임상시험 심사위원회(IRB) 설치, 운영의 실제

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서울의대

인간을 대상하는 시행하는 의학연구에 참여하는 피험자의 권익 및 안전을 보증한다는 개념은 20세기에 들어오면서부터 거론되기 시작하였으며, 나치의 비윤리적 생체시험, 1950년대말의 thalidomide 약화 사건을 거치며 1964년 세계 의사회의 Helsinki 선언으로 의학 연구에 있어서 피험자의 권익, 안전을 위한 윤리 강령이 자리를 잡아가게 되었다. 이러한 의학 연구의 일환인 신약개발과 관련한 의약품 임상시험도 같은 맥락의 윤리적 문제가 존재하여, 1978년 미국의 FDA는 의약품 임상시험과 관련하여 과학성과 윤리성 검토를 시행하는 시설내 시험심사위원회(IRB ; Institutional Review Board) 운영에 대한 지침을 발표하게 되었고 1981년 이후 임상시험과 관련하는 타 지침들과 통합되어 의약품의 임상시험 실시에 반드시 지켜야 되는 법적 효력을 지닌 의약품 임상시험 기준(Current GCPs)으로 발전하게 되었다. 이후 구미, 일본등 선진국에서도 GCP를 시행하고 있으며 국내에서도 1995년 10월에 보건복지부는 KGCP 기준을 시행하고 있다.

GCP 기준에 따른 임상시험의 진행에 있어 IRB는 임상시험이 진행되는 의료기관내에서 핵심적 구심체 역할을 하기 때문에 IRB의 건실한 운영은 매우 중요하다. 더욱이, 국내에서는 이와 관련한 여건에서 선진국과 달리 의료기관내 IRB 운영의 역사가 일천하여 현재 운영되고 있는 IRB들의 운영체계 및 운영내용에 있어서 많은 문제점을 갖고 있는 것으로 지적되고 있다. 따라서, 본 연자는 KGCP 및 미국 FDA의 IRB 규정을 기반으로 IRB의 설치 및 운영등과 관련한 실제적인 문제들을 집어 봄으로써 국내 IRB 운영의 견실화에 보탬이 되고자 한다. 참고로 미국 FDA의 IRB 운영등과 관련한 규정과 IRB Self-Evaluation Check List을 첨부하여 각 기관의 IRB 운영에 참조토록 한다.

Title 21—Chapter I—Food and Drug Administration
Subchapter A—General
Part 56—Institutional Review Boards

SUBPART A—GENERAL PROVISIONS

§56.101 Scope.

(a) This part contains the general standards for the composition, operation, and responsibility of an Institutional Review Board (IRB) that reviews clinicalinvestigations regulated by the Food and Drug Administration under sections 505(i), 507(d), and 520(g) of the act, as well as clinical investigations that support applications for research or marketing permits for products regulated by the Food and Drug Administration, including food and color additives, drugs for human use, medical devices for human use, biological products for human use, and electronic products. Compliance with this part is intended to protect the rights and welfare of human subjects involved in such investigations.

(b) References in this part to regulatory sections of the Code of Federal Regulations are to chapter I of title 21, unless otherwise noted.

§56.102 Definitions.

As used in this part:

(a) *Act* means the Federal Food, Drug, and Cosmetic Act, as amended (secs. 201-902, 52 Stat. 1040 et seq., as amended (21 U.S.C. 321-392)).

(b) *Application for research or marketing permit* includes:

(1) A color additive petition, described in part 71.

(2) Data and information regarding a substance submitted as part of the procedures for establishing that a substance is generally recognized as safe for a use which results or may reasonably be expected to result, directly or indirectly, in its becoming a component or otherwise affecting the characteristics of any food, described in §170.35.

(3) A food additive petition, described in part 171.

(4) Data and information regarding a food additive submitted as part of the procedures regarding food additives permitted to be used on an interim basis pending additional study, described in §180.1.

(5) Data and information regarding a substance submitted as part of the procedures for establishing a tolerance for unavoidable contaminants in food and food-packaging materials, described in section 406 of the act.

(6) An investigational new drug application, described in part 312 of this chapter.

(7) A new drug application, described in part 314.

(8) Data and information regarding the bioavailability or bioequivalence of drugs for human use submitted as part of the procedures for issuing, amending, or repealing a bioequivalence requirement, described in part 320.

