CHAPTER 7: OPINIONS ON RESEARCH & INNOVATION

The Opinions in this chapter are offered as ethics guidance for physicians and are not intended to establish standards of clinical practice or rules of law.

7.1 Physician Involvement in Research

7.2 Disseminating Research Results

7.3 Special Issues in Research

7.1.1 Physician Involvement in Research

Biomedical and health research is intended to contribute to the advancement of knowledge and the welfare of society and future patients, rather than to the specific benefit of the individuals who participate as research subjects.

However, research involving human participants should be conducted in a manner that minimizes risks and avoids unnecessary suffering. Because research depends on the willingness of participants to accept risk, they must be able to make informed decisions about whether to participate or continue in a given protocol.

Physician researchers share their responsibility for the ethical conduct of research with the institution that carries out research. Institutions have an obligation to oversee the design, conduct, and dissemination of research to ensure that scientific, ethical, and legal standards are upheld. Institutional review boards (IRBs) as well as individual investigators should ensure that each participant has been appropriately informed and has given voluntary consent.

Physicians who are involved in any role in research with human participants have an ethical obligation to ensure that participants' interests are protected and to safeguard participants' welfare, safety, and comfort.

To fulfill these obligations, individually, physicians who are involved in research should:

(a) Participate only in those studies for which they have relevant expertise.

(b) Ensure that voluntary consent has been obtained from each participant or from the participant's legally authorized representative if the participant lacks the capacity to consent, in keeping with ethics guidance. This requires that:

    (i) prospective participants receive the information they need to make well-considered decisions, including informing them about the nature of the research and potential harms involved;

    (ii) physicians make all reasonable efforts to ensure that participants understand the research is not intended to benefit them individually;

    (iii) physicians also make clear that the individual may refuse to participate or may withdraw from the protocol at any time.

(c) Assure themselves that the research protocol is scientifically sound and meets ethical guidelines for research with human participants. Informed consent can never be invoked to justify an unethical study design.

(d) Demonstrate the same care and concern for the well-being of research participants that they would for patients to whom they provide clinical care in a therapeutic relationship. Physician researchers should advocate for access to experimental interventions that have proven effectiveness for patients.

(e) Be mindful of conflicts of interest and assure themselves that appropriate safeguards are in place to protect the integrity of the research and the welfare of human participants.

(f) Adhere to rigorous scientific and ethical standards in conducting, supervising, and disseminating results of the research.

AMA Principles of Medical Ethics: I,II,III,V

7.1.2 Informed Consent in Research

Informed consent is an essential safeguard in research. The obligation to obtain informed consent arises out of respect for persons and a desire to respect the autonomy of the individual deciding whether to volunteer to participate in biomedical or health research. For these reasons, no person may be used as a subject in research against his or her will.

Physicians must ensure that the participant (or legally authorized representative) has given voluntary, informed consent before enrolling a prospective participant in a research protocol. With certain exceptions, to be valid, informed consent requires that the individual have the capacity to provide consent and have sufficient understanding of the subject matter involved to form a decision. The individual's consent must also be voluntary.

A valid consent process includes:

(a) Ascertaining that the individual has decision-making capacity.

(b) Reviewing the process and any materials to ensure that it is understandable to the study population.

(c) Disclosing:

(i) the nature of the experimental drug(s), device(s), or procedure(s) to be used in the research;

(ii) any conflicts of interest relating to the research, in keeping with ethics guidance;

(iii) any known risks or foreseeable hazards, including pain or discomfort that the participant might experience;

(iv) the likelihood of therapeutic or other direct benefit for the participant;

(v) that there are alternative courses of action open to the participant, including choosing standard or no treatment instead of participating in the study;

(vi) the nature of the research plan and implications for the participant;

(vii) the differences between the physician's responsibilities as a researcher and as the patient's treating physician.

(d) Answering questions the prospective participant has.

(e) Refraining from persuading the individual to enroll.

(f) Avoiding encouraging unrealistic expectations.

(g) Documenting the individual's voluntary consent to participate.

Participation in research by minors or other individuals who lack decision-making capacity is permissible in limited circumstances when:

(h) Consent is given by the individual's legally authorized representative, under circumstances in which informed and prudent adults would reasonably be expected to volunteer themselves or their children in research.

(i) The participant gives his or her assent to participation, where possible. Physicians should respect the refusal of an individual who lacks decision-making capacity.

