and Human Research Protections Program is responsible for this policy.

Reviewed 08/23/2013

Replaces DOHP 400-4.8-08

VII. Signature Block with Effective Date

Ana M. Viamonte Ros, M.D., M.P.H.
State Surgeon General
Department of Health

Date

I. Policy

It is the policy of the Department of Health (DOH) Institutional Review Board (IRB) to assure that provisions are made to obtain legally authorized informed consent prospectively from each research participant or permission from his or her legally authorized representative.

II. Authority

A. Chapter 381.86, Institutional Review Board, Florida Statutes

B. Rule 64H-2.001, Institutional Review Board, *Florida Administrative Code*

III. Supportive Data

A. 45 CFR 46.111

B. 45 CFR 46.116 and 46.117

C. 21 CFR 50.24, 50.25 and 50.55

D. 38 CFR 16 and 17

E. OHRP Guidance Document: Informed Consent, Legally Effective and Prospectively Obtained (OPRR REPORTS 95-03)

IV. Definitions

See DOHP 400-11.1, “Definitions”

V. Procedures

A. Presumption of Informed Consent in Research

The IRB assures that provisions are made to obtain legally effective informed consent prospectively from each research participant, or permission from his/her legally authorized representative. However, there are circumstances in which the IRB may grant a waiver of informed consent in accordance with Federal regulations.

B. Presumption that Informed Consent will be Documented

Documentation of informed consent is obtained unless alternate procedures are approved by the IRB. The IRB reviews all informed consent documents to assure the adequacy of the information contained in the consent document, and adherence to Federal regulations regarding the required elements of informed consent.

C. Presumption that Consent will be obtained Prior to Research

Informed consent is obtained from the participant or permission from a legally authorized representative prior to initiating research activities. This includes recruitment and screening procedures.

1. Children. For subjects who meet the Food and Drug Administration (FDA) and Department of Health and Human Services (DHHS) definition of "children" their parents or guardians are the legally authorized representatives who may grant permission for their participation in research. Parental permission and minor assent will be obtained per DOHP 400-6.3, "Special Categories of Research: Children"

2. Cognitively Impaired Adult Subjects. If a researcher intends to enroll adult subjects who lack the capacity to consent, legal counsel will be consulted on a protocol-by-protocol basis to determine who is authorized to grant permission for participation in research prior to IRB approval.

3. Research over Extended Periods. Studies involving subjects who are decisionally-impaired may take place over extended periods of time. The IRB considers whether and when periodic reconsenting of individuals is required to assure that a subject's continued involvement is voluntary. The IRB may require that the Investigator reconsent subjects after taking into account the study's anticipated length and the condition of the individuals to be included (e.g., subjects with progressive neurological disorders). Additionally, the IRB considers whether and when to require a reassessment of decision-making capacity

VI. History Notes

The Office of Public Health Research, Ethics and Human Research Protections Program is responsible for this policy.

Reviewed 08/23/2013

VII. Signature Block with Effective Date

Ana M. Viamonte Ros, M.D., M.P.H.
State Surgeon General
Florida Department of Health

Date

I. Policy

It is the policy of the Department of Health (DOH) Institutional Review Board (IRB) that informed consent be documented in writing as determined in the IRB review and approval process.

II. Authority

A. Chapter 381.86, Institutional Review Board, *Florida Statutes*

B. Rule 64H-2.001, Institutional Review Board, *Florida Administrative Code*

III. Supportive Data

A. 45 CFR 46.111

B. 45 CFR 46.116 and 46.117

C. 21 CFR 50.24, 50.25 and 50.55

D. 38 CFR 16 and 17

E. OHRP Guidance Document: Informed Consent, Legally Effective and Prospectively Obtained (OPRR REPORTS 95-03)

IV. Definitions

See DOHP 400-11.1, Definitions

V. Procedures

A. All documentation of informed consent shall include the following contact information for participants or prospective participants and their representatives to contact to voice concerns, ask questions, or obtain information about their rights as a research participant:

1. The Principal Investigator or a senior research team member;

2. The Investigator's local IRB if it is not the DOH IRB;

3. Where to go and whom to contact in the event of a research-related injury when medical interventions or treatments are involved in the research;

4. The DOH IRB, including the toll-free telephone number; and

5. If the research site is in a county health department facility, the Medical Director of the facility.

B. Three Options for Documentation of Informed Consent

1. The IRB may approve procedures for documentation of informed consent that involve either:

    a. A written consent form signed by the participant;

    b. A short form written consent with oral presentation; or

    c. In limited circumstances, a waiver of the signed written consent form.

    Each of these options is described in detail below.

2. It is the responsibility of the IRB Committee to determine which of the procedures described below is appropriate for documenting informed consent in research applications that it reviews. Generally, only Option One will be appropriate.

C. Option One: Written Consent Form Signed by the Participant or Legally Authorized Representative.

1. In most circumstances, the IRB should require that informed consent is documented by the use of a written consent form approved by the IRB and signed and dated by the participant or the participant's legally authorized representative.

2. This consent form must embody the required elements of informed consent required by IRB Procedure 5.2.2 “Incorporating the Elements of Informed Consent”), in addition to any applicable additional elements that are required by the Federal regulations. This form may be read to the participant or the participant’s legally authorized representative. However, the Investigator should allow the participant or the legally authorized representative adequate opportunity to read and consider the consent document before it is signed. A copy of the signed and dated document must be given to the person signing the form.

    a. The written informed consent document should embody, in language understandable to the participant, all the required elements necessary for legally effective informed consent (*See* DOH IRB Policy 5.1, “Legally Effective and Prospectively Obtained Informed Consent”).

    b. Participants who do not speak English should be presented with an informed consent document written in a language understandable to them.

D. Option Two: Oral Presentation Using the Short Form

1. As an alternative to standard written informed consent documents, oral

presentation of informed consent information may be used, and documented using the "short form" consent document. The "short form" consent document should generally only be used when the research involves no more than minimal risk to subjects or, if the research involves more than minimal risk, presents the prospect of direct benefit to individual subjects. The "short form' consent document attests that the elements of consent have been presented orally. In such cases, the participant must be provided with both:

a. A short form written informed consent document stating that the required basic and appropriate additional elements of consent (*See* DOH IRB Policy 5.1, Legally Effective and Prospectively Obtained Informed Consent) have been presented orally to the participant or the participant's legally authorized representative; and

b. A signed and dated copy of the written summary of the information, approved by the IRB, that is presented orally to the participant or the participant's legally authorized representative.

2. Witness Required. A witness to the oral presentation is required. The witness must sign and date both the short form written informed consent document and a copy of the written summary.

3. The participant or the legally authorized representative must sign and date the short form written consent document.

4. The person obtaining consent (e.g., the Principal Investigator) must sign and date a copy of the written summary of the information that is presented orally. The person obtaining consent may not be the witness to the consent.

5. Participants Who Do Not Speak English

a. It is preferable that the written informed consent documents for non-English speaking participants embody, in a language understandable to the participant, all the required elements necessary for legally effective informed consent.

b. Alternatively, the regulations permit oral presentation of informed consent information in conjunction with a short form written consent document (stating that the elements of consent have been presented orally) and a written summary of what is presented orally. A witness to the oral presentation is required, and the participant must be given signed and dated copies of the short form informed consent document and the summary. When this procedure is used with participants who do not speak English, the following are required:

(1) The oral presentation and the short form written informed consent document should be in a language understandable to the participant;

(2) The IRB-approved English language informed consent document may serve as the summary; and

(3) A witness who is fluent in both English and the language of the participant should be present.

c. The IRB Committee must review and approve all foreign language versions of the informed consent document or the short form informed consent documents prior to use.

d. Expedited review of these versions is acceptable if the convened IRB Committee has already approved the research study, the full English language informed consent document, and the English language version of the short form document.

E. Option Three: Waiver of Documentation See DOHP 400-5.3, "Waiver or Alteration of Informed Consent"

F. No Verbal Consent. Verbal agreement to participate in a research study is not permitted unless the documentation or process of informed consent is waived by the IRB.

G. Use of Facsimile, Mail or Email to Document Informed Consent

1. The IRB may approve a process that allows the informed consent document to be delivered by mail, facsimile to the potential participant or the potential participant's legally authorized representative and to conduct the consent interview by telephone when the participant or the legally authorized representative can read the consent document as it is discussed. A document may also be sent as an attachment via email for the participant to print out and sign and return.

2. All other applicable conditions for documentation of informed consent must also be met when using this procedure.

H. Standard Surgical Consent Documents

1. Standard surgical or medical treatment consent documents may be used in lieu of specific research informed consent documents but they must include all the elements of consent as required by DOH policy (*See* DOHP 400-5.1, "Legally Effective And Prospectively Obtained Informed Consent ") and Federal regulations for standard research consent documents, in addition to applicable additional elements, and must be approved by the IRB prior to its use for research.

2. Reliance on such documents for research generally requires a formal waiver of consent in accordance with Federal Regulations and DOH IRB Policy.

VI. History Notes

The Office of Public Health Research, Ethics and Human Research Protections Program is responsible for this policy.

Reviewed 08/23/2013

Replaces DOHP 400-5.2-07

VII. Signature Block with Effective Date

Ana M. Viamonte Ros, M.D., M.P.H.
State Surgeon General
Florida Department of Health

Date

I. Policy

It is the policy of the Department of Health (DOH) Institutional Review Board (IRB) to grant a waiver from informed consent for research or an exception from informed consent for qualifying emergency research in congruence with the Federal regulations and DOH IRB policies and procedures.

II. Authority

A. Chapter 381.86, Institutional Review Board, Florida Statutes

B. Rule 64H-2.001, Institutional Review Board, *Florida Administrative Code*

III. Supportive Data

A. 45 CFR 46

B. 45 CFR 46.116

C. 21 CFR 50 and 56

D. 21 CFR 50.24

E. OHRP Guidance Document; Emergency Research Informed Consent Requirements (OPRR 96-01)

F. 45 CFR 46 Waiver Of Informed Consent Requirements in Certain Emergency Research (Federal Register, Vol. 61, No. 192, pp. 51531-51533, October 2, 1996)

G. FDA Guidance for Institutional Review Boards and Clinical Investigators, 1998 Update.

H. DOH IRB Policy, “Legally Effective and Prospectively Obtained Informed Consent”

I. DOH IRB Policy, “Emergency Use of FDA Regulated Products”

IV. Definitions

See DOHP 400-11.1, Definitions

VI. Procedures

A. The IRB follows the criteria in 45 CFR 46.116(c-d), 45 CFR 46.117, and 21 CFR 177(c), 21 CFR 56.109(c)(1) and 21 CFR §56.109(d) to determine whether the IRB can waive the requirement to obtain written documentation of the consent process.

B. The IRB follows the criteria in 45 CFR 46.116(c-d), 45 CFR 46.117, and 21 CFR 177(c), 21 CFR 56.109(c)(1) and 21 CFR 56.109(d) determine whether the IRB can waive or alter the consent process.

C. Procedures for waiving or altering the process and documentation of parental permission and minor assent are described in DOHP 400-6.3, "Research Involving Children."

D. Exception from Informed Consent Requirements for Emergency Research Subject to FDA Regulation

IMPORTANT NOTE: Do not confuse with Emergency Use of FDA Regulated Products – *See* DOH IRB Policy 7.5, "Emergency Use of FDA Regulated Products and Emergency Use Authorizations."

The IRB may review and approve a clinical investigation without requiring prospective informed consent of <u>all</u> research subjects if the IRB (with the concurrence of a licensed physician who is a member of or consultant to the IRB and who is not otherwise participating in the clinical investigation) finds and documents each of the following:

1. The target population for the research is in a life-threatening situation, available treatments are unproven or unsatisfactory, and the collection of valid scientific evidence, which may include evidence obtained through randomized placebo-controlled investigations, is necessary to determine the safety and effectiveness of particular interventions.

2. Obtaining informed consent is not feasible because:

    a. The subjects will not be able to give their informed consent as a result of their medical condition;

    b. The intervention under investigation must be administered before consent from the subjects' legally authorized representatives is feasible; and

    c There is no reasonable way to identify prospectively the individuals likely to become eligible for participation in the clinical investigation.

3. Participation in the research holds out the prospect of direct benefit to the subjects because:

    a. The subjects are facing a life-threatening situation that necessitates intervention;

    b. Appropriate animal and other preclinical studies have been conducted, and the information derived from those studies and

related evidence support the potential for the intervention to provide a direct benefit to the individual subjects; and

c. The risks associated with the investigation are reasonable in relation to what is known about the medical condition of the potential class of subjects and the risks and benefits of the proposed intervention or activity.

4. The clinical investigation could not practicably be carried out without the waiver.

5. The proposed investigational plan defines the length of the potential therapeutic window based on scientific evidence, and the Investigator has committed to attempting to contact a legally authorized representative for each subject within that window of time and, if feasible, to asking the legally authorized representative contacted for consent within that window rather than proceeding without consent. The Investigator must agree to summarize efforts made to contact legally authorized representatives and make this information available to the IRB at the time of continuing review.

6. The IRB has reviewed and approved informed consent procedures and an informed consent document consistent with Federal regulations and IRB policies and procedures. The informed consent procedures and the informed consent document are to be used with subjects or their legally authorized representatives in situations where use of such procedures and documents is feasible.

7. Additional protections of the rights and welfare of the subjects will be provided, including, at least:

a. Consultation (including, where appropriate, consultation carried out by the IRB) with representatives of the communities in which the clinical investigation will be conducted and from which the subjects will be drawn;

b. Prior to the initiation of the clinical investigation, public disclosure to the communities in which the clinical investigation will be conducted and from which the subjects will be drawn of plans for the investigation and its risks and expected benefits;

c. At the completion of the clinical investigation there are plans for public disclosure of sufficient information to apprise the community and researchers of the study. The information must include the demographic characteristics of the research population and results of the clinical investigation.

d. Establishment of an independent data and safety monitoring committee to exercise oversight of the clinical investigation; and

e. If obtaining informed consent is not feasible and a legally authorized representative is not reasonably available, the Investigator must commit to attempting to contact within the therapeutic window, the subject's family member who is not a legally authorized representative, and asking whether he/she objects to the subject's participation in the clinical investigation. The Investigator will summarize efforts made to contact family members and make this information available to the IRB at the time of continuing review.

8. Procedures must be in place to inform, at the earliest feasible opportunity, each subject, or if the subject remains incapacitated, a legally authorized representative of the subject, or if such a representative is not reasonably available, a family member, of the subject's inclusion in the clinical investigation, the details of the investigation and other information contained in the informed consent document, specifically that the subject, the legally authorized representative, or the family member may discontinue the subject's participation at any time without penalty or loss of benefits of which the subject is other wise entitled.

9. If a legally authorized representative or family member is told about the clinical investigation and the subject's condition improves, the subject is also to be informed as soon as feasible.

10. If a subject is entered into a clinical investigation with waived consent and the subject dies before a legally authorized representative or family member can be contacted, information about the clinical investigation is to be provided to the subject's legally authorized representative or family member, if feasible.

11. All clinical investigation records, including regulatory files, must be maintained for at least three years after the completion of the clinical investigation and will be accessible for inspection and copying by the regulatory authorities, as applicable.

12. Clinical investigations that are granted an exception to the informed consent requirement under this section must be performed under a separate investigational new drug application (IND) or investigational device exemption (IDE) that clearly identifies that the clinical investigation may include subjects who are unable to consent. The submission of these clinical investigations to the FDA for a separate IND or IDE is required even if an IND for the same drug product or an IDE for the same device already exists. Applications for this IND or IDE may not be submitted as an amendment to the existing IND or IDE.

13. If the IRB determines it cannot approve a request for exception from informed consent requirements in emergency research because the clinical investigation does not meet the criteria according to Federal regulations, IRB policies and procedures, or other relevant ethical concerns, the IRB must document its findings and provide these findings

promptly in writing to the clinical investigator who will forward to the sponsor of the clinical investigation.

E. Emergency Research Not Subject to FDA Regulation

The IRB review finds:

1. The research activity is not subject to FDA regulations in 21 CFR 50 or will not be carried out under an FDA investigational new drug application (IND) or an FDA investigational device exemption (IDE), the application for which has clearly identified the protocols that would include participants who are unable to consent; and

2. Items D 1-10 as stated in option three above are met.

F. DOH does not permit planned emergency research requesting a waiver of informed consent to enroll:

1. Pregnant women and fetuses

2. Prisoners

3. Children

G. No Deferred Consent or Un-Approved Waivers of Informed Consent

Informed consent procedures, which provide for other than legally authorized and prospectively obtained consent, fail to constitute informed consent under Federal regulations for the protection of human subjects in research. Therefore, waiving informed consent using a method other than those described in this policy is a violation of IRB policy and Federal regulations and is subject to reporting to the appropriate Federal, State, and Institutional officials.

VI. History Notes

The Office of Public Health Research, Ethics and Human Research Protections Program is responsible for this policy.

Revised 04/20/2010
Reviewed 08/23/2013

VII. Signature Block with Effective Date

Ana M. Viamonte Ros, M.D., M.P.H. Date
State Surgeon General,

I. Policy

It is the policy of the Department of Health (DOH) Institutional Review Board (IRB) to assure that adequate provisions are made for soliciting the assent and dissent of children and cognitively impaired adults who lack decision-making capacity.

II. Authority

A. Chapter 381.86, Institutional Review Board, Florida Statutes

B. Rule 64H-2.001, Institutional Review Board, *Florida Administrative Code*

III. Supportive Data

A. *The Belmont Report*

B. 45 CFR 46, Subpart D

C. 21 CFR 50, Subpart D

D. DOHP 400-5.1, “Legally Effective and Prospectively Obtained Informed Consent”

E. DOHP 400-6.3, “Research Involving Children”

IV. Definitions

See DOHP 400-11.1, “Definitions”

V. Procedures

A. In instances where the participant is not legally capable of giving informed consent (e.g., minors) or where the participant is cognitively impaired, the IRB must find that adequate provisions are made for soliciting the assent of the participant when, in the judgment of the IRB, the participant is capable of providing assent.

B. In determining whether participants are capable of assenting, the IRB shall take into account the age, maturity, and psychological state of the participant involved. This judgment may be made for all participants to be involved in research under a particular protocol, or for each participant, as the IRB deems appropriate. If the IRB determines that the capability of some or all of the participants is so limited that they cannot reasonably be consulted or that the intervention or procedure involved in the research holds out a prospect of direct benefit that is important to the health or well-being of the participant and is available only in the context of the research, the assent of the participant is not a necessary condition for proceeding with the research. Even where the IRB determines that the participants are capable of assenting, the IRB may still waive the assent requirement under circumstances in which consent may be waived in accord with IRB Policy.

C. When the IRB determines that assent is required, it shall also determine whether and how assent must be documented.

VI. History Notes

The Office of Public Health Research, Ethics and Human Research Protections Program is responsible for this policy.

Revised 05/15/2010
Reviewed 08/23/2013

Replaces DOHP 400-5.4-07

VII. Signature Block with Effective Date

Ana M. Viamonte Ros, M.D., M.P.H. Date
State Surgeon General,

I. Policy

It is the policy of the Department of Health (DOH) Institutional Review Board (IRB) to review research in compliance with applicable regulations to ensure that, when research involves pregnant women who are vulnerable to coercion or undue influence, safeguards are included in the research design to protect the rights and welfare of participants in research.