(9) Data and information regarding an over-the-counter drug for human use submitted as part of the procedures for classifying such drugs as generally recognized as safe and effective and not misbranded, described in part 330.

(10) Data and information regarding an antibiotic drug submitted as part of the procedures for issuing, amending, or repealing regulations for such drugs, described in §314.300 of this chapter.

(11) An application for a biological product license, described in part 601.

(12) Data and information regarding a biological product submitted as part of the procedures for determining that licensed biological products are safe and effective and not misbranded, as described in part 601.

(13) An Application for an Investigational Device Exemption, described in parts 812 and 813.

(14) Data and information regarding a medical device for human use submitted as part of the procedures for classifying such devices, described in part 860.

(15) Data and information regarding a medical device for human use submitted as part of the procedures for establishing, amending, or repealing a standard for such device, described in part 861.

(16) An application for premarket approval of a medical device for human use, described in section 515 of the act.

(17) A product development protocol for a medical device for human use, described in section 515 of the act.

(18) Data and information regarding an electronic product submitted as part of the procedures for establishing, amending, or repealing a standard for such products, described in section 358 of the Public Health Service Act.

(19) Data and information regarding an electronic product submitted as part of the procedures for obtaining a variance from any electronic product performance standard, as described in §1010.4.

(20) Data and information regarding an electronic product submitted as part of the procedures for granting, amending, or extending an exemption from a radiation safety performance standard, as described in §1010.5.

(21) Data and information regarding an electronic product submitted as part of the procedures for obtaining an exemption from notification of a radiation safety defect or failure of compliance with a radiation safety performance standard, described in subpart D of part 1003.

(c) *Clinical investigation* means 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), 507(d), or 520(g) of the act, or need not meet the requirements for prior submission to the Food and Drug Administration under these sections of the 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 term does not include experiments that must meet the provisions of part 58, regarding nonclinical laboratory studies. The terms *research, clinical research, clinical study, study, and clinical investigation* are deemed to be synonymous for purposes of this part.

(d) *Emergency use* means the use of a test article 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.

(e) *Human subject* means 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.

(f) *Institution* means any public or private entity or agency (including Federal, State, and other agencies). The term facility as used in section 520(g) of the act is deemed to be synonymous with the term institution for purposes of this part.

(g) *Institutional Review Board* (IRB) means any board, committee, or other group formally designated by an institution to review, to approve the initiation of, and to conduct periodic review of, biomedical research involving human subjects. The primary purpose of such review is to assure the protection of the rights and welfare of the human subjects. The term has the same meaning as the phrase institutional review committee as used in section 520(g) of the act.

(h) *Investigator* means an individual who actually conducts a clinical investigation (i.e., under whose immediate direction the test article is administered or dispensed to, or used involving, a subject) or, in the event of an investigation conducted by a team of individuals, is the responsible leader of that team.

(i) *Minimal risk* means that 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.

(j) *Sponsor* means a person or other entity that initiates a clinical investigation, but that does not actually conduct the investigation, i.e., the test article is administered or dispensed to, or used involving, a subject under the immediate direction of another individual. A person other than an individual (e.g., a corporation or agency) that uses one or more of its own employees to conduct an investigation that it has initiated is considered to be a sponsor (not a sponsor-investigator), and the employees are considered to be investigators.

(k) *Sponsor-investigator* means an individual who both initiates and actually conducts, alone or with others, a clinical investigation, i.e., under whose immediate direction the test article is administered or dispensed to, or used involving, a subject. The term does not include any person other than an individual, e.g., it does not include a corporation or agency. The obligations of a sponsor-investigator under this part include both those of a sponsor and those of an investigator.

(l) *Test article* means any drug for human use, biological product for human use, medical device for human use, human food additive, color additive, electronic product, or any other article subject to regulation under the act or under sections 351 or 354-360F of the Public Health Service Act.

(m) *IRB approval* means the determination of the IRB that the clinical investigation has been reviewed and may be conducted at an institution within the constraints set forth by the IRB and by other institutional and Federal requirements.

§56.103 Circumstances in which IRB review is required.

(a) Except as provided in §§56.104 and 56.105, any clinical investigation which must meet the requirements for prior submission (as required in parts 312, 812, and 813) to the Food and Drug Administration shall not be initiated unless that investigation has been reviewed and approved by, and remains subject to continuing review by, an IRB meeting the requirements of this part.