(j) There is potential for the individual to benefit from the study.

In certain situations, with special safeguards in keeping with ethics guidance, the obligation to obtain informed consent may be waived in research on emergency interventions.

AMA Principles of Medical Ethics: I,III,V

7.1.3 Study Design & Sampling

To be ethically justifiable, biomedical and health research that involves human subjects must uphold fundamental principles of respect for persons, beneficence, and justice. These principles apply not only to the conduct of research, but equally to the selection of research topics and study design.

Well-designed, ethically sound research aligns with the goals of medicine, addresses questions relevant to the population among whom the study will be carried out, balances the potential for benefit against the potential for harm, employs study designs that will yield scientifically valid and significant data, and generates useful knowledge. For example, research to develop biological or chemical weapons is antithetical to the goals of the medical profession, whereas research to develop defenses against such weapons can be ethically justifiable.

Physicians who engage in biomedical or health research with human participants thus have an ethical obligation to ensure that any study with which they are involved:

(a) Is consistent with the goals and fundamental values of the medical profession.

(b) Addresses research question(s) that will contribute meaningfully to medical knowledge and practice.

(c) Is scientifically well designed to yield valid data to answer the research question(s), including using appropriate population and sampling controls, clear and appropriate inclusion/exclusion criteria, a statistically sound plan for data collection and analysis, appropriate controls, and when applicable, criteria for discontinuing the study (stopping rules).

(d) Minimizes risks to participants, including risks associated with recruitment and data collection activities, without compromising scientific integrity.

(e) Provides mechanisms to safeguard confidentiality.

(f) Does not disproportionately recruit participants from historically disadvantaged populations or populations whose ability to provide fully voluntary consent is compromised. Participants who otherwise meet inclusion/exclusion criteria should be recruited without regard to race, ethnicity, gender, or economic status.

(g) Recruits participants who lack the capacity to give informed consent only when the study stands to benefit that class of participants and participants with capacity would not yield valid results. In this event, assent should be sought from the participant and consent should be obtained from the prospective participant's legally authorized representative, in keeping with ethics guidance.

(h) Has been reviewed and approved by appropriate oversight bodies.

AMA Principles of Medical Ethics: I,II,III,V,VII

7.1.4 Conflicts of Interest in Research

Increasing numbers of physicians, both within and outside academic health centers, are becoming involved in partnerships with industry to conduct biomedical and health research. As they do so, physicians must be mindful of the conflicts such engagement poses to the integrity of the research and the welfare of human participants. In addition to financial conflicts of interest created by incentives to conduct trials and recruit subjects, physicians must be sensitive to the differing roles of clinician and investigator, which may require them to balance dual commitments to participants and science. This conflict of commitment is particularly acute when a physician-investigator has treated or continues to treat a patient who is eligible to enroll as a participant in a clinical trial the physician is conducting.

Minimizing and mitigating conflicts of interest in clinical research is imperative if the medical community is to justify and maintain trust in the medical research community.

Physicians who engage in research should:

(a) Decline financial compensation that awards in excess of the physician's research efforts and does not reflect fair market value. Physicians should not accept payment solely for referring patients to research studies.

(b) Ensure that the research protocol includes provision for funding participants' medical care in the event of complications associated with the research. A physician should not double-bill a third-party payer for additional expenses related to conducting the trial if he or she has already received funds from a sponsor for those expenses.

(c) As part of the informed consent process, disclose to prospective participants the nature and source of funding and financial incentives offered to the investigators. This disclosure should be included in any written consent materials.

(d) Avoid engaging in any research where there is an understanding that limitations can be placed on the presentation or publication of results by the research sponsor.

(e) Refrain from knowingly participating in a financial relationship with a commercial entity with whom they have a research relationship until the research relationship ends and the research results have been published or otherwise disseminated to the public.

(f) Disclose material ties to companies whose products they are investigating or other ties that create real or perceived conflicts of interest to:

    (i) institutions where the research will be carried out;

    (ii) organizations that are funding the research;

    (iii) any journal or publication where the research results are being submitted.

(g) Physicians who have leadership roles in institutions that conduct biomedical and health research as well as the entities that fund research with human participants should promote the development of guidelines on conflicts of interest that clarify physician-investigators responsibilities.