II. Authority

A. Chapter 381.86, Institutional Review Board, *Florida Statutes*

III. Supportive Data

A. 45 CFR 46 Subpart B

B. 21 CFR §56.111(b)

C. 40 CFR 26.304, 40 CFR 26.404-405

D. 390.0111(6) Florida Statutes, Experimentation on Fetus Prohibited; exception

IV. Definitions

See DOHP 400-11.1, “Definitions”

V. Procedures

A. IRB Review and Approval of Research Involving Pregnant Women

Research involving women who are or may become pregnant shall receive special attention from the IRB because of women's additional health concerns during pregnancy and because of the need to avoid unnecessary risk to the fetus. Further, in the case of a pregnant woman, the IRB shall determine when informed consent of the father is required for research. Special attention is justified because of the involvement of a third party (the fetus) who may be affected but cannot give consent and because of the need to prevent harm or injury to future members of society. Procedural protections beyond the basic requirements for participant protection are prescribed in the federal regulations for research involving pregnant women.

B. 46.204: Research Involving Pregnant Women or Fetuses

Pregnant women or fetuses may be involved in research when all of the following conditions are met:

1. Where scientifically appropriate, preclinical studies, including studies on pregnant animals, and clinical studies, including studies on non-pregnant

women, have been conducted and provide data for assessing potential risks to pregnant women and fetuses; and

2. The risk to the fetus is caused solely by interventions or procedures that hold out the prospect of direct benefit for the woman or the fetus; or when there is no such prospect of benefit, the risk to the fetus is not greater than minimal and the purpose of the research is the development of important knowledge (for research conducted or supported by federal funds, the knowledge is limited to biomedical knowledge) which cannot be obtained by any other means; and

3. Any risk is the least possible for achieving the objectives of the research; and

4. When the research holds out the prospect of direct benefit to the pregnant woman, the prospect of a direct benefit both to the pregnant woman and the fetus, or no prospect of benefit for the woman nor the fetus when risk to the fetus is not greater than minimal and the purpose of the research is the development of important knowledge (or, when the research is federally-funded, important biomedical knowledge) that cannot be obtained by any other means, the woman's consent is obtained in accord with the informed consent provisions of 45 CFR 46 Subpart A; and

5. When the research holds out the prospect of direct benefit solely to the fetus then the consent of the pregnant woman and the father is obtained in accord with the informed consent provisions of 45 CFR 46 Subpart A, except that the father's consent need not be obtained when he is unable to consent because of unavailability, incompetence, or temporary incapacity or the pregnancy resulted from rape or incest; and

6. Each individual providing consent under (4) or (5) above, is fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate; and

7. For children as defined in 45 CFR 46.402(a) who are pregnant, assent and permission are obtained in accord with the provisions of 45 CFR 46 Subpart D (*See* IRB Policy, DOHP 400-6.3 "Research Involving Children"); and

8. No inducements, monetary or otherwise, will be offered to terminate a pregnancy; and

9. Individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy; and

10. Individuals engaged in the research will have no part in determining the viability of a neonate;

11. Experimentation on a fetus is prohibited, except as necessary to protect or preserve the life and health of such fetus or premature infant. (390.0111(6) F.S.)

C. 46.205: Research Involving Neonates

1. Neonates of uncertain viability and nonviable neonates may be involved in research when all of the following conditions are met:

   a. Where scientifically appropriate, preclinical and clinical studies have been conducted and provide data for assessing potential risks to neonates; and

   b. Each individual providing consent under paragraph B.2 or C.5 of this section is fully informed regarding the reasonably foreseeable impact of the research on the neonate; and

   c. Individuals engaged in the research will have no part in determining the viability of the neonate; and

   d. The requirements of paragraph B or C of this section have been met as applicable;

   e. Experimentation on a fetus is prohibited, except as necessary to protect or preserve the life and health of such fetus or premature infant. (390.0111(6) *F.S.)*

2. Neonates of uncertain viability

   Until it has been ascertained whether or not a neonate is viable, a neonate may not be involved in research covered by this policy unless the following additional conditions have been met:

   a. The IRB must determine that:

      (1) The research holds out the prospect of enhancing the probability of survival of the neonate to the point of viability, and any risk is the least possible for achieving that objective; or

      (2) The purpose of the research is the development of important knowledge (or, when the research is federally-funded, important biomedical knowledge) which cannot be obtained by other means and there will be no added risk to the neonate resulting from the research; and

   b. The legally effective informed consent of either parent of the neonate, or when neither parent is able to consent because of unavailability, incompetence, or temporary incapacity, the legally

effective informed consent of either parent's legally authorized representative is obtained in accord with 45 CFR 46 Subpart A, except that the consent of the father or his legally authorized representative need not be obtained when the pregnancy resulted from rape or incest;

c. Experimentation on a fetus is prohibited, except as necessary to protect or preserve the life and health of such fetus or premature infant. (390.0111(6) F.S.)

3. Viable neonates

When a neonate is judged viable (i.e. being able, after delivery, to survive, given the benefit of available medical therapy, to the point of independently maintaining heartbeat and respiration) the neonate is then called an infant and should be treated as a child for purpose of research participation. A neonate, after delivery, that has been determined to be viable may be included in research only to the extent permitted by and in accord with the requirements of 45 CFR 46 Subparts A and D.

D. 46.206: Research Involving, After Delivery, the Placenta, the Dead Fetus, or Fetal Material.

1. Research involving, after delivery, the placenta; the dead fetus; macerated fetal material; or cells, tissue, or organs excised from a dead fetus, shall be conducted only in accord with any applicable federal, state, or local laws and regulations regarding such activities.

2. When information associated with material described in paragraph 1 of this section is recorded for research purposes in a manner that living individuals can be identified, directly or through identifiers linked to those individuals, those individuals are research subjects and all pertinent subparts of the regulations are applicable.

E. 46.207: Research Not Otherwise Approvable Which Presents an Opportunity to Understand, Prevent, or Alleviate a Serious Problem Affecting the Health or Welfare of Pregnant Women, Fetuses, or Neonates

Per federal Regulations, the Secretary of the Department of Health and Human Services (DHHS) will conduct or fund research that the IRB does not believe meets the requirements of 45 CFR 46.204 or 45 CFR 46.205 only when:

1. The IRB finds that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of pregnant women, fetuses, or neonates; and

2. Per federal regulations, the Secretary of DHHS, after consultation with a panel of experts in pertinent disciplines (for example: science, medicine,

ethics, law) and following opportunity for public review and comment, including a public meeting announced in the *Federal Register*, has determined either:

a. That the research, in fact, satisfies the conditions of 46.204, as applicable; or

b. The following:

(1) The research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of pregnant women, fetuses, or neonates; and

(2) The research will be conducted in accord with sound ethical principles; and

(3) Informed consent will be obtained in accord with the informed consent provisions of 45 CFR 46 Subpart A and other applicable subparts of 45 CFR 46.

3. Modification or Waiver of Specific Requirements. Per federal Regulations, upon the request of the Investigator (with the approval of the IRB), the Secretary of the Department of Health and Human Services may modify or waive any of the above requirements of this policy.

F. Studies in Which Pregnancy is Coincidental to Subject Selection.

1. Any study in which women of childbearing potential are possible subjects may inadvertently include pregnant women. Federal regulations require that, when appropriate, subjects be provided a statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, when the subject is or may become pregnant) which are currently unforeseeable as part of the informed consent process.

a. The IRB must judge whether the mother's participation would pose any risk to the fetus or nursing infant. In some studies, the IRB may need to assure that non-pregnant subjects are advised to avoid pregnancy or nursing for a time during or following the research. Furthermore, where appropriate, subjects should be advised to notify the Investigator immediately should they become pregnant. In some instances, there may be potential risk sufficient to justify requiring that pregnant women either be specifically excluded from the research or studied separately.

G. Exemption from Review.

Note that with the revision of Subpart B on November 13, 2001, the exemptions from IRB review listed at 45 CFR 46.101(b) may now be applied to research

involving pregnant women, human fetuses, and neonates in accordance with 45 CFR 46.201(b).

H. Research on Transplantation of Fetal Tissue

The IRB must assure that the following provisions have been met before approving such research activities:

1. Research involving the transplantation of human fetal tissue for therapeutic purposes may be conducted only when the woman providing the tissue makes a statement, in writing and signed by the woman, declaring that:

    a. The woman donates the fetal tissue for research; and

    b. The donation is made without any restriction regarding the identity of individuals who may be the recipients of transplantations of the tissue; and

    c. The woman has not been informed of the identity of any such individuals.

2. Research involving the transplantation of human fetal tissue for therapeutic purposes may be conducted only when the attending physician with respect to obtaining the tissue from the woman involved makes a statement, in writing and signed by the attending physician, declaring that:

    a. In the case of tissue obtained pursuant to an induced abortion:

        (1) The consent of the woman for the abortion was obtained prior to requesting or obtaining consent for a donation of the tissue for use in such research; and

        (2) No alteration of the timing, method, or procedures used to terminate the pregnancy was made solely for the purposes of obtaining the tissue; and

        (3) The abortion was performed in accordance with applicable State law; and

    b. The tissue has been donated by the woman in accordance with paragraph A of this section; and

    c. Full disclosure has been provided to the woman with regard to:

        (1) Such physicians interest in the research to be conducted with the tissue; and

(2) Any known medical risks to the woman or risks to her privacy that might be associated with the donation of the tissue and that are in addition to risks of such type that are associated with the woman's medical care.

3. Research involving transplantation of human fetal tissue for therapeutic purposes may be conducted only when the Investigator makes a signed statement declaring that the Investigator:

a. Is aware that:

(1) The tissue is human fetal tissue; and

(2) The tissue may have been obtained pursuant to a spontaneous or induced abortion or pursuant to a stillbirth; and

(3) The tissue was donated for research purposes; and

4. The Investigator has provided such information to other individuals with responsibilities regarding the research; and

a. The Investigator will require, prior to obtaining the consent of an individual to be a recipient of a transplantation of the tissue, written acknowledgment of receipt of such information by such recipient; and

b. The Investigator has had no part in any decisions as to the timing, method, or procedures used to terminate the pregnancy made solely for the purpose of the research.

5. Research involving transplantation of human fetal tissue for therapeutic purposes may be conducted only when the head of the agency or other entity conducting the research involved certifies to the Secretary of the Department of Human Services (DHHS) that the statements required under paragraphs B and C of this section will be available for audit by the Secretary of DHHS.

6. Research involving transplantation of human fetal tissue for therapeutic purposes may be conducted only when it is conducted in accordance with applicable federal, state and local laws and institutional policies and procedures.

I. Research funded by the Environmental Protection Agency

1. For research conducted or supported by EPA, or for research not conducted or supported by any federal agency that has regulations for protecting human research participants but where the intention of the research is submission to the EPA, research involving the intentional

exposure of pregnant women, nursing women, or children to any substance is prohibited.

2. For observational research involving children that does not involve greater than minimal risk, the IRB may approve such research only if the IRB finds that adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians, as set forth in 40 CFR 26.406.

3. The IRB shall review observational research involving pregnant women and fetuses using 40 CFR 26 and 45 CFR 46 Subpart B.

J. Equivalent protections for review of research involving pregnant women that is not conducted or supported by DHHS

1. Researchers provide the same information for review by the IRB regardless of source of funding

2. IRB members review the same materials regardless of source of funding

3. IRB members make the same protocol-specific determinations concerning research involving children regardless of funding

VI. History Notes

The Office of Statewide Research, Ethics and Human Research Protections Program are responsible for this policy.

Revised 06/15/2010
Reviewed 08/23/2013
Replaces DOHP 400-6.1-09

VII. Signature Block with Effective Date

Ana M. Viamonte Ros, M.D., M.P.H.
State Surgeon General
Florida Department of Health

Date

I. Policy

It is the policy of the Department of Health (DOH) Institutional Review Board (IRB) to review and approve all research involving prisoners with additional ethical and regulatory considerations applicable to prisoners under 45 CFR 46, Subpart C, *"Additional DHHS Protections Pertaining to Biomedical and Behavioral Research Involving Prisoners as Subjects."*

II. Authority

A. Chapter 381.86, Institutional Review Board, *Florida Statutes*

B. Rule 64H-2.001, Institutional Review Board, *Florida Administrative Code*

III. Supportive Data

A. 45 CFR 46 Subpart C

B. 28 CFR 512

C. OHRP Guidance Document: "OHRP Guidance on Involvement of Prisoners in Research", May 23, 2003

D. OHRP Letter dated January 15, 2004: Informal 45 CFR 46 Subpart C Guidance

E Waiver of the Applicability of Certain Provisions of Department of Health and Human Services Regulations for Protection of Human Research Subjects for Department of Health and Human Services Conducted or Supported Epidemiologic Research Involving Prisoners as Subjects, *Federal Register* (October 7, 2002) (67 FR 62432)

IV. Definitions

See DOHP 400-11.1, Definitions.

V. Procedures

A. IRB Review and Approval of Research Involving Prisoners.

The special vulnerability of prisoners makes consideration of involving them as research subjects particularly important. Prisoners may be under constraints because of their incarceration, which could affect their ability to make a truly voluntary and uncoerced decision whether or not to participate as subjects in research. To safeguard their interests and to protect them from harm, special ethical and regulatory considerations apply for reviewing research involving prisoners. Therefore, when a protocol involves the use of prisoners as participants, both the general IRB policies and procedures apply and the additional ones outlined in this policy. The IRB may approve research involving prisoners only when these special provisions are met.

1. Research involving prisoners as participants must be reviewed and approved by both DOH IRB policies and procedures, and additional considerations for prisoners as determined by federal, state, county, and local regulations.

2. For research involving prisoners, the definition of minimal risk differs from the definition of minimal risk in the Common Rule. The definition for prisoners requires reference to physical or psychological harm, as opposed to harm or discomfort, to risks normally encountered in the daily lives, or routine medical, dental or psychological examination of healthy persons. See definition in DOHP 400-11.1, Definitions.

3. The DOH IRB must review research in which prisoners are the target population, the participant is a prisoner at the time of enrollment, or when a currently enrolled participant becomes incarcerated and research interventions and interactions would occur during the incarceration period or when identifiable private information will be obtained during the incarceration period.

4. Persons who are released on parole in the community, or in community-based alternate settings, such as “half-way houses” are not considered prisoners.

5. Persons confined by civil commitment proceedings to A. G. Holley State Tuberculosis Hospital are not prisoners. However, the IRB shall take into account their special circumstances.

6. When the IRB is reviewing a protocol in which a prisoner is participant, the convened IRB Committee or reviewer using the expedited procedure, must make, in addition to requirements under 45 CFR 46, Subpart A, seven additional findings under 45 CFR 46.305(a), as follows:

    a. The research under review represents one of the following categories of research permissible under 45 CFR 46.306(a)(2):

        1). A study of the possible causes, effects, and processes of incarceration, and of criminal behavior, provided that the study presents no more than minimal risk and no more than inconvenience to the participants;

        2). A study of prisons as institutional structures or of prisoners as incarcerated persons, provided that the study presents no more than minimal risk and no more than inconvenience to the participants;

        3). Research on conditions particularly affecting prisoners as a class (e.g., vaccine trials and other research on hepatitis which is much more prevalent in prisons than elsewhere;

and research on social and psychological problems such as alcoholism, drug addiction, and sexual assaults) provided that the study may proceed only after the DHHS Secretary (through OHRP) has consulted with appropriate experts including experts in penology, medicine, and ethics and published notice, in the Federal Register, of his intent to approve such research; or

4). Research on practices, both innovative and accepted, which have the intent and reasonable probability of improving the health or well-being of the participant. In cases in which those studies require the assignment of prisoners in a manner consistent with protocols approved by the IRB to control groups which may not benefit from the research, the study may proceed only after the DHHS Secretary (through OHRP) has consulted with appropriate experts including experts in penology, medicine, and ethics and published notice, in the Federal Register, of his intent to approve such research.

5) For certain epidemiological research conducted or supported by DHHS the sole purpose of which is to describe the incidence or prevalence of a disease by identifying all cases or to study risk factor associated with a disease, and where the Department certifies to OHRP that the research presents no more than minimal risk and no more than minimal inconvenience to the prisoner-subjects and prisoners are not a particular focus of the research.

b. Any possible advantages accruing to the prisoner through his or her participation in the research, when compared to the general living conditions, medical care, quality of food, amenities and opportunity for earnings in the prison, are not of such a magnitude that his or her ability to weigh the risks of the research against the value of such advantages in the limited choice environment of the prisoner is impaired;

c. The risks involved in the research are commensurate with risks that would be accepted by non-prisoner volunteers;

d. Procedures for the selection of participants within the prison are fair to all prisoners and immune from arbitrary intervention by prison authorities or prisoners. Unless the Principal Investigator provides to the IRB justification in writing for following some other procedures, control participants must be selected randomly from the group of available prisoners who meet the characteristics needed for that particular research project;

e. The information is presented in language which is understandable to the participant population;

f. Adequate assurance exists that parole boards will not take into account a prisoner's participation in the research in making decisions regarding parole, and each prisoner is clearly informed in advance that participation in the research will have no effect on his or her parole; and

g. Where the IRB finds there may be a need for follow-up examination or care of participants after the end of their participation, adequate provision has been made for such examination or care, taking into account the varying lengths of individual prisoners' sentences, and for informing participants of this fact.

B. Composition of IRB when Prisoners are Involved in Research.

1. When reviewing research involving prisoners, special composition requirements for IRB membership exist. This section describes additional requirements for the composition of the IRB in addition to those listed in DOHP-400-4.2, "Review of Human Subjects Research: Conduct of Meetings by the Convened IRB" See 45 CFR 46.304 (a) and (b)

a.. A majority of the IRB (exclusive of prisoner members) shall have no association with the prison(s) involved, apart from their membership on the IRB

b. When reviewing research involving prisoners, at least one member of the IRB must be a prisoner, or a prisoner representative with appropriate background and experience to serve in that capacity. The prisoner representative must have a close working knowledge, understanding and appreciation of prison conditions from the perspective of a prisoner. Suitable individuals could include present or former prisoners; prison chaplains; prison psychologists, prison social workers, or other prison service providers; persons who have conducted advocacy for the rights of prisoners; or individuals who are qualified to represent the rights and welfare of prisoners by virtue of appropriate background and experience.

c. The IRB must meet the special composition requirements for all types of review for the protocol: initial review, continuing review, review of protocol amendments, review of problems requiring prompt reporting to the IRB (See DOHP 400-4.6, "Problems Requiring Prompt Reporting to the IRB"), or in the event an individual becomes a prisoner while participating in a research protocol.

2. Initial review by the convened IRB when research involves prisoners: When an IRB reviews a protocol involving prisoners as participants, the composition of the IRB must satisfy the following requirements:

    a. The prisoner representative must be a voting member of the IRB.

    b. The prisoner representative must review research involving prisoners.

    c. The prisoner representative must be assigned as a primary reviewer, and must receive all materials pertaining to the research.

    d. The prisoner representative must be present at a convened meeting when the research involving prisoners is reviewed. If the prisoner representative is not present, research involving prisoners cannot be reviewed or approved. The prisoner representative may attend the meeting via conference call, but the prisoner representative must receive all materials pertaining to the research.

    e. The prisoner representative must provide a written review using a reviewer comment worksheet submitted in IRBWise, and present his/her review orally at the convened meeting of the IRB when the research involving prisoners is reviewed.