(b) Except as provided in §§56.104 and 56.105, the Food and Drug Administration may decide not to consider in support of an application for a research or marketing permit any data or information that has been derived from a clinical investigation that has not been approved by, and that was not subject to initial and continuing review by, an IRB meeting the requirements of this part. The determination that a clinical investigation may not be considered in support of an application for a research or marketing permit does not, however, relieve the applicant for such a permit of any obligation under any other applicable regulations to submit the results of the investigation to the Food and Drug Administration.

(c) Compliance with these regulations will in no way render inapplicable pertinent Federal, State, or local laws or regulations.

§56.104 Exemptions from IRB requirement.

The following categories of clinical investigations are exempt from the requirements of this part for IRB review:

(a) Any investigation which commenced before July 27, 1981 and was subject to requirements for IRB review under FDA regulations before that date, provided that the investigation remains subject to review of an IRB which meets the FDA requirements in effect before July 27, 1981.

(b) Any investigation commenced before July 27, 1981 and was not otherwise subject to requirements for IRB review under Food and Drug Administration regulations before that date.

(c) Emergency use of a test article, provided that such emergency use is reported to the IRB within 5 working days. Any subsequent use of the test article at the institution is subject to IRB review.

(d) Taste and food quality evaluations and consumer acceptance studies, if wholesome foods without additives are consumed or 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.

§56.105 Waiver of IRB requirement.

On the application of a sponsor or sponsor-investigator, the Food and Drug Administration may waive any of the requirements contained in these regulations, including the requirements for IRB review, for specific research activities or for classes of research activities, otherwise covered by these regulations.

SUBPART B—ORGANIZATION AND PERSONNEL

§56.107 IRB membership.

(a) Each IRB shall have at least five members, with varying backgrounds to promote complete and adequate review of research activities commonly conducted by the institution. The IRB shall be sufficiently qualified through the experience and expertise of its members, and the diversity of the members, including consideration of race, gender, cultural backgrounds, and sensitivity to such issues as community attitudes, to promote respect for its advice and counsel in safeguarding the rights and welfare of human subjects. In addition to possessing the professional competence necessary to review the specific research activities, the IRB shall be able to ascertain the acceptability of proposed research in terms of institutional commitments and regulations, applicable law, and standards or professional conduct and practice. The IRB shall therefore include persons knowledgeable in these areas. If an IRB regularly reviews research that involves a vulnerable category of subjects, such as children, prisoners, pregnant women, or handicapped or mentally disabled persons, consideration shall be given to the inclusion of one or more individuals who are knowledgeable about and experienced in working with those subjects.

(b) Every nondiscriminatory effort will be made to ensure that no IRB consists entirely of men or entirely of women, including the instituton's consideration of qualified persons of both sexes, so long as no selection is made to the IRB on the basis of gender. No IRB may consist entirely of members of one profession.

(c) Each IRB shall include at least one member whose primary concerns are in the scientific area and at least one member whose primary concerns are in nonscientific areas.

(d) Each IRB shall include at least one member who is not otherwise affiliated with the institution and who is not part of the immediate family of a person who is affiliated with the institution.

(e) No IRB may have a member participate in the IRB's initial or continuing review of any project in which the member has a conflicting interest, except to provide information requested by the IRB.

(f) An IRB may, in its discretion, invite individuals with competence in special areas to assist in the review of complex issues which require expertise beyond or in addition to that available on the IRB. These individuals may not vote with the IRB.

SUBPART C—IRB FUNCTIONS AND OPERATIONS

§56.108 IRB functions and operations.

In order to fulfill the requirements of these regulations, each IRB shall:

(a) Follow written procedures: (1) For conducting its initial and continuing review of research and for reporting its findings and actions to the investigator and the institution; (2) for determining which projects require review more often than annually and which projects need verification from sources other than the investigator that no material changes have occurred since previous IRB review; (3) for ensuring prompt reporting to the IRB of changes in research activity; and (4) for ensuring that changes in approved research, during the period for which IRB approval has already been given, may not be initiated without IRB review and approval except where necessary to eliminate apparent immediate hazards to the human subjects.

(b) Follow written procedures for ensuring prompt reporting to the IRB, appropriate institutional officials, and the Food and Drug Administration of:

(1) Any unanticipated problems involving risks to human subjects or others;

(2) any instance of serious or continuing noncompliance with these regulations or the requirements or determinations of the IRB; or (3) any suspension or termination of IRB approval.