AMA Principles of Medical Ethics: II,IV,V

7.1.5 Misconduct in Research

Biomedical and health research is intended to advance medical knowledge to benefit future patients. To achieve those goals physicians who are involved in such research maintain the highest standards of professionalism and scientific integrity.

Physicians with oversight responsibilities in biomedical or health research have a responsibility to ensure that allegations of scientific misconduct are addressed promptly and fairly. They should ensure that procedures to resolve such allegations:

(a) Do not damage science.

(b) Resolve charges expeditiously.

(c) Treat all parties fairly and justly. Review procedures should be sensitive to parties' reputations and vulnerabilities.

(d) Maintain the integrity of the process. Real or perceived conflicts of interest must be avoided.

(e) Maintain accurate and thorough documentation throughout the process.

(f) Maintain the highest degree of confidentiality.

(g) Take appropriate action to discharge responsibilities to all individuals involved, as well as to the public, research sponsors, the scientific literature, and the scientific community.

AMA Principles of Medical Ethics: I,III,V

7.2.1 Principles for Disseminating Research Results

Physicians have an ethical responsibility to learn from and contribute to the total store of scientific knowledge. When they engage in biomedical or health research, physicians have obligations as scientists, which include disseminating research findings. Prompt presentation to scientific peers and publication of research findings are foundational to good medical care and promote enhanced patient care, early evaluation of clinical innovations, and rapid dissemination of improved techniques.

To fulfill their ethical responsibilities with respect to sharing research findings for the ultimate benefit of patients, physicians should:

(a) Advocate for timely and transparent dissemination of research data and findings. Physicians should not intentionally withhold information for reasons of personal gain.

(b) Report the results of research accurately, including subsequent negative findings. This is particularly important where the findings do not support the research hypothesis.

(c) Maintain a commitment to peer review.

(d) Disclose sponsorship and conflicts of interest relating to the research, in keeping with ethics guidance.

(e) Be responsible in their release of research results to the media, ensuring that any information the researcher provides is prompt and accurate and that informed consent to the release of information has been obtained from research participants (or participants' legally authorized representative when the participant lacks decision-making capacity) prior to releasing any identifiable information.

In rare circumstances, the potential for misuse of research results could affect the decision about when and whether to disseminate research findings. Physician-researchers should assess foreseeable ramifications of their research in an effort to balance the promise of benefit against potential harms from corrupt application. Only under rare circumstances should findings be withheld, and then only to the extent required to reasonably protect against misuse.

AMA Principles of Medical Ethics: I,II,III,V,VII

7.2.2 Release of Data from Unethical Experiments

Research that violates the fundamental principle of respect for persons and basic standards of human dignity, such as Nazi experiments during World War II or from the US Public Health Service Tuskegee Syphilis Study, is unethical and of questionable scientific value. Data obtained from such cruel and inhumane experiments should virtually never be published. If data from unethical experiments can be replaced by data from ethically sound research and achieve the same ends, then such must be done. In the rare instances when ethically tainted data have been validated by rigorous scientific analysis, are the only data of such nature available, and human lives would certainly be lost without the knowledge obtained from the data, it may be permissible to use or publish findings from unethical experiments.

Physicians who engage with data from unethical experiments as authors, peer reviewers, or editors of medical publications should:

(a) Disclose that the data derive from studies that do not meet contemporary standards for the ethical conduct of research.

(b) Clearly describe and acknowledge the unethical nature of the experiment(s) from which the data are derived.

(c) Provide ethically compelling reasons for which the data are being released or cited, such as the need to save human lives when no other relevant data are available.

(d) Pay respect to those who were the victims of the unethical experimentation.

AMA Principles of Medical Ethics: II,V,VII

7.2.3 Patents & Dissemination of Research Products

A patent grants the holder the right, for a limited time, to prevent others from commercializing his or her inventions. By requiring full disclosure of the invention, and thus enabling another trained in the art to replicate it, the patent system protects the holder's discovery, yet also fosters information sharing. Patenting is also thought to encourage private investment into research.

With respect to genetic research, patenting raises unique questions. Arguments have been made that the patenting of human genetic material sets a troubling precedent for the ownership or commodification of human life. However, DNA sequences are not tantamount to human life and it is unclear where and whether qualities uniquely human are found in genetic material. Moreover, while genetic research holds great potential for developing new medical therapies it remains unclear what role patenting will play in ensuring such development.