3. Initial review using the expedited procedure for certain research involving prisoners

    a. Research involving prisoners involving interaction with prisoners (including obtaining consent from prisoners) may be reviewed by the expedited procedure, if a determination is made that the research is minimal risk for the prison population being studied or included.

        i. The prisoner representative must concur with the determination of minimal risk.

        ii. The prisoner representative must review the research as a reviewer designated by the IRB Chair. This may be as the sole reviewer or in addition to another reviewer. The prisoner representative must provide a written review using a reviewer comment worksheet submitted in IRBWise .

    b. Research involving prisoners that does not involve interaction with prisoners (for example, research involving existing data or record review, including epidemiological research involving prisoners)

may be reviewed by the expedited procedure, if a determination is made that the research is minimal risk for the prison population being studied or included.

c. The prisoner representative may review the research as a reviewer if designated by the IRB chair, but review by the prisoner representative is not required.

4. Review of amendments when research involves prisoners

a. Substantial modifications reviewed by the convened IRBs must use the same procedures for initial review including the responsibility of the prisoner representative.

b. Minor modifications to previously approved research may be reviewed using either of the two procedure described above at V.B.3.a or V.B.3.b, based on the type of modification.

i. Review of amendments must use the same procedures for initial review using the expedited procedure including the responsibility of the prisoner representative.

5. Continuing review when research involves prisoners

a. Continuing review by the convened IRB must use the same procedures for initial review including the responsibility of the prisoner representative.

b. For continuing review of studies involving prisoners that meet criteria for expedited review, the continuing review may be reviewed using either of the two procedure described above for initial review using the expedited procedure at V.B.3.a or V.B.3.b.

i. Continuing review of studies must use the same procedures for initial review using the expedited procedure including the responsibility of the prisoner representative.

C. Measures that are to be Taken When a Current Research Participant Becomes a Prisoner.

1. When a participant becomes a prisoner after enrolling in a research study, the Investigator is responsible for <u>immediately</u> reporting the event in IRBWise using the Problems Requiring Prompt Reporting form. This is not required when the study was previously approved by the IRB for prisoner participation.

2. When research interactions and interventions or obtaining identifiable private information will not occur during the incarceration, IRB review and approval under Subpart C is not required.

3. When the study was not previously reviewed and approved by the IRB in accordance with the requirements of Subpart C, all research interactions and interventions with, and obtaining identifiable private information must cease until the requirements of Subpart C (for DHHS-funded research) or equivalent protections are satisfied.

4. Review must meet requirements describe above at V.B.2.Initial review by the convened IRB when research involves prisoners, or V.B.3, initial review using the expedited procedure

D. Research Conducted or Supported by DHHS.

1. For research conducted or supported by DHHS to involve prisoners, two actions must occur:

   a. The institution engaged in the research must certify to the DHHS Secretary (through OHRP) that the IRB designated under its assurance of compliance has reviewed and approved the research under 45 CFR 46.305; and

   b. The DHHS Secretary (through OHRP) must determine that the proposed research falls within the categories of research permissible under 45 CFR 46.306(a)(2).

2. When an Investigator wishes to engage in non-DHHS supported research, certification is not required. However, the IRB should apply the standards of this policy and the federal regulations in reviewing the research.

3. When either of the following are true, the research should only proceed after the IRB has consulted with the appropriate experts, as determined by the IRB:

   a. The research involves conditions particularly affecting prisoners as a class as explained in Section A.4.a(1) above; or

   b. The research does not satisfy the stipulations at Section A.4.a above.

E. Additional Approvals

1. The Federal Bureau of Prisons places special restrictions on research that takes place within the Bureau of Prisons under 28 CFR 512. The provisions under 28 CFR 512 specify additional requirements for prospective investigators (both employees and non-employees) to obtain

approval to conduct research within the Bureau of Prisons (Bureau) and responsibilities of Bureau staff in processing proposals and monitoring research projects.

F. Additional Considerations.

1. When a prisoner is also a child (e.g. an adolescent detained in a juvenile detention facility is a prisoner), DOHP 400-6.3, "Special Categories of Research: Children", will also apply.

2. Reviews by the expedited procedure of research involving prisoners is not allowed. The full, convened IRB Committee must review research involving prisoners as human subjects.

3. Exemption from review of research involving prisoners is not allowed. Research that would otherwise be exempt from the requirement that it receive IRB approval is not exempt when the research involves prisoners.

G. Equivalent protections for review of research involving prisoners that is not conducted or supported by DHHS

1. Researchers provide the same information for review by the IRB regardless of source of funding

2. IRB members review the same materials regardless of source of funding

3. IRB members make the same protocol-specific determinations concerning research involving prisoners

VI. History Notes

The Office of Public Health Research, Ethics and Human Research Protections Program is responsible for this policy.

Revised 7/8/2010
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Replaces DOHP 400-6.2-09

VII. Signature Block with Effective Date

Ana M. Viamonte Ros, M.D., M.P.H.
State Surgeon General
Florida Department of Health

Date

I. Policy

It is the policy of the Department of Health (DOH) Institutional Review Board (IRB) to review research in compliance with applicable regulations to ensure that, when research involves children who are vulnerable to coercion or undue influence, safeguards are included in the research design to protect the rights and welfare of children.

II. Authority

A. Chapter 381.86, Institutional Review Board, *Florida Statutes*

B. Rule 64H-2.001, Institutional Review Board, *Florida Administrative Code*

III. Supportive Data

A. 45 CFR §46.101(e)-(f)

B. 45 CFR §46.102(c)

C. 45 CFR §46.402(d)-(e)

D. 21 CFR §50.3(l)

E. 21 CFR §50.3(o)

F. 21 CFR §50.3(s)

G. 21 CFR §56.103(c)

H. 40 CFR 26 Subpart D

I. OHRP Report 98-03, NIH Policy Guidance on the Inclusion of Children in Research

J. OHRP Guidance, Children Involved as Subjects in Research: Guidance on the DHHS 45 CFR 46.407 (“407”) Review Process at: http://www.hhs.gov/ohrp/children/guidance_407process.html

K. OHRP IRB Guidebook Online, Chapter 6, Section C, “Children and Minors” at: http://www.hhs.gov/ohrp/irb/irb_guidebook.htm

L. DOHP 400-5.1, “Legally Effective and Prospectively Obtained Informed Consent”

M. DOHP 400-5.2, “Documentation of Informed Consent”

IV. Definitions

See DOHP 400-11.1, “Definitions.”

V. Procedures

A. Procedure for Determining when Research Involves Children

1. Persons under the age of 18 years of age are children as defined in DHHS regulation, regardless of whether the research is funded or supported by DHHS, except as provided elsewhere in Florida law:

   a. A person under the age of 18 years of age who has had the disability of nonage removed by a circuit court is no longer a child and may consent to treatments and procedures in research; §743.015 *F.S*.

   b. A person under the age of 18 years of age who is married or has been married, including one whose marriage is dissolved, or who is widowed or widowered is no longer a child and may consent to treatments and procedures in research; §743-01 *F.S*.

   c. An unwed pregnant person under the age of 18 years of age may consent to the performance of medical or surgical care or services relating to her pregnancy, or relation to her child, including not greater than minimal risk research relating to her pregnancy or her child, and such consent is valid and binding as if she had achieved her majority; §743.065 *F.S*.

   d. A person under the age of 18 years of age seeking medical care or services related to sexually transmitted disease may consent to such treatments and procedures, including not greater than minimal risk research related to sexually transmitted diseases, and the consent of the parents or guardians of a minor is not a prerequisite; §384.30 *F.S*.

2. If IRB staff are uncertain whether the researcher's proposed plans to enroll in research persons who are less than 18 years of age involve children, the IRB staff will consult with legal counsel to determine whether the research involves children under DHHS regulations, regardless of whether the research is funded or supported by DHHS. IRB staff will convey findings of legal counsel to the convened IRB or reviewer using the expedited procedure.

3. When the research involves children, it will be reviewed under Subpart D, or equivalent protections.

4. When individuals less than 18 years of age can consent to the procedures or treatment in research under Florida law, then the research will not be reviewed under Subpart D.

B. Procedure for Determining who is a Guardian

1. The only individuals who may provide permission for children to participate in research under Florida law are

    a. A natural or adoptive parent

    b. A guardian appointed by a court, having been granted specific authority to the guardian to enroll the child in research.

2. Legally authorized representatives may not give permission for research involving children unless they are a guardian appointed by a court, having been granted specific authority to the guardian to enroll the child in research.

3. If IRB staff are uncertain who may serve as a guardian, the IRB staff will consult with legal counsel to determine who may serve as a guardian for the protocol. IRB staff will convey findings of legal counsel to the IRB or representative.

C. IRB Review and Approval of Research Involving Children

The special vulnerability of children and adolescents makes consideration of involving them as research participants particularly important. To safeguard their interests and to protect them from harm, special ethical and regulatory considerations apply for reviewing research involving children. The IRB may approve research involving children only when special provisions are met. The IRB must classify research involving children into one of four categories and document their discussions of the risks and benefits of the research study. The four categories of research involving children that may be approved by the IRB Committee are based on degree of risk and benefit to individual subjects.

D. Categories of Research Involving Children

1. Category 404: Research Not Involving Greater than Minimal Risk to Children (45 CFR 46.404). When the IRB finds that no greater than minimal risk to children is presented, the IRB may approve the research only when the IRB finds that adequate provisions are made for soliciting the assent of the children and permission of their parents or guardians, as set forth below.

2. Category 405: Research Involving Greater than Minimal Risk but Presenting the Prospect of Direct Benefit to the Individual Child (45 CFR 46.405). When the IRB finds that more than minimal risk to children is presented by an intervention or procedure that holds out the prospect of direct benefit for the individual child, or involves a monitoring procedure that is likely to contribute to the child's well-being, the IRB may approve the research only when the IRB finds that:

    a. The risk is justified by the anticipated benefit to the participants;

b. The relation of the anticipated benefit to the risk presented by the study is at least as favorable to the participants as that provided by available alternative approaches; and

c. Adequate provisions are made for soliciting the assent of the children and permission of their parents or guardians, as set forth below

3. Category 406: Research Involving Greater than Minimal Risk and No Prospect of Direct Benefit to the Individual Child, but Likely to Yield Generalizable Knowledge about the Child's Disorder or Condition (45 CFR 46.406). When the IRB finds that more than minimal risk to children is presented by an intervention or procedure that does not hold out the prospect of direct benefit for the individual child, or involves a monitoring procedure which is not likely to contribute to the well-being of the child, the IRB may approve the research only when the IRB finds that:

   a. The risk represents a minor increase over minimal risk;

   b. The intervention or procedure presents experiences to participants that are reasonably commensurate with those inherent in their actual or expected medical, dental, psychological, social, or educational situations;

   c. The intervention or procedure is likely to yield generalizable knowledge about the participants' disorder or condition which is of vital importance for the understanding or amelioration of the participants' disorder or condition; and

   d. Adequate provisions are made for soliciting assent of the children and permission of their parents or guardians, as set forth below.

4. Research Not Otherwise Approvable, which Presents an Opportunity to Understand, Prevent, or Alleviate a Serious Problem Affecting the Health or Welfare of Children (45 CFR 46.407). When the IRB finds the research does not meet the requirements set forth in categories 46.404, 46.405 or 46.406 as described above, the IRB may approve the research only when:

   a. The IRB finds that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children; and

   b. When Federally funded, the Secretary of the Department of Health and Human Services (DHHS), after consultation with a panel of experts in pertinent disciplines (for example: science, medicine, education, ethics, law) and following opportunity for public review and comment, has determined either:

(1) That the research in fact satisfies the conditions of categories 46.404, 46.405, or 46.406; or

(2) The following:

(a) The research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children;

(b) The research will be conducted in accordance with sound ethical principles; and

(c) Adequate provisions are made for soliciting the assent of children and the permission of their parents or guardians, as set forth below in Paragraph F.

E. Requirements for Permission by Parents or Guardians and for Assent by Children

1. Adequate Provisions for Child's Assent

The IRB must find that adequate provisions are made for soliciting the assent of child participants when in the judgment of the IRB the children are capable of providing assent.

a. In determining whether children are capable of assenting, the IRB shall take into account the ages, maturity, and psychological state of the children involved. This judgment may be made for children to be involved in research under a particular protocol, or for each child, as the IRB deems appropriate. The child should be given an explanation of the proposed research procedures in a language that is appropriate to the child's age, experience, maturity, and condition.

b. Waiver of Assent

When the IRB determines either of the following to be true, then the assent of the children is not a necessary condition for proceeding with the research:

(1) The capability of the children is so limited that they cannot reasonably be consulted; or

(2) The intervention or procedure involved in the research holds out a prospect of direct benefit that is important to the health or wellbeing of the children and is available only in the context of the research.

(a) Therefore, when the research offers the child the possibility of a direct benefit that is important to the health or wellbeing of the child and is available only in the context of the research, the IRB may determine that the assent of the child is not necessary.

(b) Additionally, in such circumstances, a child's dissent, which should normally be respected, may be overruled by the child's parents at the IRB's discretion. When research involves the provision of experimental therapies for life threatening diseases such as cancer, however, the IRB should be sensitive to the fact that parents may wish to try anything, even when the likelihood of success is marginal and the probability of extreme discomfort is high. Should the child not wish to undertake such experimental therapy, difficult decisions may have to be made. In general, when the child is a mature adolescent and death is imminent, the child's wishes should be respected.

(c) Finally, even where the IRB determines that the child participants are capable of assenting, the IRB may still waive or alter the assent requirement under circumstances in which consent may be waived or altered for adults in accordance with DOHP 400-5.3, “Waiver and Alteration of Informed Consent” regarding waiver or alteration of informed consent generally.

F. Adequate Provisions for Parents’ or Guardians’ Permission

The IRB must find that adequate provisions are made for soliciting the permission of each child's parents or guardians.

1. Research not involving greater than minimal risk to children or research involving greater than minimal risk but presenting the prospect of direct benefit to the individual child. The IRB must determine whether

   a. the permission of both parents is required unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child; or

   b. whether the permission of one parent is sufficient.

2. Research involving greater than minimal risk and no prospect of direct benefit to the individual child, but likely to yield generalizable knowledge about the child's disorder or condition. The IRB must determine that the permission of both parents is required unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child.

3. Research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children. When the research is approved under Paragraph D.4 above and permission is to be obtained from parents, both parents must give their permission unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child.

G. Waiver of Parents' or Guardians' Permission

When the IRB determines that, a research protocol is designed for conditions or for a participant population for which parental or guardian permission is not a reasonable requirement to protect the participants (for example, neglected or abused children), it may waive the consent requirements described above, provided that all of the following are true:

1. An appropriate mechanism for protecting the children who will participate as subjects in the research is substituted; and

2. The waiver is not inconsistent with federal, state, or local law. The choice of an appropriate mechanism would depend upon the nature and purpose of the activities described in the protocol, the risk and anticipated benefit to the research participants, and their age, maturity, status, and condition.

3. The research is not subject to Food and Drug Administration regulation.

H. Wards of the State or Other Agency

Children who are wards of the state or any other agency, institution, or entity can be included in research in categories 45 CFR 46.406 or 45 CFR 46.407 above approved under sections G (permission of guardian) or F (waiver of consent/assent) above only if the IRB finds and documents that such research is:

1. Related to their status as wards; or

2. Conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of children involved as participants are not wards.

3. If the research is approved under 45 CFR 46.406 or 45 CFR 46.407 , the IRB must require appointment of an advocate for each child who is a ward, in addition to any other individual acting on behalf of the child as representative, guardian or *in loco parentis*. One individual may serve as

advocate for more than one child. The advocate shall be an individual who has the background and experience to act in, and agrees to act in, the best interests of the child for the duration of the child's participation in the research and who is not associated in any way (except in the role as advocate or member of the IRB) with the research, the Investigators, or the guardian organization.

I. Pediatric Expertise on IRB Committee

An IRB Committee considering a protocol involving children as participants shall:

1. Assess its needs for pediatric expertise among the IRB voting membership to assure that it possesses the professional competence necessary to review the specific research activities; and

2. Include one or more individuals who are knowledgeable about and experienced in working with children. To fulfill this requirement, the IRB Committee may invite nonvoting individuals to assist in the review of issues which require expertise beyond, or in addition to, that available among voting IRB members.

J. Research funded by the Environmental Protection Agency

1. For research conducted or supported by EPA, or for research not conducted or supported by any federal agency that has regulations for protecting human research participants but where the intention of the research is submission to the EPA, research involving the intentional exposure of pregnant women, nursing women, or children to any substance is prohibited.

2. For observational research involving children that does not involve greater than minimal risk, the IRB may approve such research only if the IRB finds that adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians, as set forth in 40 CFR 26.406.

3. For observational research involving children that presents greater than minimal risk but presents the prospect of direct benefit to the individual participants, the IRB may approve only if the IRB finds and documents that:

   a. The intervention or procedure holds out the prospect of direct benefit to the individual participant or is likely to contribute to the participant's well-being.

   b. The risk is justified by the anticipated benefit to the participants.

   c. The relation of the anticipated benefit to the risk is at least as

favorable to the participants as that presented by available alternative approaches.

d. Adequate provisions are made for soliciting the assent of the children and permission of their parents or guardians, as set forth in 40 CFR 26.406.

K. Equivalent protections for review of research involving children that is not conducted or supported by DHHS

1. Researchers provide the same information for review by the IRB regardless of source of funding

2. IRB members review the same materials regardless of source of funding

3. IRB members make the same protocol-specific determinations concerning research involving children.

VI. History Notes

The Office of Public Health Research, Ethics and Human Research Protections Program is responsible for this policy.

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VII. Signature Block with Effective Date

Ana M. Viamonte Ros, M.D., M.P.H.
State Surgeon General
Florida Department of Health

Date

I. Policy

It is the policy of the Department of Health (DOH) Institutional Review Board (IRB) to review, approve, and provide guidance on the special ethical considerations when cognitively impaired participants are involved in human subjects research.

II. Authority

A. Chapter 381.86, Florida Statutes, Institutional Review Board

III. Supportive Data

A. The *Belmont Report*

B. Am J Psychiatry 155:11, November 1998, "Guidelines for Assessing the Decision-Making Capacities of Potential Research Subjects with Cognitive Impairment"

C. The Office of Human Subjects Research (OHSR), National Institutes of Health, Information Sheet #7, "Research Involving Cognitively Impaired Subjects: A Review of Some Ethical Considerations"

IV. Definitions

See DOHP 400-11.1, "Definitions"

V. Procedures

A. IRB Review and Approval of Research Involving Cognitively Impaired Participants

1. Because cognitively impaired individuals may have diminished autonomy that may limit their capacity to provide consent or their ability to withdraw, research involving cognitively impaired participants should be reviewed and approved through consideration of the DOH IRB policies and the special considerations as determined by the *Belmont Report*, federal and state regulations, and guidance documents.

2. The DOH IRB must review all research in which cognitively impaired individuals will be considered as participants to assure that the Investigator has provided additional safeguards to protect the rights and welfare of this vulnerable population.

3. The IRB must consider the degree of cognitive impairment of the participant, the level of risk, and the potential benefit to the individual participant.

B. Requirements for Evaluating Decision-Making Capacity for Cognitively Impaired Participants

1. The IRB must find that appropriate provisions are made for determining the participant's ability to provide consent or their ability to withdraw, through evidence of one or more of the following pertaining to the individual:

    a. The ability to make a choice;

    b. The ability to understand relevant information;

    c. The ability to appreciate the situation and its likely consequences; and

    d. The ability to manipulate information rationally.