(c) Except when an expedited review procedure is used (see §56.110), review proposed research at convened meetings at which a majority of the members of the IRB are present, including at least one member whose primary concerns are in nonscientific areas. In order for the research to be approved, it shall receive the approval of a majority of those members present at the meeting.

§56.109 IRB review of research.

(a) An IRB shall review and have authority to approve, require modifications in (to secure approval), or disapprove all research activities covered by these regulations.

(b) An IRB shall require that information given to subjects as part of informed consent is in accordance with §50.25. The IRB may require that information, in addition to that specifically mentioned in §50.25, be given to the subjects when in the IRB's judgment the information would meaningfully add to the protection of the rights and welfare of subjects.

(c) An IRB shall require documentation of informed consent in accordance with §50.27, except that the IRB may, for some or all subjects, waive the requirement that the subject or the subject's legally authorized representative sign a written consent form if it finds that the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside the research context. In cases where the documentation requirement is waived, the IRB may require the investigator to provide subjects with a written statement regarding the research.

(d) An IRB shall notify investigators and the institution in writing of its decision to approve or disapprove the proposed research activity, or of modifications required to secure IRB approval of the research activity. If the IRB decides to disapprove a research activity, it shall include in its written notification a statement of the reasons for its decision and give the investigator an opportunity to respond in person or in writing.

(e) An IRB shall conduct continuing review of research covered by these regulations at intervals appropriate to the degree of risk, but not less than once per year, and shall have authority to observe or have a third party observe the consent process and the research.

§56.110 Expedited review procedures for certain kinds of research involving no more than minimal risk, and for minor changes in approved research.

(a) The Food and Drug Administration has established, and published in the *Federal Register*, a list of categories of research that may be reviewed by the IRB through an expedited review procedure. The list will be amended, as appropriate, through periodic republication in the *Federal Register*.

(b) An IRB may use the expedited review procedure to review either or both of the following: (1) Some or all of the research appearing on the list and found by the reviewer(s) to involve no more than minimal risk, (2) minor changes in previously approved research during the period (of 1 year or less) for which approval is authorized. Under an expedited review procedure, the review may be carried out by the IRB chairperson or by one or more experienced reviewers designated by the IRB chairperson from among the members of the IRB. In reviewing the research, the reviewers may exercise all of the authorities of the IRB except that the reviewers may not disapprove the research. A research activity may be disapproved only after review in accordance with the nonexpedited review procedure set forth in §56.108(c).

(c) Each IRB which uses an expedited review procedure shall adopt a method for keeping all members advised of research proposals which have been approved under the procedure.

(d) The Food and Drug Administration may restrict, suspend, or terminate an institution's or IRB's use of the expedited review procedure when necessary to protect the rights or welfare of subjects.

§56.111 Criteria for IRB approval of research.

(a) In order to approve research covered by these regulations the IRB shall determine that all of the following requirements are satisfied:

(1) Risks to subjects are minimized: (i) By using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk, and (ii) whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes.

(2) Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may be expected to result. In evaluating risks and benefits, the IRB should consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies that subjects would receive even if not participating in the research). The IRB should not consider possible long-range effects of applying knowledge gained in the research (for example, the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility.

(3) Selection of subjects is equitable. In making this assessment the IRB should take into account the purposes of the research and the setting in which the research will be conducted and should be particularly cognizant of the special problems of research involving vulnerable populations, such as children, prisoners, pregnant women, handicapped, or mentally disabled persons, or economically or educationally disadvantaged persons.

(4) Informed consent will be sought from each prospective subject or the subject's legally authorized representative, in accordance with and to the extent required by part 50.

(5) Informed consent will be appropriately documented, in accordance with and to the extent required by §50.27.

(6) Where appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects.

(7) Where appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.

(b) When some or all of the subjects, such as children, prisoners, pregnant women, handicapped, or mentally disabled persons, or economically or educationally disadvantaged persons, are likely to be vulnerable to coercion or undue influence additional safeguards have been included in the study to protect the rights and welfare of these subjects.

§56.112 Review by institution.

Research covered by these regulations that has been approved by an IRB may be subject to further appropriate review and approval or disapproval by officials of the institution. However, those officials may not approve the research if it has not been approved by an IRB.

§56.113 Suspension or termination of IRB approval of research.