Physicians who develop medical innovations may ethically patent their discoveries or products but should uphold the following guidelines:

(a) Not use patents (or other means, such as trade secrets or confidentiality agreements) to limit the availability of medical innovations. Patent protection should not hinder the goal of achieving better medical treatments and technologies.

(b) Not allow patents to languish. Physicians who hold patents should negotiate and structure licensing agreements in such a way as to encourage the development of better medical technology.

(c) For patents on genetic materials recognize that:

(i) patents on processes, e.g. to isolate and purify gene sequences, are ethically preferable to patents on the substances themselves;

(ii) patents on purified proteins (substance patents) are ethically preferable to patents on genes or DNA sequences.

Descriptions for (substance) patents on proteins, genes, or genetic sequences should be carefully constructed to ensure that the patent holder does not limit the use of a naturally occurring form of the substance in question.

AMA Principles of Medical Ethics: V,VII

7.3.1 Ethical Use of Placebo Controls in Research

A fundamental requirement of biomedical and health research is that it must provide scientifically valid data. In some research, this can best be achieved by comparing an intervention against a control to identify the effects of the intervention. Used appropriately, a placebo control can provide valuable data, particularly when there is no accepted therapy for the condition under study.

The existence of an accepted therapy does not necessarily preclude use of placebo controls, but because use of a placebo deprives participants in the control arm of access to accepted therapy for some period of time, it requires thoughtful ethical justification. In general, the use of a placebo control will more easily be justified as the severity and number of negative side effects of standard therapy increase.

To ensure that the interests of human participants are protected, physician-researchers and those who serve on oversight bodies should give careful attention to issues of methodological rigor, informed consent, characteristics of the medical condition under study, and safety and monitoring, in keeping with the following guidelines:

(a) Evaluate each study protocol to determine whether a placebo control is scientifically necessary or an alternative study design using a different type of control would be sufficient for the purposes of the research. Placebo controls are ethically justifiable when no other research design will yield the requisite data.

(b) Assess the use of placebo controls in relation to the characteristics of the condition under study in keeping with the following considerations:

(i) Studies that involve conditions likely to cause death or irreversible damage cannot ethically employ placebo controls if an alternative therapy would prevent or slow the progression of illness;

(ii) Studies that involve illnesses characterized by severe or painful symptoms require a thorough exploration of alternatives to the use of a placebo control;

(iii) In general, the more severe the consequences or symptoms of the illness under study, the more difficult it will be to justify the use of a placebo control when alternative therapy exists. Consequently, there will almost certainly be conditions for which placebo controls cannot ethically be justified.

(c) Design studies to minimize the amount of time participants are on placebo without compromising the scientific integrity of the study or the value of study data.

(d) Pay particular attention to the informed consent process when enrolling participants in research that uses a placebo control. In addition to general guidelines for informed consent in research, physician-researchers (or other health care professionals) who obtain informed consent from prospective subjects should:

(i) describe the differences among the research arms, emphasizing the essential intervention(s) that will or will not be performed in each;

(ii) be sensitive to the possible need for additional safeguards in the consent process, such as having a neutral third party obtain consent or using a consent monitor to oversee the consent process.

(e) Ensure that interim data analysis and monitoring are in place to allow researchers to terminate a study because of either positive or negative results, thus protecting participants from remaining on placebo longer than needed to ensure the scientific integrity of the study.

(f) Avoid using surgical placebo controls—i.e., a control arm in which participants undergo surgical procedures that have the appearance of therapeutic interventions but during which the essential therapeutic maneuver is not performed—when there is a standard treatment that is efficacious and acceptable to the patient and forgoing standard treatment would result in significant injury. In these situations, physician-researchers must offer standard treatment as part of the study design. Use of surgical placebo controls may be justified when:

(i) an existing, accepted surgical procedure is being tested for efficacy. Use of a placebo control is not justified to test the effectiveness of an innovative surgical technique that represents only a minor modification of an existing, accepted surgical procedure;

(ii) a new surgical procedure is developed with the prospect of treating a condition for which there is no known surgical therapy. In such cases, the use of placebo must be evaluated in light of whether the current standard of care includes a nonsurgical treatment and the risks, benefits, and side effects of that treatment;

(iii) the standard (nonsurgical) treatment is not efficacious or not acceptable to the patient;

(iv) Additional safeguards are in place in the informed consent process.