C. Determination of Capacity to Consent or Ability to Withdraw

The determination of capacity to consent or ability to withdraw may be made through a standardized measure or consultation with another qualified professional. The IRB must approve the process for making such a determination.

1. Because the capacity to consent or the ability to withdraw may fluctuate, the IRB must evaluate the process for continued verification of understanding and willingness to participate.

    a. The consent procedures should describe a plan for protecting individuals who may lose their capacity to provide consent or their ability to withdraw while participating in research activities (e.g., use of an ombudsman).

    b. The IRB may require that an outside witness observe and confirm the consenting process.

2. For participants who lack decision-making capacity, the permission of the individual's legally authorized representative is required and assent should be obtained from the participant (*See* DOHP 400-5.1, "Legally Effective and Prospectively Obtained Informed Consent").

3. In research situations where there is the potential for direct benefit to the participant, the IRB may waive the requirement to obtain assent. However, permission from the legally authorized representative must be obtained.

4. Even where the IRB determines that the individuals are capable of consenting or withdrawing, the IRB may still waive the consent requirements under the circumstances described in the DOH IRB informed consent policy (*See* DOHP 400-5.1, "Legally Effective and Prospectively Obtained Informed Consent").

5. The IRB must also review and approve the appropriate consent documents with the required elements of consent written in a language understandable to the participant.

D. Procedure for Determining Who is a Legally Authorized Representative

1. Under Florida law (765 *F.S.*), several classes of persons can consent for incapacitated adults. They are listed below in order of priority. Consent must be sought first from the person at the top of the list.

   Only if that option is not reasonably available, willing, or competent to consent, does the next option apply, and so on down the list. If the first reasonably available person refuses consent, however, that refusal is final.

   a. Health care surrogate: Any competent adult expressly designated to make health care decisions for a particular incapacitated individual. The designation must be in writing in accordance with Florida law.

   b. Attorney in fact ("power of attorney"): A competent adult to whom the subject has delegated authority to make health care decisions by means of a validly executed durable power of attorney.

   c. Judicially appointed guardian (in the absence of a Surrogate or where a court revokes the authority of the Surrogate). All persons who have been adjudged incompetent should have a judicially appointed guardian.

   d. Proxy: Under Florida Law (765.401 *F.S.*), a proxy (substitute decision maker) may consent (where the participant has not executed an advanced directive, or designated a Surrogate to make health care decisions, or a court has not appointed a guardian) to experimental treatment, provided, the experimental treatment has been approved by an IRB and the proxy reasonably believes that the patient would have made the decision under the circumstances. If none of the above are reasonably available, then a competent adult who has not been expressly designated to make health care decisions for a particular incapacitated individual but who is available, willing, and competent to act is the next option for consent. The following possible proxies should be sought, again in order of priority,

working down the list when an option is not reasonably available, or is unwilling or incompetent to act as proxy.

i. The subject's spouse

ii. An adult child of the subject. If the subject has more than one adult child then obtain permission from a majority of the adult children who are reasonably available

iii. A parent of the subject

iv. The adult sibling of the subject. If the subject has more than one adult sibling then obtain permission from a majority of the adult siblings who are reasonably available

v. An adult relative of the subject who has exhibited special care and concern for the subject and who has maintained regular contact with the subject and who is familiar with the subject's activities, health, and religious or moral beliefs

vi. A close personal friend 18 years of age or older who has exhibited special care and concern for the patient

2. If HRPP staff are uncertain who may serve as a legally authorized representative for an incapacitated adult, the IRB staff will consult with legal counsel to determine who may serve as a legally authorized representative for the protocol. IRB staff will convey findings of legal counsel to the IRB or representative.

3. When it is determined by the Investigator that the participant lacks decision-making capacity, the IRB must find that appropriate provisions are made for soliciting the permission of each individual's legally authorized representative unless the criteria are met to approve a waiver of informed consent (*See* DOHP 400-5.1, "Legally Effective and Prospectively Obtained Informed Consent").

E. Institutionalized Participants

1. The IRB must consider the rationale and justification for involvement of institutionalized participants, including an explanation as to why non-institutionalized individuals could not be used.

2. Research proposals where involuntarily institutionalized participants are to be included shall also be reviewed consistent with additional criteria as specified in IRB Policy on Prisoners.

F. Composition of IRB when Cognitively Impaired Participants are involved in Research

1. When reviewing research involving cognitively impaired participants, the IRB Committee will include into its composition one or more individuals who are knowledgeable about and experienced in working with the cognitively impaired.

2. When the study requires review by the full IRB Committee, it must meet the special composition requirements when conducting reviews for initial review, continuing review, protocol amendments, and problems requiring prompt reporting to the IRB when the research involves cognitively impaired individuals.

VI. History Notes

The Office of Statewide Research, Ethics and Human Research Protections Program are responsible for this policy.

Revised 07/18/2010
Reviewed 08/23/2013
Replaces DOHP 400-6.4-08

VII. Signature Block with Effective Date

Ana M. Viamonte Ros, M.D., M.P.H.
State Surgeon General
Florida Department of Health

Date

I. Policy

It is the policy of the Department of Health (DOH) Institutional Review Board (IRB) that human participant research involving the use of investigational articles (drugs or medical devices) complies with regulations governing investigational articles.

II. Authority

A. Chapter 381.86, Florida Statutes, Institutional Review Board

B. Rule 64H-2.001, Institutional Review Board, *Florida Administrative Code*

III. Supportive Data

A. 21 CFR §11, 21 CFR §54, 21 CFR §210, 21 CFR §211, 21 CFR §312, 21 CFR §314, 21 CFR §320, 21 CFR §330, 21 CFR §601, 21 CFR §807, 21 CFR §812, 21 CFR §814, 21 CFR §820, 21 CFR §860

B. FDA Information Sheets

IV. Definitions

See DOHP 400-11.1, “Definitions”

V. Procedures

A. When research involves the use of a drug other than a marketed drug in the course of medical practice, or when research is conducted to evaluate the safety or effectiveness of a device:

1. Sponsors are responsible for obtaining an IND or providing information using the IRBWise application sufficient for the HRPP to determine exemptions from regulatory requirements (21 CFR §312.2(b)) are met.

2. Sponsors are responsible for obtaining an IDE or providing information using the IRBWise application sufficient for the HRPP to determine the research use of a device meets requirements for an investigational device exemption (21 CFR 812.2(b)(1)) or is exempt from the requirement for an IDE (21 CFR 812.2(c)).

3. For investigator-initiated research, where the researcher holds the IND or IDE, the researcher is responsible for arranging to have a contract research organization (CRO) ensure all regulatory requirements are met. The IRB may approve investigator-initiated research by university researchers provided documentation is provided that the university is responsible for ensuring all regulatory requirements are met, and that the university human research protection program is accredited by the Association for Accreditation of Human Research Protection Programs.

Investigators shall not conduct research that is not monitored by a sponsor or CRO.

B. Process to confirm that the test article has an IND or IDE, or that the protocol meets one of the FDA exemptions from the requirement to have an IND or IDE.

1. Staff confirms that the drug has an IND, or that the drug meets exceptions to have an IND (21 CFR §312.2(b)) using the Investigational Article Worksheet. Acceptable forms of documentation are the presence of an IND on the Sponsor protocol, or communication from the Sponsor, or communication from the FDA. Staff may require the Sponsor to provide documentation from the FDA that an IND is not required.

2. Staff confirms that the IDE is valid, or that the device meets requirements for an abbreviated investigational device exemption (21 CFR 812.2(b)(1)) or is exempt from the requirement for an IDE (21 CFR 812.2(c)). Acceptable forms of documentation are the presence of an IDE on the Sponsor protocol, or communication from the Sponsor, or communication from the FDA. Staff may require the Sponsor to provide documentation from the FDA that an IDE is not required.

3. For investigator-initiated research, staff confirms that a contract-research-organization will ensure compliance, or that a university with a human research protection program accredited by AAHRPP will ensure compliance.

4. The completed Investigational Article Worksheet is stored in IRBWise and is available to the IRB as documentation of the validity of the IND or IDE.

C. IRB review of the use of an investigational drug is conducted using the IND Worksheet completed by the Primary Reviewer

D. IRB Review of the Use of an Investigational Device is conducted using the IDE Worksheet completed by the Primary Reviewer

VI. History Notes

The Office of Statewide Research, Ethics and Human Research Protections Program are responsible for this policy.

Reviewed 08/28/2013

VII. Signature Block with Effective Date

Ana M. Viamonte Ros, M.D., M.P.H.
State Surgeon General
Florida Department of Health

Date

I. Policy

It is the policy of the Department of Health (DOH), Institutional Review Board (IRB) that all investigational drugs and devices are used only in approved research protocols and under the direction of approved Researchers in accordance with applicable laws and regulations.

II. Authority

A. Chapter 381.86, Institutional Review Board, *Florida Statutes*

B. Rule 64H-2.001, Institutional Review Board, *Florida Administrative Code*

III. Supportive Data

A. 45 CFR 46

B. 21 CFR §312.61, 21 CFR §312.62, 21 CFR §312.69, 21 CFR §812.100, 21 CFR §812.110, 21 CFR §812.140(a)

IV. Definitions

See DOHP 400-11.1, “Definitions.”

V. Procedures

A. Control of Investigational Drugs and Devices

1. The IRB conducts protocol-by-protocol review and approval of the researcher’s plans to control investigational articles. Acceptable methods include:

    a. For research on patients at A. G. Holley Tuberculosis Hospital, control shall be provided by the Pharmacy under supervision of a licensed pharmacist

    b. For outpatient research at County Health Departments, control may be provided by the pharmacy or by the Investigator in the research clinic consistent with all legal requirements.

    c. For research involving in vitro diagnostic devices, control may be provided by the Investigator in the laboratory consistent with all legal requirements.

    d. For other settings, control by the Investigator consistent with all legal requirements.

B. Storage of Investigational Drugs and Devices

1. For research on patients at A. G. Holley Tuberculosis Hospital, or for research where investigational drugs are stored in a County Health Department pharmacy, it is the responsibility of a licensed pharmacist to comply with all Institutional, State, and Federal law regarding storage of investigational drugs, including controlled substances. Controlled substances may only be used at A. G. Holley State Tuberculosis Hospital under the supervision of licensed pharmacist.

2. When not controlled by a pharmacy, it is the responsibility of the Investigator to comply with all Institutional, State, and Federal law regarding storage of investigational drugs.

3. When not controlled by a pharmacy, investigational drugs used in the context of research must be stored in areas under the direct supervision of the Investigator and in accordance with the Sponsor protocol, when applicable.

4. Investigational agent storage facilities must be in compliance with Institutional, State, Federal (Food and Drug Administration) laws, and when applicable, Joint Commission on Accreditation of Hospital Organizations (JCAHO) requirements. Pharmacy monitoring may be incorporated into the IRB auditing process as needed to assure compliance.

D. Dispensing of Investigational Drugs

1. Investigational drugs administered to research participants may be provided to research participants through a pharmacy, or by the Investigator in a research clinic

2. It is the responsibility of the Investigator to assure that dispensing is in accordance with all Institutional, State, Federal, and when applicable JCAHO requirements.

3. Compounding of drugs for research may occur only at A. G. Holley State Tuberculosis Hospital. Preparation and dispensing of compounded medications shall be done by a pharmacist with a compounding license.

E. The Investigator is responsible for the tracking and oversight of FDA-regulated devices in research and must meet the following requirements in order to use an investigational device in research conducted under the jurisdiction of the DOH IRB:

1. The investigational device must be used only by the Investigator or under his/her direct supervision;

2. The investigational device must be used only as approved by the FDA and as described in the currently approved IRB documents;

3. The Investigator must not supply the investigational device to persons not authorized under the IDE; and

4. Informed consent from the participant or the participant's legally authorized representative must be prospectively obtained.

E. Investigations of issues related to the potential mishandling of investigational drugs will be conducted by the Division of Medical Quality Assurance or other state agency with responsibility for compliance and promptly reported to the IRB

VI. History Notes

The Office of Public Health Research, Ethics and Human Research Protections Program is responsible for this policy.

Revised 5/9/2010
Reviewed 08/23/2013
Replaces DOHP 400-7.1-09

VII. Signature Block with Effective Date

Ana M. Viamonte Ros, M.D., M.P.H. Date
State Surgeon General
Florida Department of Health

I. Policy

It is the policy of the Department of Health (DOH), Institutional Review Board (IRB) that all investigational device use be reviewed and approved by the IRB in accordance with applicable laws and regulations.

II. Authority

A. Chapter 381.86, Institutional Review Board, *Florida Statutes*

B. Rule 64H-2.001, Institutional Review Board, *Florida Administrative Code*

III. Supportive Data

A. 45 CFR 46

B. 21 CFR 50 and 56

C. 21 CFR 812

IV. Definitions

See DOHP 400-11.1, “Definitions.”

V. Procedures

A. Significant Risk (SR) vs. Non-Significant (NSR) Risk Devices

1. Unless exempt by the Investigational Device Exemption (IDE) regulations, an investigational device must be categorized as either a Significant Risk (SR) device or a Non-Significant Risk (NSR) device. The initial risk assessment is determined by the sponsor, but the IRB must make a formal determination during a convened meeting regarding the appropriate SR/NSR category. See Section C below.

2. Research involving the use of a Significant Risk (SR) device must be conducted in accordance with the full requirements of the FDA and must have an approved IDE from the FDA.

3. Research involving the use of a Non-significant Risk (NSR) device must be conducted in accordance with the “abbreviated” requirements of the FDA as described in the FDA regulations 21 CFR Sec. 812.2(b). In some cases, the FDA may notify the sponsor that it does not agree with the NSR determination and will require the submission of an IDE.

B. Exemptions from IDE requirements

1. The device can be exempt from the IDE requirements. A claim that the device is exempt must reference the exemption category being claimed. There are seven exemption categories that may be claimed. The first two categories pertain to devices that were either manufactured before 1976 or similar products manufactured after 1976. Categories 3 and 4 are the most commonly applied for exemptions. Categories 5 and 6 are pertinent to the use of devices in animals. Category 7 pertains to custom devices and is rarely utilized. Full information regarding the seven exemption categories that may be claimed can be found in the FDA regulations 21 CFR Sec. 812.2(c).

2. The exemption category most commonly claimed is 21 CFR Sec. 812.2(c)(3). In addition to the sponsor's compliance with applicable requirements in 21 CFR Sec. 809.10(c), the device testing must comply with the following:

    a. Is noninvasive;

    b. Does not require an invasive sampling procedure that presents significant risk;

    c. Does not by design or intention introduce energy into a participant; and

    d. Is not used as a diagnostic procedure without confirmation of the diagnosis by another, medically established diagnostic product or procedure.

3. Another common exemption category claimed is 21 CFR Sec. 812(c)(4). To qualify for this exemption, the device testing must not be for the purposes of determining safety and effectiveness and must not put participants at risk. The device testing must be limited to the following:

    a. Consumer preference testing;

    b. Testing of a modification; or

    c. Testing of a combination of two or more devices in commercial distribution.

4. It is the sponsor's responsibility to provide sufficient justification to support the exemption category being claimed.

5. An exemption from the IDE requirement is not an exemption from the requirement for prospective IRB review or informed consent.

C. DOH IRB Approval of the Use of an Investigational Device

1. Where a protocol is participant to review under more than one department or agency's regulations, the requirements of each set of regulations must be met. This situation may arise, for example, with IDEs where both the FDA and DHHS have jurisdiction over the research. The use of an unapproved significant risk IDE requires an FDA IDE.

2. The IRB must determine whether it is in agreement with the rendering of the decision by the sponsor of the device being a non-significant risk or a significant risk device. When the IRB is in agreement with the sponsor's determination of NSR, no report to the FDA is required until the data are submitted. However, the sponsor must be notified when the IRB disagrees with the sponsor's NSR determination.

3. The IRB may approve or disapprove the proposed research based on local context and its responsibilities to protect human participants in research even when approval of the device has been granted by the FDA.

4. The Investigator is responsible for the tracking and oversight of FDA-regulated devices in research and must meet the following requirements in order to use an investigational device in research conducted under the jurisdiction of the DOH IRB:

    a. The investigational device must be used only by the Investigator or under his/her direct supervision;

    b. The investigational device must be used only as approved by the FDA and as described in the currently approved IRB documents;

    c. The Investigator must not supply the investigational device to persons not authorized under the IDE; and

    d. Informed consent from the participant or the participant's legally authorized representative must be prospectively obtained.

5. Research with the use of an investigational device must be conducted under DOH IRB applicable policies and procedures.

D. Advertising or Recruitment for Studies That Involve an IDE (DOHP 400-4.7, "Recruitment and Advertising")

1. Advertisements or recruiting tools must not include the term "new treatment", without explaining that the IDE is "investigational, meaning non-FDA approved". A phrase such as "receive new treatment" implies that study participants will be receiving newly marketed products of proven worth. It is not a treatment because its effectiveness has not been proven or established. The term "new" is misleading as it gives the participant hope of a new intervention when the outcome is unknown. This could be viewed as coercive; and

2. Advertisements or recruiting tools must not include the promise of “free medical treatment” when the intent is only to say that participants will not be charged for taking part in the investigation or experimental intervention (e.g. device). The use of the word “free” could be viewed as coercive as it may entice someone to participate in a study for the perceived benefits.

E. Informed Consent in Research That Involves an IDE

1. Informed consent must meet the requirements outlined in the IRB Informed Consent policies and procedures (See DOHPs 400-5.1 - 5.5 and corresponding procedures);

2. No claims are to made which state or imply, directly or indirectly, that the IDE is safe or effective for the purposes under investigation or that the device is in any way superior to any other device;

3. The informed consent document must contain a statement that the IDE is “investigational, meaning non-FDA approved”;

4. The informed consent document must contain a statement that the FDA may have access to the participant’s medical records as they pertain to the study; and

5. The Investigator must ensure that throughout the consenting process and study participation the participant understands that the IDE is experimental, and that its benefits for the condition under study are unproven.

F. Additional Reporting Requirements

1. Devices may have an unanticipated adverse device effect to participants or others. An investigator must submit to the sponsor and to the DOH IRB any problems requiring prompt reporting to the IRB (See DOHP 400-4.6, “Problems Requiring Prompt Reporting to the IRB”) occurring during an investigation as soon as possible, but in no event later than 10 working days after the Investigator first learns of the effect. Should the IRB determine that the new information gained in the adverse effect report changes its risk assessment, the IRB has the ability to reconsider its prior NSR decision and ask for FDA review.

2. A sponsor must immediately conduct an evaluation of any unanticipated adverse device effect to participants or others.

   a. A sponsor who determines that an unanticipated adverse device effect presents an unreasonable risk to participants must terminate or suspend all investigations or parts of investigations presenting that risk as soon as possible. Termination or suspension must occur no later than five working days after the

sponsor makes this determination and no later than 15 working days after the sponsor first received notice of the effect.

b. When the device is a significant risk device, a sponsor may not resume a terminated or suspended investigation without IRB and FDA approval. When the device is not a significant risk device, a sponsor may not resume a terminated or suspended investigation without IRB approval and, when the investigation was terminated or suspended for an unanticipated adverse device effect that presented an unreasonable risk to participants or others, FDA approval.