An IRB shall have authority to suspend or terminate approval of research that is not being conducted in accordance with the IRB's requirements or that has been associated with unexpected serious harm to subjects. Any suspension or termination of approval shall include a statement of the reasons for the IRB's action and shall be reported promptly to the investigator, appropriate institutional officials, and the Food and Drug Administration.

§56.114 Cooperative research.

In complying with these regulations, institutions involved in multi-institutional studies may use joint review, reliance upon the review of another qualified IRB, or similar arrangements aimed at avoidance of duplication of effort.

SUBPART D—RECORDS AND REPORTS

§56.115 IRB records.

(a) An institution, or where appropriate an IRB, shall prepare and maintain adequate documentation of IRB activities, including the following:

(1) Copies of all research proposals reviewed, scientific evaluations, if any, that accompany the proposals, approved sample consent documents, progress reports submitted by investigators, and reports of injuries to subjects.

(2) Minutes of IRB meetings which shall be in sufficient detail to show attendance at the meetings; actions taken by the IRB; the vote on these actions including the number of members voting for, against, and abstaining; the basis for requiring changes in or disapproving research; and a written summary of the discussion of controverted issues and their resolution.

(3) Records of continuing review activities.

(4) Copies of all correspondence between the IRB and the investigators.

(5) A list of IRB members identified by name; earned degrees; representative capacity; indications of experience such as board certifications, licenses, etc., sufficient to describe each member's chief anticipated contributions to IRB deliberations; and any employment or other relationship between each member and the institution; for example: full-time employee, part-time employee, a member of governing panel or board, stockholder, paid or unpaid consultant.

(6) Written procedures for the IRB as required by section 56.108 (a) and (b).

(7) Statements of significant new findings provided to subjects, as required by §50.25.

(b) The records required by this regulation shall be retained for at least 3 years after completion of the research, and the records shall be accessible for inspection and copying by authorized representatives of the Food and Drug Administration at reasonable times and in a reasonable manner.

(c) The Food and Drug Administration may refuse to consider a clinical investigation in support of an application for a research or marketing permit if the institution or the IRB that reviewed the investigation refuses to allow an inspection under this section.

SUBPART E—ADMINISTRATIVE ACTIONS FOR NONCOMPLIANCE

§56.120 Lesser administrative actions.

(a) If apparent noncompliance with these regulations in the operation of an IRB is observed by an FDA investigator during an inspection, the inspector will present an oral or written summary of observations to an appropriate representative of the IRB. The Food and Drug Administration may subsequently send a letter describing the noncompliance to the IRB and to the parent institution. The agency will require that the IRB or the parent institution respond to this letter within a time period specified by FDA and describe the corrective actions that will be taken by the IRB, the institution, or both to achieve compliance with these regulations.

(b) On the basis of the IRB's or the institution's response, FDA may schedule a reinspection to confirm the adequacy of corrective actions. In addition, until the IRB or the parent institution takes appropriate corrective action, the agency may:

(1) Withhold approval of new studies subject to the requirements of this part that are conducted at the institution or reviewed by the IRB;

(2) Direct that no new subjects be added to ongoing studies subject to this part;

(3) Terminate ongoing studies subject to this part when doing so would not endanger the subjects; or

(4) When the apparent noncompliance creates a significant threat to the rights and welfare of human subjects, notify relevant State and Federal regulatory agencies and other parties with a direct interest in the agency's action of the deficiencies in the operation of the IRB.

(c) The parent institution is presumed to be responsible for the operation of an IRB, and the Food and Drug Administration will ordinarily direct any administrative action under this subpart against the institution. However, depending on the evidence of responsibility for deficiencies, determined during the investigation, the Food and Drug Administration may restrict its administrative actions to the IRB or to a component of the parent institution determined to be responsible for formal designation of the IRB.

§56.121 Disqualification of an IRB or an institution.

(a) Whenever the IRB or the institution has failed to take adequate steps to correct the noncompliance stated in the letter sent by the agency under §56.120(a), and the Commissioner of Food and Drugs determines that this noncompliance may justify the disqualification of the IRB or of the parent institution, the Commissioner will in-

stitute proceedings in accordance with the requirements for a regulatory hearing set forth in part 16.

(b) The Commissioner may disqualify an IRB or the parent institution if the Commissioner determines that:

(1) The IRB has refused or repeatedly failed to comply with any of the regulations set forth in this part, and

(2) The noncompliance adversely affects the rights or welfare of the human subjects in a clinical investigation.