AMA Principles of Medical Ethics: I,V

7.3.2 Research on Emergency Medical Interventions

Emergency medicine often applies standard interventions that have not been scientifically evaluated for safety and effectiveness in the context of emergency care and may render unsatisfactory outcomes. However, in life-threatening situations, patients may not be able to give informed consent and a surrogate

decision maker may not be readily available, making it challenging to carry out ethically sound research. Soliciting input from the community before a research protocol is approved can help address some concerns, but not all.

Given the insufficiency of standard treatment alternatives, it can be appropriate, in certain situations and with special safeguards, to provide experimental treatment without a participant's informed consent.

To protect the rights and welfare of participants in research on emergency medical interventions, physician-researchers must adhere to the following criteria:

(a) The experimental intervention has a realistic probability of providing benefit equal to or greater than standard care.

(b) The risks associated with the research are reasonable in light of the critical nature of the medical condition and the risks associated with standard treatment.

(c) Study participants are randomized fairly.

(d) The trial is overseen by an independent data and safety monitoring board.

(e) The prospective participant lacks the capacity to give informed consent at the time he or she must be enrolled due to the emergency situation and requirements of the research protocol and it would not have been feasible to obtain prospective informed consent because the life-threatening emergency situation could not have been anticipated.

(f) The window of opportunity to administer the experimental intervention is so narrow as to make it unfeasible to obtain consent from the prospective participant's surrogate or other legally authorized representative.

(g) Participants, or their representatives, are informed as soon as possible that the individual has been enrolled in the research and asked to give consent to further participation.

(h) The representative of a patient who dies while participating in the research must be informed that the individual was involved in an experimental protocol.

(i) Study results will be publicly disclosed.

AMA Principles of Medical Ethics: I,V

7.3.3 International Research

Biomedical and health research in international settings often raises special ethical questions, particularly when research is carried out in resource-poor settings by sponsors or researchers from resource-rich countries. Physicians engaged in international research may encounter differing cultural traditions, economic conditions, health care systems, and ethical or regulatory standards and traditions than in the US.

While fundamental requirements to ensure scientifically sound research and to protect the welfare, safety, and comfort of human participants apply in any research setting, physicians who are involved in international research may need to address special concerns about selection of research topic and study design, informed consent, and the impact of the research on the participating community.

In addition to following general ethical guidelines for biomedical and health research, physicians who are involved in international research have obligations to:

Study design

(a) Ensure that the research responds to a medical need in the region in which it is undertaken.

(b) Ensure that the research does not exploit the populations and communities from which participants will be drawn.

(c) Be sensitive to special considerations in assessing the risks and benefits of the research in the particular setting and employ a research design that minimizes risks to the participant population by:

    (i) ascertaining that there is genuine uncertainty within the clinical community about the comparative merits of the experimental intervention and the intervention that will be offered as a control for the population to be enrolled;

    (ii) obtaining relevant input from representatives of the host community and from the research population;

    (iii) considering the harm that is likely to result for the host community or research population if the research is not carried out.

(d) In some instances, a three-pronged protocol that offers the standard of care in the US, an intervention that meets a level of care that can be attained in and sustained by the host community, and a placebo may offer the most ethically desirable means for evaluating the safety and efficacy of an intervention in a given population.

Informed consent

(e) Ensure that a suitable process for informed consent is in place. If consent is to be meaningful, physicians (or other health professionals) who obtain consent must communicate with sensitivity to local customs. Notwithstanding, they should always ensure that individual participants are informed and that their voluntary consent is sought.

Impact on the host community

(f) Foster research with the potential for lasting benefits to the host community, especially when the research is carried out among populations that are severely deficient in health care resources. This can be achieved by:

    (i) facilitating development of a health care infrastructure that will be of use during and after the research period itself;

    (ii) encouraging sponsors to provide interventions that have been demonstrated to be beneficial to all study participants after the study concludes.

AMA Principles of Medical Ethics: I,IV,VII,VIII,IX

7.3.4 Maternal-Fetal Research

Maternal-fetal research, i.e., research intended to benefit pregnant women and/or their fetuses, must balance the health and safety of the woman who participates and the well-being of the fetus with the desire to develop new and innovative therapies. One challenge in such research is that pregnant women may face external pressure or expectations to enroll from partners, family members, or others that may compromise their ability to make a fully voluntary decision about whether to participate.