3. Within 90 days after termination or completion of the investigation or the Investigator's part of the investigation, the Investigator must submit a final report to the sponsor and the DOH IRB.

VI. History Notes

The Office of Public Health Research, Ethics and Human Research Protections Program is responsible for this policy.

Revised 05/15/2010
Reviewed 08/23/2013
Replaces DOHP 400-7.2-09

VII. Signature Block with Effective Date

Ana M. Viamonte Ros, M.D., M.P.H.
State Surgeon General
Florida Department of Health

Date

I. Policy

It is the policy of the Department of Health (DOH), Institutional Review Board (IRB) that the use of investigational drugs, agents, and/or biologics be reviewed and approved for use in accordance with the federal regulations.

II. Authority

A. Chapter 381.86, Institutional Review Board, *Florida Statutes*

B. Rule 64H-2.001, Institutional Review Board, *Florida Administrative Code*

III. Supportive Data

A. 21 CFR 50 and 56, 312, and 509

B. U.S. Food and Drug Administration Information Sheet: Investigational Use of Marketed Drugs, Biologics and Medical Devices, 1998.

IV. Definitions

See DOHP 400-11.1, “Definitions.”

V. Procedures

A. IRB Requirements for the Use of an Investigational Drug, Agent or Biologic.

1. The Department of Health, IRB will conduct initial approval and ongoing monitoring of investigational drugs, agents, and biologics used in human subjects research under its jurisdiction. Included in this process is a review by a pharmacist on the IRB committee. Prospective IRB review is required even when a waiver from IRB regulations has been granted by the FDA for use of the investigational drug, agent, or biologic.

2. FDA regulations allow certain individuals not enrolled in clinical trials to obtain expanded access to investigational drugs, agents, or biologics through the following methods:

a. Compassionate Use: The term “compassionate use” is erroneously used to refer to the provision of investigational drugs outside of an ongoing clinical trial to a limited number of patients who are desperately ill and for whom no standard alternative therapies are available. The term “compassionate use” does not, however, appear in FDA or DHHS regulations. It is preferable, instead, to use the names of the specific access programs when discussing the use of investigational articles outside of formal clinical trials.

b. Group C Treatment Investigational New Drug (IND): A means for the distribution of investigational drugs, agents, or biologics to oncologists for the treatment of cancer under protocols outside controlled clinical trials. Group C drugs, agents, or biologics usually have shown evidence of relative and reproducible efficacy in a specific tumor type. Although the FDA typically grants a waiver for most drugs used in Group C Treatment IND protocols, the DOH IRB requires prospective IRB review and approval.

c. Open – Label Protocol: A study designed to obtain additional safety data, typically done when the controlled trial has ended and treatment continues. The purpose of such a study is to allow participants to continue to receive the benefits of the investigational drug, agent, or biologic until marketing approval is obtained. Prospective IRB review and approval is required.

d. Parallel Track: A method approved by the FDA that expands the availability of investigational drugs, agents, or biologics as quickly as possible to persons with AIDS and other HIV-related diseases. These drugs, agents or biologics are utilized in separate protocols that “parallel” the controlled clinical trials and are essential to establish the safety and effectiveness of these new drugs, agents or biologics. Although the Secretary of the Department of Health and Human Services may, on a protocol-by-protocol basis, waive the provisions of 45 CFR 46 where adequate protections are provided through other mechanisms, prospective IRB review and approval is required by the DOH IRB.

e. Treatment IND or Biologics: A mechanism for providing eligible participants with investigational drugs (as early in the drug development process as possible) for the treatment of serious and life-threatening illnesses for which there are no satisfactory alternative treatments. The FDA defines an immediately life-threatening disease as a stage of a disease in which there is a reasonable likelihood that death will occur within a matter of months or in which premature death is likely without early treatment. The FDA will permit an investigational drug to be used under a treatment IND after sufficient data have been collected to show that the drug “may be effective” and does not have unreasonable risks. Prospective IRB review and approval is required.

f. There are four requirements that must be met before a treatment IND can be issued:

1) The drug is intended to treat a serious or immediately life-threatening disease;

2) There is no satisfactory alternative treatment available;

3) The drug is already under investigation or trials have been completed; and

4) The trial sponsor is actively pursuing marketing approval.

g. The FDA identifies two special considerations when a patient is to be treated under a Treatment IND:

1) Informed Consent. Informed consent is especially important in treatment use situations because the participants are desperately ill and particularly vulnerable. They will be receiving medications which have not been proven either safe or effective in a clinical setting. Both the setting and their desperation may work against their ability to make an informed assessment of the risk involved. Therefore, the IRB should ensure that potential participants are fully aware of the risks involved in participation.

2) Charging for Treatment INDs. The FDA permits charging for the drug, agent, or biologic when used in a Treatment IND. Therefore, the IRB Committee should pay particular attention to Treatment INDs in which the participants will be charged for the cost of the drugs. When participants will be charged for the use of the test article, economically disadvantaged persons will likely be excluded from participation. Charging for participation may preclude economically disadvantaged persons as a class from receiving access to test articles. The IRB should balance this interest against the possibility that unless the sponsor can charge for the drug, it will not be available for treatment use until it receives full FDA approval.

h. Single-Patient Use: The use of an investigational drug outside of a controlled clinical trial for a patient, usually in a desperate situation, who is unresponsive to other therapies or in a situation where no approved or generally recognized treatment is available. There is usually little evidence that the proposed therapy is useful, but may be plausible on theoretical grounds or anecdotes of success. Access to investigational drugs for use by a single, identified patient may be gained either through the sponsor under a treatment protocol, or through the FDA, by first obtaining the drug from the sponsor and then submitting a treatment IND to the FDA requesting authorization to use the investigational drug for treatment use. Prospective IRB review and approval is required (See B.3. below)

i. Emergency IND: The emergency use of an unapproved investigational drug, agent or biologic requires an emergency IND. The FDA has established mechanisms and guidance for obtaining an Emergency IND for the use of investigational drugs, agents, or biologics. Additional DOH IRB guidance regarding emergency IND is provided in the "Emergency Use of FDA Regulated Product" policy (See DOH IRB Policy 7.5, "Emergency Use of FDA-regulated products" for details).

3. Where the protocol is subject to review under more than one department or agency's regulations, the requirements of each set of regulations must be met. This situation may arise, for example, with Treatment Investigational New Drugs where both the FDA and DHHS have jurisdiction over the research. The use of an unapproved investigational drug, agent or biologic requires an FDA investigational new drug application (IND).

B. Use of an Investigational Drug, Agent or Biologic by an Investigator.

1. In order for an investigational drug, agent or biologic to be used in clinical research at DOH, an Investigational New Drug (IND) must be on file with the FDA and an IND number granted.

2. Clinical Investigations of a drug, agent, or biologic that is lawfully marketed in the United States are exempt from the requirements of an IND, when the following conditions are met:

a. Use of the investigational drug, agent or biologic is not intended to be reported to the FDA in support of a new indication for use nor support any significant change in labeling for the product;

b. The use of the investigational drug, agent, or biologic is not intended to support a significant change in the advertising of the product;

c. The use of the product does not involve a route of administration, dosage level, and/or use in a subpopulation, or other factors that significantly increase the risks, or decrease the acceptability of the risks associated with the use of the drug, agent, or biologic.

d. The use will be conducted in compliance with the IRB approval and informed consent procedures;

e. The use will be conducted in compliance with the requirements concerning the promotion and sale of the drug, agent, or biologic as described in FDA regulations 21 CFR Sec 312.7; and

f. The use does not intent to invoke exception from informed consent requirements for emergency use.

3. Research involving combinations of FDA approved drugs, agents, or biologics that are currently approved as single use, do not require an IND. However, use of these drugs, agents or biologics in research must still be prospectively reviewed and approved by the IRB.

4. The Investigator administering an investigational drug, agent or biologic must meet the following requirements in order to use an investigational drug, agent or biologic in research conducted under the jurisdiction of the DOH IRB.

    a. The drug, agent or biologic must be used only in accordance with the plan of investigation as described by the FDA-approved IND application and the IRB-approved protocol;

    b. The drug, agent, or biologic may only be used in participants under the Investigator's personal supervision or under the supervision of physicians who are directly responsible to the Investigator; and

    c. Informed consent from the participant or the participant's legally authorized representative is prospectively obtained, unless a waiver of consent has been approved by the DOH IRB.

5. Research with the use of an investigational drug, agent, or biologic must be conducted in accordance with Department of Health IRB policies.

C. Advertising or Recruitment for Studies Involving Investigational Drugs, Agents, or Biologics (*See* DOH IRB Policy 400-4.7, "Recruitment and Advertising")

1. Advertisements or recruiting tools must not include the term "new treatment," without explaining that the drug, agent, and biologic is "investigational, meaning non-FDA approved." A phase, such as "receive new treatment" implies that study participants will be receiving newly marketed products of proven worth. It is not a treatment because its effectiveness has not been proven or established. The term "new" is misleading as it gives the participant hope of a new intervention when the outcome is unknown. This could be viewed as coercive; and

2. Advertisements or recruiting tools must not include the promise of "free medical treatment" when the intent is only to say that participants will not be charged for taking part in the investigation or experimental intervention (e.g. drug, agent, biologic.) The use of the word "free" could be viewed as coercive as it may entice someone to participate in a study for the perceived benefits.

D. Informed Consent in Research That Involves an Investigational Drug, Agent, or Biologic.

1. Informed consent must meet the requirements outlined in the IRB Informed Consent policies and procedures (*See* DOH IRB Policies 400-5.1 – 5.5 and corresponding procedures);

2. No claims are to made which state or imply, directly or indirectly, that the investigational drug, agent, or biologic is safe or effective for the purposes under investigation or that the drug is in any way superior to another drug;

3. The informed consent document must contain a statement that the drug, agent, or biologic is "investigational, meaning non-FDA approved;"

4. The informed consent document must contain a statement that the FDA may have access to the participant's medical records as they pertain to the study; and

5. The Investigator must assure that throughout the consenting process and study participation the participant understands that the investigational drug, agent, or biologic is under investigation, and that its benefits for the condition under study are unproven.

6. For Phase I studies, the informed consent document must disclose that the purpose of the research includes examining the drug's safety. For Phase II and Phase III studies, the informed consent document must disclose that the purpose of the research includes examining the drug's safety and efficacy.

VI. History Notes

The Office of Public Health Research, Ethics and Human Research Protections Program is responsible for this policy.

Revised 9/23/2009
Reviewed 08/23/2013

VII. Signature Block with Effective Date

Ana M. Viamonte Ros, M.D., M.P.H.
State Surgeon General
Florida Department of Health

Date

I. Policy

It is the policy of the Department of Health (DOH), Institutional Review Board (IRB) to review and approve the use of all Humanitarian Use Devices.

II. Authority

A. Chapter 381.86, Institutional Review Board, *Florida Statutes*

B. Rule 64H-2.001, Institutional Review Board, *Florida Administrative Code*

III. Supportive Data

A. 21 CFR 814, 803.30

B. U.S. Food and Drug Administration Device Exemptions Regulation" Questions and Answers; Final Guidance for Industry, July 12, 2001.

C. U.S. Food and Drug Administration Device Regulations, June 26, 1996.

IV. Definitions

See DOHP 400-11.1, "Definitions."

V. Procedures

A. IRB review of HUD Use.

1. In order for a HUD to be used in treatment, diagnosis, or research at DOH, the IRB and the FDA must approve it and a Humanitarian Device Exemption (HDE) issued.

    a. The IRB approval must verify that the use of the HUD, as proposed, is congruent with current labeling of the device, and does not exceed the scope of the FDA approved indication.

    b. The IRB may impose more stringent restrictions for use of the HUD as a means of additional protections, as deemed necessary.

2. The initial review of a HUD is to be completed by the full IRB Committee. The full Committee may make the determination at initial review that subsequent continuing reviews meet expedited criteria.

3. The physician utilizing the HUD for treatment, diagnosis or research must use the HUD only in accordance with the labeling of the device, intended purpose, and in the designated population for which the FDA approved its use.

a. Only the holder of the HUD agreement with the FDA must use the HUD; and

b. Informed consent is required from a patient prior to the use of a HUD when:

1) the HUD is the subject of a clinical investigation; or

2) the IRB requires use of informed consent.

B. Considerations for prompt reporting

1. Whenever the physician or health care provider receives or otherwise becomes aware of information, from any source, that reasonably suggests that a HUD has or may have caused or contributed to the death or serious injury of a patient, the physician or health care provider must report such findings to the FDA and the IRB as soon as possible, but no later than 10 working days after the Investigator first learns of the effect or problem (See IRB Policy 400-4.6 “Problems Requiring Prompt Reporting to the IRB”) This reporting is in addition to, not a substitute for, FDA and/or manufacturer reporting requirements in accordance with 21 CFR 803.30.

2. The physician or health care provider shall promptly report FDA action(s) regarding the HUD to the IRB.

3. Modifications to the HUD or the clinical use of the HUD are to be promptly reported to the DOH IRB in accordance with the DOH IRB Policy 400-4.5, “Amendments to Approved or Exempt Research.”

VI. History Notes

The Office of Public Health Research, Ethics and Human Research Protections Program is responsible for this policy.

Revised 9/30/2009
Reviewed 08/23/2013

VII. Signature Block with Effective Date

Ana M. Viamonte Ros, M.D., M.P.H.
State Surgeon General
Florida Department of Health

Date

I. Policy

It is the policy of the Department of Health (DOH) Institutional Review Board (IRB) to recognize the provisions found in the Food and Drug Administration (FDA) regulations for the emergency use of investigational drugs, biologics, agents, or devices.

II. Authority

A. Chapter 381.86, Florida Statutes, Institutional Review Board

III. Supportive Data

A. 21 CFR §50.23

B. 21 CFR §50.24

C. 21 CFR §50.25(d),

D. 21CFR §56.102(d)

E. 21 CFR §56.104(c)

F. FDA Information Sheets: Frequently Asked Questions: IRB Procedures

G. FDA Information Sheets: Emergency Use of an Investigation Drug or Biologic, Emergency Use of Unapproved Medical Devices

H. FDA Guidance: Emergency Use Authorization of Medical Products http://www.fda.gov/RegulatoryInformation/Guidances/ucm125127.htm

I. Section 564 of the Federal Food, Drug and Cosmetic Act (FD&C Act).

J. Project BioShield Act of 2004, Public Law 108–276

K. Nightingale SL, Prasher JM, Simonson S. Emergency Use Authorization (EUA) to enable use of needed products in civilian and military emergencies, United States. Emerg Infect Dis [serial on the Internet]. Available from http://www.cdc.gov/EID/content/13/7/1046.htm

IV. Definitions

See DOHP 400-11.1, “Definitions”

V. Procedures

A. Nothing in this policy is intended to limit the authority of a physician to provide emergency medical care for patients who need such care, to the extent the physician is permitted to do so under FDA regulation and other applicable law.

B. Emergency use of a test article is not human research subject to DHHS regulations (45 CFR 46). Data from an emergency use may not be reported in a way that implies that the activity was a prospectively planned systematic investigation designed to develop or contribute to generalizable knowledge.

C. Emergency use of a test article is research involving human subjects subject to FDA regulation. The patient given the investigational article is a participant in FDA-regulated research. The FDA may require data from an emergency use to be reported in a marketing application. The IRB may allow data from an emergency use to be published in a retrospective report and all other uses required by FDA.

D. The emergency use provision in the FDA regulations [21 CFR 56.104(c)] is an exemption from prior review and approval by the IRB when it meets several conditions. To insure that emergency use is consistent with regulation, investigators should notify the Human Research Protection Administrator designated in the Department's Assurance, HRPP Staff, or an IRB Chair first.

1. The Human Research Protection Administrator designated in the Department's Assurance or IRB Chair will review the situation with the investigator to make sure the criteria allowing exemption from IRB review under FDA regulation and Department policy concerning emergency use are met:

    a. The patient is in a life-threatening or severely debilitating situation.

    b. No standard acceptable treatment is available.

    c. There is not sufficient time to obtain IRB approval

    d. The use is reported to the IRB within five (5) days by the investigator administering the investigational article.

    e. Informed consent will be obtained and documented in accordance with 21 CFR 50 or the situation meets the waiver criteria in 21 CFR 50.23

    f. The emergency use of an unapproved investigational drug or biologic requires an IND. If the subject does not meet the criteria of an existing approved protocol, the investigator should contact manufacturer of drug/biologic to determine if it can be provided under an existing IND or, if not available through the manufacturer, contact the FDA for an Emergency IND.

    g. Permission of the sponsor exists prior to use..

    h. The activity does not meet the DHHS definition of "research" involving "human subjects" as defined by DHHS.

2. Documentation that the situation is a life-threatening emergency should be provided in both the patient's medical record and in a letter to the IRB.

E. If there is no time to contact the Human Research Protection Administrator or IRB Chair prior to use, the Human Research Protection Administrator or IRB Chair will make the determination retrospectively based on the report that is provided within five (5) days and issue a letter indicating whether the activity met the exemption requirements at 21 CFR 56.103(c).

F. Notification of the Human Research Protection Administrator or IRB Chair should not be construed as IRB approval. The investigator is required to submit notification using IRBWise within five working days, and notifying the Human Research Protection Administrator or Chair is used to initiate tracking and insure the investigator files this report as required in FDA regulation (21 CFR 56.104(c).

G. If the chair determines, based on retrospective evaluation, that the activity does not meet the exemption requirements at 21 CFR 56.103(c) the issue will be handled according to DOHP 400-10.1, "Investigating any Non-Compliance, Serious or Continuing Non-Compliance".

H. Not all emergency use requires exemption from prior IRB review. It there is sufficient time to allow IRB review, investigators will complete a new IRBWise application which will be scheduled for review at the next possible meeting. FDA regulations [21 CFR 56.102(d)] permit one emergency use, but any subsequent use must have prior IRB review and approval [21 CFR 56.104(c)]. If an investigator anticipates the possible subsequent use of the agent will occur, the investigator should complete an IRBWise application.

I. Manufacturers or sponsors that agree to allow the use of the investigational drug, agent, biologic or device, but will not ship without "an IRB approval letter", will be provided a written statement that the IRB is aware of the proposed use and based on the information it has been provided by the Investigator that the proposed use meets the requirements of 21 CFR 56.102(d).

J. During a public health emergency it may be necessary to give a test article to more than one patient. Project BioShield Act of 2004 provided a mechanism for population-level emergency use of unapproved medical products. EUAs represent a different mechanism for authorizing shipment and use of unapproved medical products than INDs and IDEs. An Emergency Use Authorization, or EUA, allows the use of drugs, biologics and medical devices that are not approved, licensed or cleared respectively (unapproved medical products) in an emergency to diagnose, treat, or prevent a serious or life-threatening disease or condition when there are no adequate, approved, or available alternatives.

K. Review by the DOH IRB is not required for EUAs. However, the HRPP may assist in providing information and guidance to local hospitals about why IRB review is not required

L. Procedure for Emergency Use Authorizations

1. Declaration of an emergency

   a. The Secretary of Homeland Security determines there is a domestic emergency, or a significant potential for a domestic emergency, involving a heightened risk of attack with a specified biological, chemical, radiologic, or nuclear agent or agents;

   b. The Secretary of Defense determines there is a military emergency, or a significant potential for a military emergency, involving a heightened risk of attack on U.S. military forces with a specified biological, chemical, radiologic, or nuclear agent or agents;

   c. The Secretary of Health and Human Services (DHHS) determines there is a public health emergency that affects, or has a significant biological, chemical, radiologic, or nuclear agent or agents, or a specified disease or condition that may be attributable to such agent or agents.

   d. Is not used as a diagnostic procedure without confirmation of the diagnosis by another, medically established diagnostic product or procedure.