(c) If the Commissioner determines that disqualification is appropriate, theCommissioner will issue an order that explains the basis for the determination and that prescribes any actions to be taken with regard to ongoing clinical research conducted under the review of the IRB. The Food and Drug Administration will send notice of the disqualification to the IRB and the parent institution. Other parties with a direct interest, such as sponsors and clinical investigators, may also be sent a notice of the disqualification. In addition, the agency may elect to publish a notice of its action in the *Federal Register*.

(d) The Food and Drug Administration will not approve an application for a research permit for a clinical investigation that is to be under the review of a disqualified IRB or that is to be conducted at a disqualified institution, and it may refuse to consider in support of a marketing permit the data from a clinical investigation that was reviewed by a disqualified IRB as conducted at a disqualified institution, unless the IRB or the parent institution is reinstated as provided in §56.123.

§56.122 Public disclosure of information regarding revocation.

A determination that the Food and Drug Administration has disqualified an institution and the administrative record regarding that determination are disclosable to the public under part 20.

§56.123 Reinstatement of an IRB or an institution.

An IRB or an institution may be reinstated if the Commissioner determines, upon an evaluation of a written submission from the IRB or institution that explains the corrective action that the institution or IRB plans to take, that the IRB or institution has provided adequate assurance that it will operate in compliance with the standards set forth in this part. Notification of reinstatement shall be provided to all persons notified under §56.121(c).

§56.124 Actions alternative or additional to disqualification.

Disqualification of an IRB or of an institution is independent of, and neither in lieu of nor a precondition to, other proceedings or actions authorized by the act. The Food and Drug Administration may, at any time, through the Department of Justice institute any appropriate judicial proceedings (civil or criminal) and any other appropriate regulatory action, in addition to or in lieu of, and before, at the time of, or after, disqualification. The agency may also refer pertinent matters to another Federal, State, or local government agency for any action that that agency determines to be appropriate.

[The next page is Appendix II, Page 41.]

A SELF-EVALUATION CHECKLIST FOR IRBs

Food and Drug Administration
October 1995

The Food and Drug Administration (FDA) has regulations that govern human subject protection aspects of research on products regulated by the Agency. In addition, other federal agencies and departments and some States have regulations that govern human subject protection. Each institution should be familiar with the laws and regulations that apply to research conducted at the institution. This checklist was developed to help institutions evaluate procedures for the protection of human subjects of research.

Through its review of IRB activities, FDA has been impressed by the variety of procedural systems that have been developed to protect human subjects. At the same time, successful IRBs make use of written procedures that, in one way or another, cover a common core of topics. This checklist is an effort to present these topics in a systematic way. Some of the items are not covered by FDA regulations (e.g., policy regarding place and time of meeting) but may be appropriate to consider when comprehensive procedures are being developed. FDA does not expect institutions to develop procedural statements responding to each item in the list. Rather, the checklist should be used to identify procedures that may be needed to meet an institution's particular situation.

Once an institution establishes its IRB structure and procedures, those procedures should be followed. FDA inspections assess compliance on both the regulatory requirements as well as on the institution's own written procedures. The institutional procedures should reflect the current processes. Therefore, policies and procedures should be reviewed on a regular basis and updated as necessary. FDA believes that when good procedures are developed, written, and followed, the rights and welfare of the subjects of research are likely to be adequately protected.

Tips on checklist use:

Three "response" columns are provided — "Yes," "No," and N/A." A "Yes" means that the institution has a policy/procedure and that it is current. A "No" may mean that a policy/procedure is lacking or needs to be updated. The "N/A" column indicates that a topic is not applicable or a procedure is not needed in the institution.

The columns may be completed by checking the appropriate box. Instead of a check-mark, some institutions record the date of issuance or revision date. Others have found it useful to record the policy/procedure number on the form. Any "No" responses indicate a need to write/revise policies and/or procedures.

References to the FDA regulations are given for additional guidance on requirements.