Physicians engaged in maternal-fetal research should demonstrate the same care and concern for the pregnant woman and fetus that they would in providing clinical care.

In addition to adhering to general guidelines for the ethical conduct of research and applicable law, physicians who are involved in maternal-fetal research should:

(a) Base studies on scientifically sound clinical research with animals and nongravid human participants that has been carried out prior to conducting maternal-fetal research whenever possible.

(b) Enroll a pregnant woman in maternal-fetal research only when there is no simpler, safer intervention available to promote the well-being of the woman or fetus.

(c) Obtain the informed, voluntary consent of the pregnant woman.

(d) Minimize risks to the fetus to the greatest extent possible, especially when the intervention under study is intended primarily to benefit the pregnant woman.

AMA Principles of Medical Ethics: I,III,V

7.3.5 Research Using Human Fetal Tissue

Research with human fetal tissue research has led to the development of a number of important research and medical advances, such as the development of polio vaccine. Fetal tissue has also been used to study the mechanism of viral infections and to diagnose viral infections and inherited diseases, as well as to develop transplant therapies for a variety of conditions, for example, parkinsonism.

However, the use of fetal tissue for research purposes also raises a number of ethical considerations, including the degree to which a woman's decision to have an abortion might be influenced by the opportunity to donate fetal tissue. Concerns have also been raised about potential conflict of interest when there is possible financial benefit to those who are involved in the retrieval, storage, testing, preparation, and delivery of fetal tissues.

To protect the interests of pregnant women as well as the integrity of science, physicians who are involved in research that uses human fetal tissues should:

(a) Abstain from offering money in exchange for fetal tissue.

(b) In all instances, obtain the woman's voluntary, informed consent in keeping with ethics guidance, including when using fetal tissue from a spontaneous abortion for purposes of research or transplantation. Informed consent includes a disclosure of the nature of the research including the purpose of using fetal tissue, as well as informing the woman of a right to refuse to participate.

(c) Ensure that when fetal tissue from an induced abortion is used for research purposes:

(i) the woman's decision to terminate the pregnancy is made prior to and independent of any discussion of using the fetal tissue for research purposes;

(ii) decisions regarding the technique used to induce abortion and the timing of the abortion in relation to the gestational age of the fetus are based on concern for the safety of the pregnant woman.

(d) Ensure that when fetal tissue is to be used for transplantation in research or clinical care:

(i) the donor does not designate the recipient of the tissue;

(ii) both the donor and the recipient of the tissue give voluntary, informed consent.

(e) Ensure that health care personnel involved in the termination of a pregnancy do not benefit from their participation in the termination, or from use of the fetal tissue for transplantation.

AMA Principles of Medical Ethics: I,III,IV,V

7.3.6 Research in Gene Therapy & Genetic Engineering

Gene therapy involves the replacement or modification of a genetic variant to restore or enhance cellular function or the improve response to nongenetic therapies. Genetic engineering involves the use of recombinant DNA techniques to introduce new characteristics or traits. In medicine, the goal of gene therapy and genetic engineering is to alleviate human suffering and disease. As with all therapies, this goal should be pursued only within the ethical traditions of the profession, which gives primacy to the welfare of the patient.

In general, genetic manipulation should be reserved for therapeutic purposes. Efforts to enhance "desirable" characteristics or to "improve" complex human traits are contrary to the ethical tradition of medicine. Because of the potential for abuse, genetic manipulation of nondisease traits or the eugenic development of offspring may never be justifiable.

Moreover, genetic manipulation can carry risks to both the individuals into whom modified genetic material is introduced and to future generations. Somatic cell gene therapy targets nongerm cells and thus does not carry risk to future generations. Germ-line therapy, in which a genetic modification is introduced into the genome of human gametes or their precursors, is intended to result in the expression of the modified gene in the recipient's offspring and subsequent generations. Germ-line therapy thus may be associated with increased risk and the possibility of unpredictable and irreversible results that adversely affect the welfare of subsequent generations.

Thus in addition to fundamental ethical requirements for the appropriate conduct of research with human participants, research in gene therapy or genetic engineering must put in place additional safeguards to vigorously protect the safety and well-being of participants and future generations.

Physicians should not engage in research involving gene therapy or genetic engineering with human participants unless the following conditions are met:

(a) Experience with animal studies is sufficient to assure that the experimental intervention will be safe and effective and its results predictable.