2. A declaration of emergency is then issued under Section 564 of the Food Drug and Cosmetic Act. This allows for the potential use of a product under an EUA provided the FDA Commissioner certifies to the Secretary of DHHS that:

   a. the agent specified in the declaration of emergency can cause a serious or life-threatening disease or condition;

   b. based on the totality of scientific evidence available, including data from adequate and well-controlled clinical trials, if available, it is reasonable to believe that the product may be effective in diagnosing, treating, or preventing a serious or life-threatening disease or condition; or a serious or life-threatening disease or condition caused by a product authorized under section 564, or approved, cleared, or licensed under the FD&C Act or PHS Act, for diagnosing, treating, or preventing a disease or condition and caused by the agent specified in the declaration of emergency

   c. that the known and potential benefits outweigh the known and potential risks of the product when used to diagnose, prevent, or treat the serious or life-threatening disease or condition that is the subject of the declaration; and

d. that there is no adequate, approved, and available alternative to the product for diagnosing, preventing, or treating such serious or life-threatening disease or condition.

3. FDA Guidance specifies the information that should be submitted to FDA for consideration of an EUA

4. The FDA Commissioner may establish conditions on the use of a product under an EUA. The provider may be required by FDA to:

   a. Inform patients that the FDA Commissioner has authorized the emergency use of the product.

   b. Inform patients of the risks and benefits of the drug.

   c. Inform patients of any alternative therapies available.

   d. Inform patients that they may refuse administration of the unapproved product.

5. An EUA will be in effect for the duration of the declaration under which it was issued, unless the EUA is revoked because the criteria of issuance are no longer met or revocation is appropriate to protect public health or safety.

6. The terms and conditions of an EUA preempt state laws governing the dispensing, administration, or labeling of unapproved medical products or approved medical products for unapproved uses.

VI. History Notes

The Office of Public Health Research, Ethics and Human Research Protections Program are responsible for this policy.

Revised 6/16/2010
Reviewed 08/23/2013
Replaces DOHP 400-7.5-0

VII. Signature Block with Effective Date

Ana M. Viamonte Ros, M.D., M.P.H.
State Surgeon General
Florida Department of Health

Date

I. Policy

It is the policy of the Department of Health (DOH) Institutional Review Board (IRB) to follow legal requirements to allow reconstruction of a complete history of all IRB actions related to the review of research under its jurisdiction.

II. Authority

A. Chapter 381.86, Institutional Review Board, *Florida Statutes*

B. Rule 64H-2.001, Institutional Review Board, *Florida Administrative Code*

III. Supportive Data

A. 45 CFR §46.115 IRB records

B. 45 CFR §115(a)-(b), OHRP Guidance on Written Institutional Review Board (IRB) Procedures

C. 21 CFR §56.115(a)(b), FDA Information Sheets: Frequently Asked Questions: IRB Records

D. 21 CFR §56.115 IRB records

IV. Definitions

See DOHP 400-11.1, Definitions.

V. Procedures

A. Records shall be maintained in a manner that contains a complete history of all IRB actions related to review and approval of a research protocol

B. Records regarding research shall be maintained in electronic form indefinitely in a secure facility meeting DOH information security requirements, and shall be retained indefinitely when practical, but for at least three (3) years after completion of the research. If the protocol is cancelled without participant enrollment, IRB records are retained indefinitely when practical, but maintained for at least three years after cancellation.

C. Records must be accessible for inspection and copying by authorized representatives of any regulatory oversight agency or sponsor at reasonable times and in a reasonable manner.

D. The Human Research Protection Administrator specified in the Department's Assurance is responsible for ensuring appropriate records are maintained.

E. IRB Policies and Procedures. The IRB will maintain written policies and procedures that will be reviewed at least annually by the Ethics and Human Research Protection Program

G. The IRB Roster and record of appointments to the IRB in electronic form indefinitely in a secure facility meeting DOH information security requirements.

H. Records of research protocols include at least:

1. Copies of all research applications reviewed, including protocols, scientific and scholarly evaluations, if any, approved sample informed consent documents, recruitment materials, data safety monitoring board/committee reports, progress reports submitted by the Researchers, investigator brochures, and reports of adverse events, unanticipated problems to participants or others, including reports of injuries to participants, and review of allegations and findings of non-compliance.

2. All correspondence between the IRB and Researchers.

3. When conducting reviews by the expedited procedure, justification for using the expedited procedure (citation of expedited categories), description of actions and determinations by the reviewer as required by law. Results of reviews using the expedited procedure are communicated to IRB members in agendas for meetings.

4. Justification for exemption determinations

5. Justification for determinations that activities do not constitute research involving human subjects (public health practice, quality improvement, research not involving human subjects).

6. Determination required by FDA regulations, including but not limited to verification of the validity of INDs and IDEs.

7. Documentation of researcher qualifications, including a curriculum vitae or resume, verification of license when appropriate, and record of research ethics education.

I. IRB minutes recording IRB deliberations and determinations include at least:

1. Actions taken by the IRB.

2. Separate deliberations for each action.

3. Votes for each protocol as numbers for, against, or abstaining.

4. Attendance at the meeting, including record of when an alternate member replaces a primary member. Record of members or alternate members

who participate through videoconference or teleconference, and documentation that those members received all pertinent material before the meeting and were able to actively and equally participate in all discussions.

5. The basis for requiring changes in research.

6. The basis for disapproving research.

7. A written summary of the discussion of controverted issues and their resolution.

8. For initial and continuing review, the approval period.

9. The names of IRB members who leave the meeting because of a conflict of interest along with the fact that a conflict of interest is the reason for the absence.

10. Required determinations and protocol-specific findings justifying those determinations for:

    a. Waiver or alteration of the consent process

    b. Research involving pregnant women and neonates; 390.0111(6) Florida Statues provides that no person shall use any live fetus or live, premature infant for any type of scientific, research, laboratory, or other kind of experimentation either prior to or subsequent to any termination of pregnancy procedure except as necessary to protect or preserve the life and health of such fetus or premature infant

    c. Research involving prisoners

    d. Research involving children

    e. Justification of any deletion or substantive modification of information concerning risks or alternative procedures contained in the DHHS-approved sample consent document, when following DHHS regulations

    f. Documentation of the rationale for significant risk/non- significant risk device determinations, when following FDA regulations

11. Record of any training and education activities conducted at meetings of the convened IRB

VI. History Notes

The Office of Public Health Research, Ethics and Human Research Protections Program is responsible for this policy.

Revised 06/28/2010
Reviewed 08/23/2013
Replaces DOHP-8.1-07

VII. Signature Block with Effective Date

Ana M. Viamonte Ros, M.D., M.P.H.
State Surgeon General
Florida Department of Health

Date

I. Policy

It is the policy of the Department of Health (DOH) Institutional Review Board (IRB) that all Investigators and key study personnel conducting human subjects research under the jurisdiction of the DOH IRB complete initial and annual human research protections training.

II. Authority

A. Chapter 381.86, Florida Statutes, Institutional Review Board

III. Supportive Data

A. National Institutes of Health (NIH) policy, "Required Education in the Protection of Human Research Participants" June 5, 2000 (Revised August 25, 2000) available at http://grants2.nih.gov/grants/guide/notice-files/NOT-OD-00-039.html

B. Collaborative IRB Training Initiative (CITI) Training: http://www.citiprogram.org

IV. Definitions

See DOHP 400-11.1, "Definitions".

V. Procedures

A. All DOH Investigators and key study personnel must complete initial research ethics education and compliance training prior to research commencing, and re-certify every two years. Individuals engaged in research must provide certification of completion to the DOH IRB:

1. Training via the Collaborative IRB Training Initiative (CITI). This internet-based course in human subjects research protection and research ethics is available at no cost and designed specifically for all personnel that have a significant involvement in the planning, conduct, and analysis of any scientific activity that employs human research participants. The course consists of training modules that are divided into two tracks: Biomedical Research and Social/Behavioral Research. The learning objectives of the CITI course are:

    a. To provide an understanding of the historical perspectives, ethical principles, and federal regulations associated with the conduct of research with human participants;

    b. To provide a clear understanding of what constitutes informed consent and how it must be applied in research involving humans;

    c. To provide basic information on the regulations and policies governing research with investigational drugs, biologics, and devices;

d. To provide a clear understanding of the ethical issues and federal regulations in force during the conduct of Social/Behavioral research, records based research, and genetics research with human participants; and

e. To provide Investigators conducting research at VA facilities a clear understanding of the special procedural and regulatory policies for human research at VA research facilities.

2. HRPP staff are responsible for ensuring that certification of training is documented in IRBWise.

3. The IRB may not approve research without CITI certification present for all researchers and key study personnel.

B. A Researcher Guide will serve as a resource manual for all study personnel that will assist investigators in smoothly navigating the IRB process and adhering to the federal regulations and IRB policies related to human research protections. The manual is located on the DOH HRPP website at: http://flpublichealthethics.net

C. All Investigators and key study personnel conducting research involving human participants at DOH are encouraged to review the core training materials including the DOH Assurance, the DOH IRB policies and procedures, the Belmont Report, and the Federal regulations including 45 CFR 46, 21 CFR 50 and 56. Links to this information plus links to other federal agencies (e.g., National Institutes of Health, Food and Drug Administration, Office of Human Research Protections, etc. governing human subjects research are available at the DOH IRB website http://flpublichealthethics.net/

D. Research studies are not approved until all researchers study personnel complete research ethics education and training. Applications may be reviewed, however the IRB will defer approval until education is complete. Verification that researchers and staff completed education requirements represents a minor change to the study, and may be reviewed using the expedited procedure.

E IRB members must complete initial research ethics education and compliance training prior to research commencing, and re-certify every two years. New IRB members in addition receive training in the use of IRBWise.

F. New members observe at least one meeting, and do not vote. In their second meeting they may vote, but are not assigned as a primary reviewer. In their third meeting they may be assigned as a primary reviewer, but may not take the lead in presenting a study. New members' understanding is assessed by HRPP Staff, and individual feedback is provided.

G. The IRB will send mass e-mail notifications, limited to a mailing list of all Investigators and key study personnel that have active studies, to alert them of

pertinent IRB issues or decisions that may impact their research.

VI. History Notes

The Office of Statewide Research, Ethics and Human Research Protections Program are responsible for this policy.

Revised 06/16/2010
Reviewed 08/23/2013
Replaces DOHP 400-9.1-08

VII. Signature Block with Effective Date

Ana M. Viamonte Ros, M.D., M.P.H.
State Surgeon General
Florida Department of Health

Date

I. Policy

It is the policy of the Department of Health (DOH) Institutional Review Board (IRB) to provide information to the public regarding the rights of research participants.

II. Authority

A. Chapter 381.86, Florida Statutes, Institutional Review Board

III. Supportive Data

A. IRB Website: http://flpublichealthethics.net/index.php/eng/participants

IV. Definitions

See DOHP 400-11.1, “Definitions”.

V. Procedures

A. The IRB will provide a toll-free contact number to contact HRPP Staff. The number provides prospective participants, participants in research, and former participants a way to contact HRPP Staff and discuss problems, concerns, or make a complaint; ask questions; obtain information; or offer input about the Department can improve the process of participating in research.

B. HRPP Staff when conducting administrative screening of applications ensure that the toll-free number appears on every informed consent document following a statement about whom the participant may contact independent of the research regarding questions or for additional information concerning the rights of participants in research.

C. The HRPP will maintain a mechanism to receive complaints from participants or others in a confidential manner. Complaints may be communicated via the toll-free number, or by using a web-based form.

D. HRPP Staff will be available to provide presentations to community groups and for DOH conferences involving public outreach to provide information and increase awareness of human research protections.

E. The HRPP makes available the brochure produced by the Office of Human Research Protection Programs, entitled “Becoming a Research Volunteer: It’s Your Decision” or equivalent. This brochure, or equivalent, includes the following:

1. Information about research understandable to the public;

2. A description of an IRB and its role;

3. The process of informed consent and information that must be made available to ensure participants can understand the research and make a voluntary decision to participate.

F. The Human Research Protection Administrator designated in the Department's Assurance is responsible for annually evaluating outreach activities and making improvements to these activities, as needed. During this annual evaluation, the Human Research Protection Administrator will seek input from the IRB Administrator, IRB Assistant Administrator, and IRB Chairs for feedback on how outreach activities may be improved.

VI. History Notes

The Office of Public Health Research, Ethics and Human Research Protections Program is responsible for this policy.

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VII. Signature Block with Effective Date

Ana M. Viamonte Ros, M.D., M.P.H.
State Surgeon General
Florida Department of Health

Date

I. Policy

It is the policy of the Department of Health (DOH) Institutional Review Board (IRB) to investigate allegations and manage findings of non-compliance with human research protection program requirements.

II. Authority

A. Chapter 381.86, Institutional Review Board, *Florida Statutes*

B. Rule 64H-2.001, Institutional Review Board, *Florida Administrative Code*

III. Supportive Data

A. 45 CFR §46.103(b)(5)(i)

B. 45 CFR §46.116(b)(5)

C. 21 CFR §50.25(b)(5)

D. 21 CFR §56.108(b)(2)

E. DOHP 400-4.6, “Problems Requiring Prompt Reporting to the IRB”

F. DOHP 400-10.1, “IRB Compliance Activities”

G. DOHP 400-10.2, “Administrative Hold, Suspension, or Termination of IRB Approval”

H. DOHP 400-10.4, “Reporting to Institutional Official, Department, or Agency Heads”

IV. Definitions

See DOHP 400-11.1, Definitions.

V. Procedures

A. Requirements for reporting allegations of non-compliance

Information regarding non-compliance in human subjects research may come to the attention of the DOH IRB through several pathways:

1. Investigators, study team members, sponsors, IRB members, and IRB staff, and those with direct supervision for researchers are required to report non-compliance.

2. Reports may also come from any source such as a participant or their family members, institutional personnel, other institutional Committees, the media, anonymous sources, or the public.

3. Reports are made to the Human Research Protection Administrator designated in the Department's Assurance.

4. Normally reports are made using IRBWise, but reports may also come via telephone, email or letter, or via an anonymous web-based form on the Ethics and Human Research Protection Program website at http://www.flpublichealthethics.net

5. The following types of information should be submitted, with as much information provided as possible so allegations of non-compliance can be assessed:

   a. Description of what happened, including the time and persons involved
   b. Name of the researcher
   c. Name of the study
   d. Location of the research

6. Researchers are required to report non-compliance to all IRBs with jurisdiction over the research, and provide documentation of their determinations to the Department.

7. Non-compliance should be reported regardless of whether it may have occured during the study, after study completion, or after participant withdrawal or completion.

B. Process for investigation of each allegation of non-compliance

1. The IRB staff conduct an investigation of all reports of alleged non-compliance to determine whether each allegation of non-compliance has a basis in fact. If the allegation of non-compliance is found not to have a basis in fact, then no further action is taken, unless the event involves unanticipated problem involving risks to participants or others. See DOHP 400-4.6, "Problems requiring prompt reporting to the IRB."

2. If the IRB staff find that an allegation of non-compliance has a basis in fact, or if staff is uncertain, then the alleged non-compliance is referred to the IRB Chair for determination, normally the IRB Chair of the committee that reviewed and approved the research.

3. The IRB Chair investigates the allegation of non-compliance and determines if the allegation is non-compliance. If the Chair determines the allegation of non-compliance has no basis in fact, then no further action is taken, unless the event involves unanticipated problem involving

risks to participants or others. See DOHP 400-4.6 "Problems requiring prompt reporting to the IRB."

4. If an allegation of non-compliance is found not to have a basis in fact by staff or the Chair, then an administrative comment is filed in IRBWise documenting the reasons and the investigator is informed using IRBWise.

C. Process for handling non-compliance found to have a basis in fact, that is neither serious nor continuing

1. The Chair evaluates each instance of non-compliance and determines whether it is serious and whether it is continuing, and whether the non-compliance involves unanticipated problem involving risks to participants or others. See DOHP 400-4.6 "Problems requiring prompt reporting to the IRB."

2. If the Chair determines the non-compliance is neither serious nor continuing, then the Chair, when appropriate

   a. Reviews a draft of the corrective action plan provided by the researcher and determines whether it is acceptable;

   b. Staff includes the information on an IRB agenda as an information item.

3. The Chair may refer non-compliance that is neither serious nor continuing to the full committee for review.

4. If the IRB Chair determines the non-compliance is serious or continuing, or is uncertain, then the Chair must refer to the full committee for review.

D. Process for handling non-compliance found to have a basis in fact, that is serious or continuing

1. The convened IRB reviews all allegations of serious or continuing non-compliance using a primary reviewer system.

   a. Reviewers are assigned by the IRB staff, where necessary in consultation with the IRB Chair. Where possible, non-compliance will be reviewed by one or more primary reviewers who conducted the most recent review of the protocol. Reviewers will have relevant subject matter expertise, and may request additional expertise. See DOHP 400-4.3, "Review of Human Subjects Research: Initial Review."

   b. All committee members have access to the allegation of non-compliance and supporting documents (including but not limited to safety monitoring board reports and sponsor reports). In addition,

all committee members have access to all documents reflecting the current IRB-approved state of the protocol, including but not limited to the protocol, consent document, and supplemental information.

c. One or more primary reviewers will review the report of non-compliance, all supporting documents, and all the documents reflecting the current IRB-approved state of the protocol.

d. All other committee members will review the report, the initial IRB application updated with any changes, any supporting documents, and the consent document.

2. The IRB will determine whether non-compliance is serious or continuing.

3. If the IRB determines non-compliance is not serious or continuing, no further action will be taken if the problem does not involve a problem requiring prompt reporting to the IRB. See DOHP 400-4.6, “Problems Requiring Prompt Reporting to the IRB”.

4. If the IRB determines non-compliance is serious or continuing, then the IRB will determine which of the following actions are appropriate regarding the protocol.

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a. Modification of the protocol.

b. Modification of the information disclosed during the consent process.

c. Providing additional information to past participants.

d. Notification of current participants when such information might relate to participants’ willingness to continue to take part in the research.

e. Requirement that current participants re-consent to participation.

f. Modification of the continuing review schedule.

g. Monitoring of the research.

h. Monitoring of the consent.

i. Suspension of the research. Suspension means all interventions or interactions with living individuals cease until the IRB determines research may commence, except when the suspension of study drugs or other interventions would place participants at risk.

j. Termination of the research. Termination means all interventions or interactions with living individuals cease. When terminating research would place participants at risks of harm, the IRB will work with the researcher to transition patients to a new study or other appropriate action.

k. Referral to other organizational entities (legal counsel, county health department director, division director, Deputy Secretary. and State Surgeon General in the role of Institutional Official.

5. The IRBs discussion is documented in minutes, including discussion of controverted issues, if any, and their resolution.

6. The investigator is informed of the IRB's determination using IRBWise.

E. Any non-compliance that is serious and continuing is reported to regulatory agencies and institutional officials or others following the DOH reporting policy. See DOHP 400-10.4, "Reporting to Institutional Official, Department or Agency Heads".