A SELF-EVALUATION CHECKLIST FOR IRBs REVIEWING STUDIES OF FDA REGULATED ARTICLES

Does the Institution have written policies or procedures that describe:	Yes	No	N/A
I. The Institutional authority under which the IRB is established and empowered.			
II. The definition of the purpose of the IRB, i.e., the protection of human subjects of research. [1]			
III. The principles which govern the IRB in assuring the rights and welfare of subjects are protected.			
IV. The authority of the IRB.			
A. The scope of authority is defined, i.e. what types of studies must be reviewed.			
B. Authority to disapprove, modify or approve studies based upon consideration of human subject protection aspects.[2]			
C. Authority to require progress reports form the investigators and oversee the conduct of the study.[3]			
D. Authority to suspend or terminate a study.[4]			
E. Authority to place restriction on a study.[5]			
V. The IRB's relationship to			
A. The top administration of the institution.			
B. The other committees and department chairpersons within the institution.			
C. The research investigators.			
D. Other institutions.			
E. Regulatory agencies.			
VI. The membership of the IRB.			
A. Number of members.[6]			
B. Qualification of members.[7]			
C. Diversity of members (for example, representation from the community, and minority groups, including representation by[8]			
— both men and women			
— multiple professions			
— non-scientific member(s)			
— non-affiliated member(s)			
D. Alternate members if (used).			
VII. Management of the IRB.			
A. The chairperson			
— selection and appointment			
— length of term/service			

Does the Institution have written policies or procedures that describe:	Yes	No	N/A
— duties			
— removal			
B. The IRB members.			
— selection and appointment			
— length of term/service and description of staggered rotation or overlapping of terms, if used			
— duties			
— attendance requirements			
— removal			
C. Training of IRB Chair and members.			
— orientation			
— continuing education			
— reference materials (IRB library)			
D. Compensation of IRB members.			
E. Liability coverage for IRB members.			
F. Use of consultants.[9]			
G. Secretarial/administrative support staff (duties).			
H. Resources (for example, meeting area, filing space, reproduction equipment, and computer access).			
I. Conflict of interest policy			
— no selection of IRB members by investigators			
— prohibition of participation in IRB deliberations and voting by investigators.[10]			
VIII. Functions of the IRB.			
A. Conducting initial and continuing review.[11]			
B. Reporting, in writing, the findings and actions of the IRB to the investigator and the institution.[12]			
C. Determining which studies require review more often that annually.[13]			
D. Determining which studies need verification from sources other than the investigators that no material changed have occurred since previous IRB review.[14]			
E. Ensuring prompt reporting to the IRB of changes in research activities.[15]			
F. Ensuring that changes in approved research are not initiated without IRB review and approval except where necessary to eliminate immediate hazards.[16]			

Does the Institution have written policies or procedures that describe:	Yes	No	N/A
G. Ensuring prompt reporting to the IRB, appropriate institutional officials, and the FDA of			
— unanticipated problems involving risks to subjects or others.[17]			
— serious or continuing noncompliance with 21 CFR parts 50 and 56 or the requirements of the IRB.[18]			
— suspension or termination of IRB approval.[19]			
H. Determining which device studies pose significant or non-significant risk.			
IX. Operations of the IRB.			
A. Scheduling of meetings.			
B. Pre-meeting distribution to members, for example, place ant time of meeting, agenda, and study material to be reviewed.			
C. The review process			
— description of the process that 1) all members review complete study documentation (see XI.B), or 2) one or more "primary reviewers"/"secondary reviewers" review the complete study documentation, report to IRB and lead discussion; if other members review summary information only, these members must have access to complete study documentation			
— role of any subcommittees of the IRB			
— emergency use notification and reporting procedures[20]			
— expedite review procedure[21] — for approval of studies that are both minimal risk and on the FDA approved list (see Appendix A) — for approval of study modifications involving no more than minimal risk			
D. Criteria for IRB approval contain all requirements of 21 CFR 56.111.			
E. Voting requirements[22]			
— quorum required to transact business			
— diversity requirements of quorum (for example requiring at least one physician when reviewing studies of FDA regulated articles)			
— percent needed to approve or disapprove study			

Does the Institution have written policies or procedures that describe:	Yes	No	N/A
— full voting rights of all members			
— no proxy votes (written or telephone)			
— prohibition against conflict-of-interest voting			
F. Further review/approval of IRB actions by others within the institution. (Override of disapprovals prohibited.)			
G. Communication from the IRB.			
— to the investigator for additional information[23]			
— to the investigator conveying IRB decison[24]			
— to the institution administration conveying IRB decision[25]			
— to sponsor of research conveying IRB decision			
H. Appeal of IRB decisions.			
— criteria for appeal			
— to whom appeal is addressed			
— how appeal is resolved (Override of IRB disapprovals by external body/official is prohibited.)			
X. IRB record requirements.			
A. IRB membership roster showing qualifications listed in 21 CFR 56.115(a)(5).			
B. Written procedures and guidelines.[26]			
C. Minutes of meetings.[27]			
— members present (any consultants/guest/others shown separately)			
— summary of discussion on debated issues			
— record of IRB decisions			
— record of voting (showing votes for, against and abstentions)			
D. Retention of protocols reviewed and approved consent documents[28]			
E. Communications to and from the IRB[29]			
F. 1) Adverse reactions reports[30], and			
2) documentation that the IRB reviews such reports.			
H. Records of continuing review.[31]			