(b) No other suitable, effective therapies are available.

(c) Gene therapy is restricted to somatic cell interventions, in light of the far-reaching implications of germ-line interventions.

(d) Evaluation of the effectiveness of the intervention includes determination of the natural history of the disease or condition under study and follow-up examination of the participants' descendants.

(e) The research minimizes risks to participants, including those from any viral vectors used.

(f) Special attention is paid to the informed consent process to ensure that the prospective participant (or legally authorized representative) is fully informed about the distinctive risks of the research, including use of viral vectors to deliver the modified genetic material, possible implications for the participant's descendants, and the need for follow-up assessments.

Physicians should be aware that gene therapy or genetic engineering interventions may require additional scientific and ethical review, and regulatory oversight, before they are introduced into clinical practice.

AMA Principles of Medical Ethics: I,V,VII

7.3.7 Safeguards in the Use of DNA Databanks

DNA databanks facilitate population-based research into the genetic components of complex diseases. These databanks derive their power from integrating genetic and clinical data, as well as data on health, lifestyle, and environment about large samples of individuals. However, the use of DNA databanks in genomic research also raises the possibility of harm to individual participants, their families, and even populations.

Breach of confidentiality of information contained in DNA databanks may result in discrimination or stigmatization and may carry implications for important personal choices, such as reproductive choices. Human participants who contribute to research involving DNA databanks have a right to be informed about the nature and scope of the research and to make decisions about how their information may be used.

In addition to having adequate training to be able to discuss genomic research and related ethical issues with patients or prospective research participants, physician-researchers who are involved in genomic research using DNA databanks should:

Research involving individuals

(a) Obtain informed consent from participants in genomic research, in keeping with ethics guidance. In addition, physicians should put special emphasis in the consent process on disclosing:

    (i) the specific privacy standards to which the study will adhere, including whether the information or biological sample will be encrypted and remain identifiable to the researcher or will be completely de-identified;

    (ii) whether participants whose data will be encrypted rather than de-identified can expect to be contacted in the future about findings or be invited to participate in additional research, either related to the current protocol or for other research purposes;

(iii) whether researchers or participants stand to gain financially from research findings, and any conflicts of interest researchers may have in regard to the research, in keeping with ethics guidance;

(iv) when, if ever, archived information or samples will be discarded;

(v) participants' freedom to refuse use of their biological materials without penalty.

Research involving identifiable communities

(b) When research is to be conducted within a defined subset of the general population, physicians should:

(i) consult with the community in advance to design a study that is sensitive to community concerns and that will minimize harm for the community, as well as for individual participants. Physicians should not carry out a study when there is substantial opposition to the research within the community of interest;

(ii) protect confidentiality by encrypting any demographic or identifying information that is not required for the study's purpose.

AMA Principles of Medical Ethics: I,IV,V,VII

7.3.8 Research with Stem Cells

Human stem cells are widely seen as offering a source of potential treatment for a range of diseases and are thus the subject of much research. Clinical studies have validated the use of adult stem cells in a limited number of therapies, but have yet to confirm the utility of embryonic stem cells.

Physicians who conduct research using stem cells obtained from any source (established tissue, umbilical cord blood, or embryos) must, at a minimum:

(a) Adhere to institutional review board (IRB) requirements.

(b) Ensure that the research is carried out with appropriate oversight and monitoring.

(c) Ensure that the research is carried out with appropriate informed consent. In addition to disclosure of research risks and potential benefits, at minimum, the consent disclosure should address:

(i) for a donor of cells to be used in stem cell research:

a the process by which stem cells will be obtained;

b. what specifically will be done with the stem cells;

c. whether an immortal cell line will result; and

d. the primary and anticipated secondary uses of donated embryos and/or derived stem cells, including potential commercial uses.

(ii) for a recipient of stem cells in clinical research:

a. the types of tissue from which the stem cells derive (e.g., established tissue, umbilical cord blood, or embryos); and

b. unique risks posed by investigational stem cell products (when applicable), such as tumorigenesis, immunological reactions, unpredictable behavior of cells, and unknown long-term health effects.