1. The report of non-compliance will be distributed to the IRB, the Human Research Protection Administrator designated in the Department's Assurance, and Director, Office of Public Health Research, the Deputy Secretary for Health, the State Surgeon General, and the OHRP, if research is covered by DHHS regulations, and other federal agencies when the research is overseen by those agencies and they require reporting separate from OHRP, and the FDA when research is FDA-regulated.

2. Reporting of non-compliance will take place in accordance with DOHP 400-10.4, "Reporting to Institutional Official, Department or Agency Heads".

F. Instances meeting the definition of research misconduct will be reported to the Division Director of the Investigator's Division, or the Dean of the Investigator's University, or the President of the Investigator's company by the Human Research Protection Administrator designated in the Department's Assurance, or by the Director, Office of Public Health Research or the Institutional Official.

1. Attempts to influence unduly an IRB Committee Member or IRB staff are considered research misconduct.

2. IRB members or staff who believe that they have been subject to undue influence must report this to the Human Research Protection Administrator designated in the Department's Assurance, or the Director of the Office of Public Health Research or the DOH Institutional Official.

3. The Human Research Protection Administrator designated in the Department's Assurance is responsible for investigating allegations of undue influence and taking corrective action, unless that person is the subject of an allegation. In such a case, the Director of the Office of Public Health Research investigates and takes corrective action. The Institutional Official may also refer the allegation to the Office of Inspector General for investigation and corrective action. If an allegation is found not to have a basis in fact, no further action is taken.

4. If an allegation is found to have a basis in fact, then the Institutional Official, Director, Office of Public Health Research, or the Human Research Protection Administrator designated in the Department's Assurance will report all attempts of undue influence of the IRB process to the Division Director of the Investigator's Division, or the Dean of the Investigator's University, or the President of the Investigator's company.

VI. History Notes

The Office of Public Health Research, Ethics and Human Research Protections Program is responsible for this policy.

Revised 07/06/2010.
Reviewed 08/23/2013

VII. Signature Block with Effective Date

Ana M. Viamonte Ros, M.D., M.P.H.
State Surgeon General
Florida Department of Health

Date

I. Policy

It is the policy of the Department of Health (DOH) Institutional Review Board (IRB) that all currently approved research is subject to modification or change in approval status, as deemed necessary by the DOH IRB, to protect participants in research. The IRB may suspend or terminate research if the research is not being conducted in accordance with the IRB's requirements or the Federal regulations or if it has been associated with unexpected serious harm to participants. Examples of a suspension include:

A. Inappropriate involvement of human subjects in research;

B. Inhibition of the rights or welfare of participants;

C. Serious non-compliance, or continuing non-compliance with Federal regulations or IRB policies; or

D. New information regarding increased risk to human participants

II. Authority

A. Chapter 381.86, *Florida Statutes*, Institutional Review Board

B. Rule 64H-2.001, Institutional Review Board, *Florida Administrative Code*

III. Supportive Data

A. 45 CFR 46.113

B. 42 CFR 50 Subpart A

C. OHRP Guidance Document, "Guidance on Continuing Review" dated July 11, 2002

D. DOH IRB Policy10.1, "Investigating Any Non-Compliance, Serious or Continuing Non-Compliance"

E. DOH IRB Policy 4.4, "IRB Continuing Review"

IV. Definitions

See DOHP 400-11.1, "Definitions"

V. Procedures

A. Sponsor-Imposed Suspensions.

1. Notification of suspension by a sponsor for whatever reason is reviewed as an unanticipated problem. See DOHP 400-4.6, "Problems requiring prompt reporting to the IRB"

C. Study Expiration.

1. If an Investigator has failed to provide continuing review information to the IRB or the IRB has not reviewed and approved a research study by the specified continuing review expiration date, the study expires. Enrollment of new participants cannot occur after the expiration of IRB approval and all research activities must stop including recruitment, enrollment, interventions, and interactions, and collection of private identifiable data.

2. Once notified of the expiration, the Investigator must immediately submit to the IRB Chairperson, a list of research participants for whom cessation of the research would cause harm.

    a. The full IRB Committee reviews this list and allows individual participants to continue participating in the research interventions or interactions only when the IRB determines that it is in their best interests.

3. The IRB notifies the Investigator in writing of the Study Expiration.

    a. The letter indicates that after the expiration date:

        1. Enrollment of new participants must stop;

        2. All research activities must stop; and

        3. Any continuation research activity is a violation of Federal regulations.

    b. The letter also indicates that the Investigator must immediately submit to the IRB, a list of research participants for whom cessation of the research would cause harm.

4. Research studies not reviewed and approved within ninety (90) calendar days of the notification of Study Expiration are administratively closed by the IRB. Reinstatement of the research requires submission of a research protocol for initial review.

D. Suspensions and Terminations of IRB Approval.

1. The convened IRB is authorized to suspend research.

2. If research needs to be suspended in an urgent manner to protect research participants, an IRB Chair, or the Human Research Protection Administrator designated in the Department's Assurance, or the State Surgeon General may suspend research. When research is suspended by someone other than the convened IRB, the convened IRB will be notified at the next meeting. In addition to notifying the convened IRB, the Director, Office of Public Health Research, Deputy Secretary, and State Surgeon General will be notified.

3. Only the convened IRB may terminate research

E. Procedure for reporting suspensions and terminations

1. The IRB reports all suspensions in writing promptly to the Investigator.

   The letter:

   a. Includes a statement of the reasons for the IRB's action;

   b. Requires the Investigator to submit to the IRB proposed procedures for withdrawal of currently enrolled subjects that considers their rights and welfare. The IRB Committee reviews the proposed procedures. The IRB may mandate oversight or transfer responsibility to another Investigator to assure implementation of these procedures;

   c. Requires the Investigator to submit to the IRB a proposed script or letter notifying all currently enrolled participants that are affected by the suspension. The IRB Committee reviews the proposed script or letter. If follow-up of subjects for safety reasons is permitted/required by the IRB, participants should be so informed. The IRB may directly contact participants to fulfill this notification; and

   d. Requires the Investigator to report any events to the IRB or sponsor that would have required reporting had the former participants continued to be enrolled in the research. The IRB may mandate oversight or transfer responsibility to another Investigator to ensure implementation of these procedures.

2. There is no need for the IRB to consider whether recurrent suspensions or terminations alone are serious or continuing non-compliance because all non-compliance that leads to a suspension or termination will be evaluated according to DOH Policy 400-10.1, “Investigating Any Non-Compliance, Serious or Continuing Non-Compliance.”

3. All suspensions and terminations will be reported according to IRB Policy 10.3, “Reporting to Institutional Officials, Department or Agency Heads”

5. When suspending research, the IRB or other authorized individual shall consider actions to protect the health and safety of research participants, in addition to recommendations from the Investigator, such as:

   a. Transferring participants to another Investigator;

   b. Making arrangements for clinical care outside of research

   c. Allowing the continuation of some research activities under the supervision of an independent monitor.

VI. History Notes

The Office of Public Health Research, Ethics and Human Research Protections Program is responsible for this policy.

Revised 5/28/2010
Reviewed 08/23/2013

VII. Signature Block with Effective Date

Ana M. Viamonte Ros, M.D., M.P.H. Date
State Surgeon General, Department of Health

I. Policy

It is the responsibility of the Department of Health (DOH) Institutional Review Board (IRB) to assure reporting occurs according to the Federal regulations, institutional policy and DOH IRB policy.

II. Authority

A. Chapter 381.86, *Florida Statutes*, Institutional Review Board

B. Rule 64H-2.001, Institutional Review Board, *Florida Administrative Code*

III. Supportive Data

A. DHHS: 45 CFR §46.103(b)(5)(ii), 45 CFR §46.113, OHRP Guidance on Reporting Incidents to OHRP

B. FDA: 21 CFR §56.108(b)(3), 21 CFR §56.113, FDA Information Sheets: Continuing Review After Study Approval

IV. Definitions

See DOHP 400-11.1, “Definitions”

V. Procedures

A. This procedure will be followed whenever any of the following occurs:

1. Any determination by an IRB that a problem is an unanticipated problem involving risk to participants or others;

2. Any determination by an IRB that an incident of noncompliance is serious non-compliance, or continuing non-compliance with this policy or the requirements or determinations of the IRB; and

3. Any suspension or termination of IRB approval.

B. Process for reporting unanticipated problems involving risks to participants or others, non-compliance determined to be serious or continuing, and suspensions or terminations of research

1. The Human Research Protection Administrator designated in the Department’s Assurance is responsible for preparing materials within 10 days of the completion of an investigation or determination.for reporting to organizational officials.

2. Reports are made to the following organizational officials at DOH:

    a. the Director, Office of Public Health Research

    b The Deputy Secretary for Health

    c. The State Surgeon General

3. Reports are made to the following other organizations:

    a. the researcher's organization

    b. any other IRBs the researcher reported in the IRBWise application at initial and continuing review as having jurisdiction over the research.

    c. DOH will attempt to work collaboratively with other IRBs to coordinate reporting, when more than one IRB will be reporting.

C. Reporting to federal officials will take place within 30 calendar days of the completion of an investigation and/or determination.

1. When research involves a drug or device regulated by the FDA, the following will be reported to the FDA:

    a. unanticipated problems involving risks to participants or others

    b. non-compliance determined to be serious or continuing

    c. suspensions or termination of research

2. When research is sponsored or supported by DHHS, the following will be reported to the Office of Human Research Protections (OHRP).

    a. unanticipated problems involving risks to participants or others

    b. non-compliance determined to be serious or continuing

    c. suspensions or termination of research

D. Any concerns regarding data integrity outside of the jurisdiction of the DOH IRB will be referred to the State Surgeon General for further consideration/action.

VI. History Notes

The Office of Public Health Research, Ethics and Human Research Protections Program is responsible for this policy.

Revised 07/07/2010
Reviewed 08/23/2013
This policy replaces DOHP 10.3-06.

VII. Signature Block with Effective Date

Ana M. Viamonte Ros, M.D., M.P.H.
State Surgeon General
Florida Department of Health

Date

I. Policy

It is the policy of the Department of Health (DOH) Institutional Review Board (IRB) to investigate all complaints received regarding human subjects research conducted under its jurisdiction.

II. Authority

A. Chapter 381.86, Institutional Review Board, *Florida Statutes*

B. Rule 64H-2.001, Institutional Review Board, *Florida Administrative Code*

III. Supportive Data

A. 45 CFR 46

IV. Definitions

A. See DOHP 400-11.1, “Definitions”

V. Procedures

A. The Human Research Protection Administrator designated in the Department’s Assurance shall investigate all complaints received regarding human subjects in research under the DOH IRB’s jurisdiction. The level of investigation will depend on the seriousness of the situation and the potential risk to participants. Complaints may come from any source including IRB Committee members, Investigators, participants and their families, Institutional personnel, other Institutional Committees, the media, anonymous sources, or the public.

B. Complaints may come from any category of research reviewed and may include anyone involved or not directly involved in the research process/study.

C. Investigations should result in finding a suitable resolution and response to the complainant in a timely manner.

D. All complaints will be handled in a confidential manner. This includes any individual involved in notifying the DOH IRB of an alleged violation of Investigator compliance.

E. Complaints that are substantiated will be further investigated through a directed audit under the direction of the Ethics and Human Research Protection Program, and actions will be taken as deemed appropriate by the IRB, including referral to the Office of Inspector General.

F. Complaints of a sensitive nature may be brought to the IRB Chairpersons for discussion and recommendation.

G. The DOH IRB offers a web page where participants in research, researchers, and study personnel, may ask questions, discuss problems or concerns or file a complaint, or request information, or offer suggestions. The suggestion box is located at:
http://flpublichealthethics.net/index.php/eng/participants

H. After the completion of the investigation all complaints processed under this policy and procedure will also be processed under DOH IRB Policy 4.6, Reporting of Unanticipated Problems and Adverse Events, as a potential unanticipated problem involving risks to participants or others.

I. All complaints processed under this policy and procedure that involve non-compliance or allegations of non-compliance will also be processed under DOH IRB Policy 10.1, Investigating Any Non-Compliance, Serious or Continuing Non-Compliance.

VI. History Notes

The Office of Public Health Research, Ethics and Human Research Protections Program is responsible for this policy.

Revised 05/25/2010
Reviewed 08/23/2013

VII. Signature Block with Effective Date

Ana M. Viamonte Ros, M.D., M.P.H.
State Surgeon General
Florida Department of Health

Date

I. Policy

It is the policy of the Department of Health (DOH) Institutional Review Board (IRB) that to improve consistency and ease maintenance of other policies, the definitions listed in this policy will be used throughout all human research protection program policies.

II. Authority

A. Chapter 381.86, *Florida Statutes*, Institutional Review Board

B. Rule 64H-2.001, Institutional Review Board, *Florida Administrative Code*

III. Supportive Data

IV. Definitions

1. Administrative Rule: Each agency statement of general applicability that implements, interprets, or prescribes law or policy or describes the procedure or practice requirements of an agency and includes any form which imposes any requirement or solicits any information not specifically required by statute or by an existing rule. The term also includes the amendment or repeal of a rule (see 120.55, *Florida Statutes*). Rules comprise the *Florida Administrative Code*.

2. Administrative Hold: A voluntary action initiated by the Investigator in response to an IRB request to place specific research activities on hold temporarily to allow for additional information to be obtained.

3. Adverse Event: any harm experienced by a participant regardless of whether the event was internal (on-site) or external (off-site) and regardless of whether the event meets the FDA definition of "serious adverse event"), which in the opinion of the principal investigator is both unexpected and related. “Adverse Events” not meeting these criteria should not be reported. See “related” and “unexpected.”.

4. Advertising: A public announcement usually by a printed notice or voice or data broadcast that describes a research study including contact information. Typically, this is used for recruitment purposes for a research study.

5. Agent: Any individual (employee or contractor) authorized to act on behalf of the Department of Health.

6. Allegation of non-compliance: written or verbal report of possible noncompliance concerning research under the oversight of the DOH IRB.

7. Alternate Member: Individuals appointed by the Institutional Official to substitute for IRB members with same responsibilities and authority. Counts toward a quorum in the absence of an IRB member whose expertise the alternate member is replacing.

8. Amendment: Any change to an IRB-approved study protocol regardless of the

level of review it receives initially (see also minor amendment and major amendment).

9. Appearance of a Conflict of Interest: If a reasonable person with knowledge of the relevant facts would question the impartiality of Investigators, study personnel, IRB members, consultants, or IRB staff, or would question the regard for the public duty or interest of Investigators, study personnel, IRB members, consultants, or IRB staff, then an appearance of a conflict of interest exists.

10. Assent: A child's affirmative agreement to participate in research. Mere failure to object should not, absent affirmative agreement, be construed as assent.

11. Assurance: A contract or agreement that establishes standards for human subjects research as approved by the Office for Human Research Protections (OHRP).

12. Bonus Payment: Compensation tied to the rate or timing of recruitment. Examples of bonus payments include but are not limited to the following: The sponsor announces that the highest enrolling site in the nation will receive a $10,000 bonus; The sponsor offers to pay an additional $10,000 to any site that enrolls five participants within a week; The sponsor offers to pay an additional $10,000 to any site that fulfils its recruitment target by the end of the month; The sponsor offers to pay an additional $1,000 for any subject who agrees to enroll within one day of initial contact. All financial interests in research must be reported to the IRB.

13. Certificate of Confidentiality: A document that provides additional protection of data from legal subpoena. The Certificate provides protection against compelled disclosure of identifying information or other identifying characteristics of a research participant enrolled in biomedical, behavioral, clinical, and other forms of sensitive research.

14. Children: are individuals who have not attained the legal age for consent to treatments or procedures involved in the research or clinical investigation, under the applicable laws of Florida. Because the legal age for consent to treatments or procedures involved in research or clinical investigations varies in Florida law based on a number of circumstances, the meaning of children will be determined on a protocol-by-protocol basis in consultation with legal counsel.

15. Clinical Investigation: Any experiment that involves a test article and one or more human subjects, and that either must meet the requirements for prior submission to the Food and Drug Administration under section 505 (i) or 520 (g) of the Federal Food, Drug, and Cosmetic Act, or need not meet the requirements for prior submission to the Food and Drug Administration under these sections of the Federal Food, Drug and Cosmetic Act, but the results of which are intended to be later submitted to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit. The terms research, clinical research, clinical study, study, and clinical investigation are synonymous for purposes of FDA regulations. (21 CFR 50.3(c), 21 CFR 56.102(c))

16. Coded Information: For the purposes of this policy, identifying information that would enable the investigator to readily ascertain the identity of the individual to whom the private information or specimens pertain has been replaced with a number, letter, symbol, or combination thereof and a key to decipher the code exists, enabling linkage of the identifying information to the private information or specimens.

17. Cognitively Impaired: Having a psychiatric disorder (e.g., psychosis, neurosis, personality or behavior disorder), an organic impairment (e.g., dementia) or a developmental disorder (e.g., mental retardation) that affects cognitive or emotional functions to the extent that capacity for judgment and reasoning is significantly diminished as determined by reasonable medical judgment. Others, including individuals under the influence of or dependent on drugs or alcohol, those suffering from degenerative diseases affecting the brain, terminally ill patients, and individuals with severely disabling physical handicaps, may also be compromised in their ability to make decisions in their best interest.

18. Collaborative IRB Training Initiative (CITI): An internet-based set of educational modules on the protection of human participants in research. It is sponsored by a consortium of IRB professionals and Investigators from Universities and Medical Schools across the country and is administered by the University of Miami.

19. Conflicting Interest: IRB Committee Members, consultants and IRB Administrators are considered to have a conflicting interest if they or a member of their immediate family have any financial interests related to the research where they have any role in the design, conduct, or reporting of the research, other individual conflict of interest.

20. Continuing Non-compliance: A pattern of repeated actions or omissions taken by an Investigator that indicates a deficiency in the ability or willingness of an Investigator to comply with Federal and State regulations, DOH IRB Policy, or determinations or requirements of the DOH IRB.

21. Continuing Review: Periodic review of research activities necessary to determine whether the risk/benefit ratio has changed, whether there are unanticipated findings involving risks to participants or others, and whether any new information regarding the risks and benefits should be provided to participants.

22. Continuous Quality Improvement (CQI): A methodology employed to improve existing processes by identifying the root cause of a problem, developing and implementing an action plan, and evaluating the outcome to assure problem resolution. The PDSA cycle incorporates the following process: Plan, Do, Study, Act.

23. Data and Safety Monitor (DSM): An individual assigned to conduct interim monitoring of accumulating data from research activities to assure the continuing safety of research participants, relevance of the study question, appropriateness of the study, and integrity of the accumulating data. The individual should have

expertise in the relevant medical, ethical, safety, and scientific issues.

24. Data and Safety Monitoring Board (DSMB): A formally appointed independent group consisting of at least three (3) members assigned to conduct interim monitoring of accumulating data from research activities to assure the continuing safety of research participants, relevance of the study question, appropriateness of the study, and integrity of the accumulating data. Membership should include expertise in the relevant field of study, statistics, and research study design.

25. Data and Safety Monitoring Committee (DSMC): Another term for DSMB.

26. Data and Safety Monitoring Plan (DSMP): A DSMP describes how the Investigator plans to oversee the research participant's safety and welfare and how adverse events will be characterized and reported. The intensity and frequency of monitoring should be tailored to fit the expected risk level, complexity, and size of the particular study.