Does the Institution have written policies or procedures that describe:	Yes	No	N/A
I. Record retention requirements. (at least 3 years after completion for FDA studies)[32]			
J. Budget and accounting records regarding acquisition and expenditure of resources.			
K. Emergency use reports.[33]			
L. Statements of significant new findings provided to subjects.[34]			
XI. Information the investigator provides to the IRB.			
A. Professional qualifications to do the research (including a description of necessary support services and facilities).			
B. Study protocol which includes/addresses[35]			
— title of study.			
— purpose of the study (including the expected benefits obtained by doing the study).			
— sponsor of the study.			
— results of previous related research.			
— subject selection criteria			
— subject exclusion criteria			
— justification for use of any special/vulnerable subject populations (for example, the mentally impaired and children)			
— study design (including as needed, a discussion of the appropriateness of research methods).			
— description for managing adverse reactions.			
— the circumstances surrounding consent procedure, including setting, subject autonomy concerns, language difficulties, vulnerable populations and other details.			
— the procedures for documentation of informed consent, including any procedures for obtaining assent form minors, using witnesses, translators and document storage.			
— compensation to subjects for their participation.			
— any compensation for injured research subjects.			
— provisions for protection of subject's privacy.			
— extra costs to subjects for their participation in the study.			

Does the Institution have written policies or procedures that describe:	Yes	No	N/A
— extra costs to third party payers because of subjects's participation.			
C. Investigator's brochure (when on exists)[36]			
D. The proposed informed consent document[37]			
— containing all requirements of 21 CFR 50.25 (a)			
— containing requirements of 21 CFR 50.25(b), that are appropriate to the study.			
— meeting all requirements of 21 CFR 50.20			
— translated consent documents, as necessary considering likely subject population(s)			
E. Requests for changes in study after initiation.[38]			
F. Reports of unexpected adverse events.[39]			
G. Progress reports.[40]			
H. Final report.			
I. Institutional forms/reports			

CHECKLIST REFERENCES

1. § 56.101(a)
2. § 56.109(a)
3. § 56.108(a)(1) and § 56.109(e)
4. § 56.108(b)(3) and § 56.113
5. § 56.109(a) and § 56.113
6. § 56.107(a)
7. § 56.107(a—f)
8. § 56.107(a—f)
9. § 56.107(f)
10. § 56.107(e)
11. § 56.108(a)(1) and § 56.109(a and e)
12. § 56.108(a)(1) and § 56.109(d)
13. § 56.108(a)(2) and § 56.109(e)
14. § 56.108(a)(2)
15. § 56.108(a)(3)
16. § 56.108(a)(4) and § 56.115(a)(1)
17. § 56.108(b)(1) and § 56.115(a)(1)
18. § 56.108(b)(2)
19. § 56.108(b)(3) and § 56.113
20. § 56.104(c)
21. § 56.110(a—c)
22. § 56.108(c) and § 56.107(c—f)
23. § 56.109(a) and § 56.115(a) (4)
24. § 56.108(a)(1) and § 56.109(d)

25. § 56.109(d)
26. § 56.108(a—b) and § 56.115(a)(6)
27. § 56.115(a)(2)
28. § 56.115(a)(1)
29. § 56.115(a)(4)
30. § 56.108(a) and § 56.115(a)(1 and 4)
31. § 56.115(a)(3)
32. § 56.115(b)
33. § 56.115(a)(4) and § 56.104(c)
34. § 56.115(a)(7)
35. § 56.103(a) and § 56.115(a)(1)
36. § 56.111(a)(2) § 56.115(a)(1) and § 312.55
37. § 56.111(a)(4—5) and § 56.111(a)(1)
38. § 56.108(a)(4) and § 56.115(a)(3—4)
39. § 56.115(a)(3—4) § 56.115(b)(1) and § 56.113
40. § 56.115(a)(1 and 3—4)

[The next page is Appendix III, Page 209.]