The professional community as well as the public remains divided about the use of embryonic stem cells for either research or therapeutic purposes. The conflict regarding research with embryonic stem cells centers on the moral status of embryos, a question that divides ethical opinion and that cannot be resolved by medical science. Regardless whether they are obtained from embryos donated by individuals or couples undergoing in vitro fertilization, or from cloned embryos created by somatic cell nuclear transfer (SCNT), use of embryonic stem cells currently requires the destruction of the human embryo from which the stem cells derive.

The pluralism of moral visions that underlies this debate must be respected. Participation in research involving embryonic stem cells requires respect for embryos, research participants, donors, and recipients. Embryonic stem cell research does not violate the ethical standards of the profession. Every physician remains free to decide whether to participate in stem cell research or to use its products. Physicians should continue to be guided by their commitment to the welfare of patients and the advancement of medical science.

Physicians who conduct research using embryonic stem cells should be able to justify greater risks for subjects, and the greater respect due embryos than stem cells from other sources, based on expectations that the research offers substantial promise of contributing significantly to scientific or therapeutic knowledge.

AMA Principles of Medical Ethics: V

7.3.9 Commercial Use of Human Biological Materials

Research using human tissues has resulted in numerous commercially available products for use in both research and treatment. The development of these products raises questions about who holds property rights in human biological materials, how to distribute profits derived from human tissues equitably, and what constitutes appropriately informed consent when patients donate biological materials to research that may ultimately result in one or more commercial products.

Physicians involved in research with human biological materials should:

(a) Disclose potential commercial applications to the tissue donor before a profit is realized on products developed from biological materials.

(b) Obtain informed consent to use biological materials in research from the tissue donor. Human biological materials and their products may not be used for commercial purposes without the consent of the tissue donor.

(c) Share profits from the commercial use of human biological materials with the tissue donor in accordance with lawful contractual agreements.

Physicians must make diagnostic and treatment recommendations in keeping with standards of good medical practice. They must not allow the commercial potential of the patient's tissue to influence professional judgment.

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E-7.3.10 – Expanded Access to Investigational Therapies

Physicians who care for patients with serious, life-threatening illness for whom standard therapies have failed, are unlikely to be effective, or do not exist should determine whether questions about access to investigational therapy through the U.S. Food and Drug Administration's "expanded access" program are likely to arise in their clinical practice. If so, physicians should familiarize themselves with the program to be better able to engage in shared decision making with patients.

When a patient requests expanded access to an investigational therapy, physicians should:

(a) Assess the patient's individual clinical situation to determine whether an investigational therapy would be appropriate, including:

  (i) whether there is a satisfactory alternative therapy available to diagnose, monitor, or treat the patient's disease or condition;

  (ii) the nature of potential risks of the investigational therapy and whether those risks are not unreasonable in the context of the patient's disease or condition;

  (iii) whether the potential benefit to the patient justifies the risks of the investigational therapy;

  (iv) whether the patient meets inclusion criteria for an existing clinical trial of the investigational therapy.

(b) As part of the informed consent process, advise the patient (or parent/guardian if the patient is a minor) that the investigational therapy has not yet been demonstrated to be effective in treating the patient's condition and may pose as yet unknown risks. Physicians should explain the importance of clinical trials, encourage patients who meet inclusion criteria to participate in an existing trial rather than seek access to investigational therapy through the FDA expanded access program, and direct patients who wish to participate in research to appropriate resources.

(c) Decline to support an application for expanded access to an investigational therapy when:

  (i) the physician judges the treatment with the investigational therapy not to be in the patient's best interest, and explain why; or

(ii) the physician does not have appropriate resources and ability to safely supervise the patient's care under expanded access.

In such cases, physicians should refer the patient to another physician with whom to discuss possible application for expanded access.

(d) Discuss the implications of expanded access for the patient and family and help them form realistic expectations about what it will mean to be treated with the investigational therapy outside a clinical trial. Physicians should alert patients:

(i) to the possibility of financial or other responsibilities associated with receiving an investigational therapy through expanded access;

(ii) to the lack of infrastructure to systematically monitor and evaluate the effects of the investigational therapy outside a clinical trial;

(iii) that they need information about how to contact the manufacturer for guidance if they seek emergency care from a health care professional who is not affiliated with a clinical trial of the investigational therapy;

(iv) that the physician has a responsibility to collect and share clinical information about the patient's course of treatment with the investigational therapy, as well as to report any adverse events that may occur over the course of treatment;

(v) to the conditions under which the physician would recommend stopping treatment with the investigational therapy.

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