27. Dead Fetus: A fetus that exhibits neither heartbeat, spontaneous respiratory activity, spontaneous movement of voluntary muscles, nor pulsation of the umbilical cord (if still attached).

28. Delivery: Complete separation of the fetus from the woman by expulsion or extraction or any other means.

29. Department of Health and Human Services (DHHS): The United States government agency for protecting the health of all Americans and providing essential human services, especially for those who are least able to help themselves.

30. Directed Audit: These audits may be conducted by the IRB staff, DOH Inspector General, or an outside third party to assess the Investigator's compliance with federal regulations, state and local laws, and DOH IRB policies and procedures. These audits of DOH IRB approved research studies are in response to identified concern(s). Concerns may be identified by an IRB Committee, an external source (e.g. OHRP, FDA or Sponsor), or an internal source (e.g. participant, family member, or DOH personnel, including IRB staff).

31. Dissent: An individual's negative expressions, verbal and/or non-verbal, that they object to participation in the research or research activities.

32. Document: Means a physical or electronic record submitted to the Department of Health Institutional Review Board

33. Emergency Research: The use of an unapproved test article (drug, agent, biologic, or device) on a human subject in a life-threatening situation in which no standard acceptable treatment is available, and in which there is not sufficient time to obtain IRB approval.

34. Emergency Treatment IDE: A mechanism through the FDA for providing eligible

participants with investigational devices for the treatment of an immediate serious or life-threatening illness for which there are no satisfactory alternatives.

35. Emergency Treatment IND: A mechanism through the FDA for providing eligible participants with investigational drugs, agents, or biologics for the treatment of an immediate serious or life-threatening illness for which there are no satisfactory alternatives.

36. Exempt Review: Studies determined by the IRB to meet the exempt criteria as defined by the Federal regulations. Exempt studies do not require periodic review by the IRB unless a change in the project is planned.

37. Expedited Review: Studies determined by the IRB to meet the expedited criteria as defined by the Federal regulations.

38. Expired Study: When continuing review of the research does not occur prior to the end of the approval period specified by the IRB, IRB approval expires automatically and requires no decision, determination, or action by the IRB. The study expires at midnight on the last approval date specified on the approval letter and the informed consent document. No activities can occur after the expiration date. Such expirations of approval are not suspensions of IRB approval, terminations of IRB approval, or administrative holds. Allowing a protocol to expire is considered non-compliance.

39. Family Member: Any one of the following legally competent persons: Spouse; children (including adopted children); brothers, sisters, and spouses of brothers and sisters; and any individual related by blood or affinity whose close association with the participant is the equivalent of a family relationship.

40. Fetus: The product of conception from implantation until delivery.

41. Financial interest related to the research: means financial interest in the sponsor, product or service being tested, or competitor of the sponsor.

42. Finder's Fee: Compensation of any type (cash, office or medical supplies, educational stipends, gift certificates, priority in authorship listings, travel reimbursement, or anything else of value) to an individual made in exchange for referral or recruitment of a participant to a research study. Such payments, generally, are made to residents, physicians, nurses, or others in a position to identify potential participants that might qualify for enrollment into a study. The fee is paid only for participants who are actually enrolled into the study. Any financial interest related to research must be reported.

43. Food and Drug Administration (FDA): The United States government office under the Department of Health and Human Services responsible for implementing regulations governing drugs, devices, and biologics.

44. Human Fetal Tissue: Tissue or cells obtained from a dead human embryo or dead fetus after a spontaneous or induced abortion, or after a stillbirth.

45. Human Participant: As defined by DHHS regulations, a living individual about whom an investigator (whether professional or student) conducting research obtains data through intervention or interaction with an individual or identifiable private information.

46. Human Subject: As defined by FDA regulations, an individual who is or becomes a participant in research, either as a recipient of the test article or as a control. A subject may be either a healthy individual or a patient. For research involving medical devices a human subject is also an individual on whose specimen an investigational device is used.

47. Human Subject Research: Any activity that either: meets the DHHS definition of "research" and involves "human subjects" as defined by DHHS regulations or meets the FDA definition of "research" and involves "human subjects" as defined by FDA regulations.

48. Humanitarian Use Device (HUD): A device that is intended to benefit patients by treating or diagnosing a disease or condition that affects fewer than 4,000 individuals in the United States per year.

49. Humanitarian Use Device Exemption (HDE): A Federal Drug Administration (FDA) approval for a physician to use a HUD in clinical treatment or as the subject of a clinical investigation.

50. Immediate Family Member: spouse, domestic partner, children, and dependents

51. Individual Conflict of Interest: A circumstance such that any action or decision in which an individual is substantially involved with the research may have direct or predictable effect on a financial interest of the individual, spouse, minor child, or organization in which the individual serves as an officer, trustee, partner or employee.

52. Informed Consent: An individual's voluntary agreement, based upon adequate knowledge and understanding of relevant information, to participate in research or to undergo a diagnostic, therapeutic, or preventive procedure.

53. Institutional Review Board (IRB): A specifically constituted review body established or designated by an entity to protect the rights and welfare of human subjects recruited to participate in research.

54. Interaction: Includes communication or interpersonal contact between an Investigator or his/her research staff and the research participant or their private identifiable information.

55. Intervention: Includes both physical procedures by which data are gathered (e.g., venipuncture) and manipulations of the subjects' environment that are performed for research purposes.

56. Investigational Agents: A pharmaceutical form of an active ingredient or placebo being tested or used as a reference in a clinical trial. This includes products with a marketing authorization when used or assembled (formulated or packaged) in a way different from the approved form, products used for an unapproved indication, or products used to gain further information about an approved use.

57. Investigational Device: Any healthcare product that does not achieve its primary intended purposes by chemical action or by being metabolized. A medical device that is the subject of a clinical study designed to evaluate the effectiveness and/or safety of the device. Investigational use also includes clinical evaluation of certain modifications or new intended uses of legally marketed devices.

58. Investigational Device Exemption: A FDA approved investigational device exemption (IDE) permits a device that otherwise would be required to comply with a performance standard or to have pre-market approval to be shipped lawfully for the purpose of conducting investigations of that device.

59. Investigational Drugs/Investigational Biologics (Test Articles): A new drug/agent or biologic that is used in a clinical investigation. The term investigational biologic also includes a biological product that is used in vitro for diagnostic purposes. Investigational drugs or biologics may include: 1. Products that are not generally recognized as being safe and effective for any use under the conditions prescribed, recommended, or suggested by the FDA; or 2. Products already approved by the FDA as safe and effective for specific indications that are being studied for new indications (or doses, strengths, or frequency).

60. Investigational New Drug (IND): FDA granting of permission that a new drug, agent, or biologic may be used in humans prior to FDA review of clinical data that has determined that a particular product is safe and effective for a specific use. The FDA permission is evidenced by the assignment of an IND number by the FDA or the granting of an IND exemption.

61. IRB Member: Individual appointed by the Insitutional Official to serve as a voting member on a designated IRB that meets requirements of expertise or experience, or community representation; membership counts toward a quorum.

62. IRB of Record: An IRB is considered the IRB of record when it assumes IRB responsibilities for another institution and is designated to do so through an approved Assurance with OHRP. A Memorandum of Understanding is required, designating the relationship, for DOH to serve as the IRB of Record.

63. Joint Commission on Accreditation of Healthcare Organizations (JCAHO): A national accrediting body for hospitals and other health care delivery organizations.

64. Key Research Personnel: The Principal Investigator and all individuals responsible for the design or conduct of the study

65. Guardian: Defined by DHHS as an individual who is authorized under applicable

State or local law to consent on behalf of a child to general medical care.

66. Legally Authorized Representative (LAR): An individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedure(s) involved in the research. LARs may not give permission for research involving children unless they are guardians.

67. Major Amendment: A proposed change in research related activities that is not a Minor Amendment.

68. Memorandum of Understanding (MOU): A formal agreement between the Department of Health and another institution that identifies the Department of Health Institutional Review Board as the IRB of record for that institution.

69. Minimal Risk: The probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests. For research involving prisoners, minimal risk means the probability and magnitude of physical or psychological harm that is normally encountered in the daily lives, or in the routine medical, dental, or psychological examinations of healthy persons.

70. Minor Amendment: A proposed change in research related activities that does not materially affect an assessment of the risks and benefits of the study, does not substantially change the specific aims or design of the study, and all added procedures that qualify for review under expedited review per 21 CFR 50.110 and 45 CFR 46.110.

71. Neonate: A newborn

72. Non-compliance: Failure to comply with Federal and State regulations, DOH IRB Policy, or the determinations or requirements of the DOH IRB.

73. Non-Human Subject Research: Any activity determined by the Institution to not represent “Human Subject Research.”

74. Non-significant Risk (NSR) Device Study: A study of a device that does not meet the definition for a significant risk device and does not present a potential for serious risk to the health, safety, or welfare of participants.

75. Nonviable Neonate: A neonate after delivery that, although living, is not viable.

76. Not-Identifiable Information: the identity of the participant is not or may not readily be ascertained by the investigator or associated with the information.

77. Not Less Than Once Per Year: All research proposals, with the exception of exempt proposals, must receive IRB continuing review at a minimum of once every year, per Federal regulations. There are no exceptions or grace periods

allowed.

78. Office for Human Research Protections (OHRP): The United States government office under the Department of Health and Human Services responsible for implementing DHHS regulations (45 CFR 46) governing biomedical and behavioral/social science research involving human subjects.

79. Office of Public Health Research: The office responsible for research and human research protections at the Florida Department of Health.

80. Parent: A child's biological or adoptive parent.

81. Pass-through funding: Where DOH receives support directly from federal agencies for non-exempt research, and all activities are conducted by community-based organizations or partners of DOH. For example, if CDC provides research funding through DOH to a community-based organization or private partner of DOH, this activity requires IRB review, even if the activity is conducted solely by agents or contractors of DOH.

82. Periodic Compliance Review: Random assessments of DOH IRB approved human research studies, including site visits, and the internal IRB program may be conducted by internal or external compliance teams. Internal compliance reviews monitor the adherence to federal regulations, state and local law, and IRB policies and procedures. Local compliance reviews monitor the adherence to federal regulations, state and local law, DOH IRB policies and procedures, adherence to the study protocol, accurate documentation and reporting of study related activities, and evaluation/observation of the informed consent process.

83. Permission: The agreement of parents or legal guardians to the participation of their child or ward in research.

84. Policy: A statement defining a plan, guiding principle, or course of action intended to determine decisions, actions, and procedures as set forth by DOH, Office of Public Health Research, and the IRB as it pertains to DOH's human research protection program (HRPP).

85. Pregnancy: Encompasses the period of time from implantation until delivery. A woman shall be assumed to be pregnant if she exhibits any of the presumptive signs of pregnancy, such as a missed menses, until the results of a pregnancy test are negative or until delivery.

86. Prisoner: Any individual involuntarily confined or detained in a penal institution. The term is intended to encompass individuals sentenced to such an institution under a criminal or civil statute, individuals detained in other facilities by virtue of statutes or commitment procedures which provide alternatives to criminal prosecution or incarceration in a penal institution, and individuals detained pending arraignment, trial or sentencing. Probation and parole are treated the same and are usually NOT considered as incarceration. Ankle bracelets/in home restrictions are considered as incarceration. Mental and substance abuse

facilities are considered incarceration if someone is mandated to attend in lieu of jail or prison; however, an individual in such a facility is NOT considered incarcerated if they voluntarily commit themselves.

87. Privacy: freedom from unauthorized intrusion or the state of being left alone and able to keep certain personal information to oneself and control other's access to that information.

88. Private Information: Includes information about behavior that occurs in a setting in which an individual can reasonably expect that no observation or recording is taking place. It includes information, which has been provided for specific purposes by an individual, and the individual can reasonably expect will not be made public (e.g., a medical record). Private information must be individually identifiable in order to be considered information to constitute research involving human participants. This may include identifiable private information obtained from a primary participant about a third party.

89. Procedure: A statement defining the internal process by which DOH policies are administered by the HRPP.

90. Prospective: Research utilizing human participants' specimens/data that will be collected after the research is approved by the IRB.

91. Public meeting: It is the intent of the Florida Legislature that there be a right of public access to government actions. The Institutional Review Board has not been exempted by the Legislature from requirements of public meetings. Members of the general public may attend IRB meetings and observe IRB meetings.

92. Quality Assurance Reviews: may be conducted by internal or external personnel to verify that the IRBWise online management system is accurate, complete, and conforms to IRB policy and procedure.

93. Radiation Exposure: The quantity used to indicate the amount of ionization in air produced by x- or gamma-ray radiation while conducting radiological procedures.

94. Radiation Safety Committee: A committee composed of individuals with expertise in various disciplines pertinent to the field of radiology, radiological sciences, nuclear medicine, and radiation oncology. Such a committee must also include an individual with special competence in radiation safety and radiation dosimetry, and must comply with all applicable law and regulation, including FDA regulations at 21 CFR 361 and state regulations at 64 E-5 Florida Administrative Code.

95. Radioactive Drug: Any substance defined as a drug under the Federal Food, Drug and Cosmetic Act that exhibits spontaneous disintegration of unstable nuclei with the emission of nuclear particles or photons. Included are any non-radioactive reagent kit or nuclide generator that is intended to be used in the preparation of a radioactive drug and "radioactive biological products." Drugs

such as carbon-containing compounds or potassium-containing salts containing trace quantities of naturally occurring radionuclides are not considered radioactive drugs.

96. Radiological Procedure: Any procedure involving radiation (e.g., X-ray) or a radioactive agent (e.g., a radionuclide).

97. Recruitment: Seeking individuals to enroll or participate in a research project.

98. Related: An adverse event is "related to the research procedures" if in the opinion of the principal investigator, it was more likely than not to be caused by the research procedures or if it is more likely that not that the event affects the rights and welfare of current participants).

99. Repository: A storage site or mechanism by which identifiable human tissue, blood, genetic material or data are stored or archived for research by multiple Investigators or multiple research projects.

100. Research: As defined by FDA regulations, any experiment that involves a test article and one or more human subjects, and that either must meet the requirements for prior submission to the FDA under section 505(i) or 520(g) of the Food, Drugs, and Cosmetics Act, or need not meet the requirements for prior submission to the FDA under these sections of the Food, Drug, and Cosmetics Act, but the results of which are intended to be later submitted to, or held for inspection by, the FDA as part of an application for a research or marketing permit. For research involving drugs, an experiment is any use of a drug except for the use of a marketed drug in the course of medical practice. The terms research, clinical research, clinical study, study, and clinical investigation are synonymous.

    (1) "Experiments that must meet the requirements for prior submission to the Food and Drug Administration under section 505(i) of the Federal Food, Drug, and Cosmetic Act" means any use of a drug other than the use of an approved drug in the course of medical practice. [21 CFR 312.3(b)]

    (2) "Experiments that must meet the requirements for prior submission to the Food and Drug Administration under section 520(g) of the Federal Food, Drug, and Cosmetic Act" means any activity that evaluates the safety or effectiveness of a medical device. [21 CFR 812.2(a)]

    (3) "Any activity in which results are being submitted to or held for inspection by FDA as part of an application for a research or marketing permit is considered to be FDA-regulated research." [21 CFR 50.3(c), 21 CFR 56.102(c)]

101. Research: As defined by DHHS regulations, any systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge.

(1) Investigation: an inquiry, examination, or search for facts, usually involving the formulation or testing of a hypothesis.

(2) Systematic: conducted according to a plan, organized method, or procedure for testing or formulation a question or hypothesis and interpreting results

(3) Designed: planned or conducted to apply to phenomena outside the observed data, or to contribute to such understanding

(4) Generalizeable Knowledge: observations, findings, information, or results that have been demonstrated with enough confidence and significance to confirm or alter the consensus within the professional norms of a community or discipline.

102. Research Misconduct: Any fabrication, falsification, or plagiarism in proposing, performing, or reviewing research, or in reporting research results or any attempt to unduly influence an IRB member or IRB staff.

103. Research Payments: Cash and non-cash payments for reimbursement of time and expenses associated with participation in research activities.

104. Retrospective: Research utilizing human participants' specimens/data that were previously collected (e.g., on the shelf) before the research was approved by the IRB.

105. Roster: Current listing of members appointed to serve on a designated IRB.

106. Secretary: The Secretary of Health and Human Services and any other officer or employee of the Department of Health and Human Services to whom authority has been delegated.

107. Sensitive Information: Includes, but is not limited to, information relating to sexual attitudes, preferences, or practices; information relating to the use of alcohol, drugs, or other addictive products; information pertaining to illegal conduct; information, that if released, might be damaging to an individual's financial standing, employability, or reputation within the community or might lead to social stigmatization or discrimination; information pertaining to an individual's psychological well-being or mental health; and genetic information.

108. Serious Non-compliance: An action or omission taken by an Investigator that any other reasonable Investigator would have foreseen as compromising the rights and welfare of, or harms, a participant.

109. Short Form Consent: A written informed consent document that summarizes the required elements of informed consent to be presented orally to the participant or his or her legally authorized representative

110. Significant Risk (SR) Device Study: A study of a device that presents a potential

for serious risk to the health, safety, or welfare of a participant and 1) is intended as an implant; 2) is used in supporting or sustaining human life; or otherwise prevents impairment of human health; 3) is of substantial importance in diagnosing, curing, mitigating or treating disease, or otherwise prevents impairment of human health; or 4) otherwise presents a potential for serious risk to the health, safety, or welfare of a participant.

111. Sponsor-Imposed Suspension: A determination from the sponsor of the study to place specific research activities on hold. This determination may be made for interim data analysis; inadequate drug availability; response to a Data Safety Monitoring Board (DSMB) report/recommendation; or a pre-planned stopping point.

112. Standard Review: Studies reviewed by the full, convened IRB Committee with a recorded vote and corresponding minutes to document the discussion.

113. Suspension of the research: all interventions or interactions with living individuals cease until the IRB determines research may commence, except when the suspension of study drugs or other interventions would place participants at risk.

114. Termination of the research: all interventions or interactions with living individuals cease. When terminating research would place participants at risks of harm, the IRB will work with the researcher to transition patients to a new study or other appropriate action.

115. Test article: Any drug (including a biological product for human use), medical device for human use, human food additive, color additive, electronic product, or any other article subject to FDA regulation.

116. Third-party: Any person or vendor (external to the DOH) who receives payment for providing research-related services and/or products.

117. Treatment IDE: A mechanism through the FDA for providing eligible participants with investigational devices for the treatment of a serious or life-threatening illness for which there are no satisfactory alternatives.

118. Unexpected: An adverse event is "unexpected" when its specificity and severity are not accurately reflected in the informed consent document.

119. Unanticipated Adverse Device Effect: any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem to participants or others associated with a device that relates to the rights, safety, or welfare of participants.

120. Unanticipated Problem Involving Risks to Participants or Others: Any problem, event or information, as determined by the Department, that (1) was unforeseen

and (2) indicates that participants or others are at increased risk of harm and (3) is related to the research.

121. Viable: As it pertains to the neonate, means being able, after delivery, to survive (given the benefit of available medical therapy) to the point of independently maintaining heartbeat and respiration.

122. Whistle-blower: As it pertains to the neonate, means being able, after delivery, to survive (given the benefit of available medical therapy) to the point of independently maintaining heartbeat and respiration.

V. Procedures

VI. History Notes

The Office of Public Health Research, Ethics and Human Research Protections Program is responsible for this policy.

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