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**Research Ethics**

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1. An investigator enters into collaboration with a pharmaceutical company to conduct a phase 1 clinical trial in children with malignant brain tumors. The investigator’s son-in-law owns $100,000 of stock in the same pharmaceutical company as an individual. The investigator is considered to
2. Have a conflict of interest with conducting the study because his son-in-law owns the stock
3. Not have a conflict of interest with conducting the study because the stock is worth less than $250,000
4. Not have a conflict of interest because his son-in-law is not considered an immediate family member
5. Have a conflict of interest because his son-in-law may transfer the stock to his daughter
6. A tenured, full-time professor on university payroll is invited to be a consultant with a startup biotech company. This biotech company is independent of the university and has no relationship with the university. His consulting activity for the company takes up approximately 15% of his time and effort. The investigator is considered to have a conflict of commitment if
7. The university allows only up to 10% of time and effort for outside consulting.
8. Fifty percent of his consulting time is spent supervising his graduate students who are working on projects related to the product development for the biotech company as a part of their research thesis.
9. He is not receiving any payment for his consulting services.
10. He does not plan to resign from the university when the company goes public after a year.
11. A hematology-oncology fellow is conducting research on the cytotoxicity of a newly developed purine analog on leukemia cell lines. He assays five different drug concentrations, and measures cell kill in triplicate. He runs out of culture media for the leukemia cell lines during the experiment and borrows culture media from a fellow researcher, which he uses for the set of experiments where he was testing the highest concentration of the drug. When assessing cell viability, he concludes that the highest concentration of the drug is most effective because the majority of leukemia cells were dead when compared to the four lower concentrations. He publishes these results. However, several other groups cannot replicate his data. He then discovers that the culture media he borrowed for his experiment was serum free, and, thus, may have affected cell viability. This is an example of
12. Falsification of results
13. Fabrication of results
14. Plagiarism of results
15. Honest error
16. A 12-year-old child is diagnosed with high-risk acute lymphoblastic leukemia (ALL). The treating oncologist discusses the treatment of high-risk ALL with the patient’s parents and offers them participation on a Phase 3 clinical trial conducted by the Children’s Oncology Group. After considering the information presented, the parents give consent for their child to participate on the clinical trial, but request the treating physician to tell the patient that his parents have given permission for treatment but not discuss the clinical trial with the patient because the child would be traumatized with the information. The physician informs the parents that
17. This is acceptable because there is a real chance that their child could benefit from participating on the clinical trial.
18. This is acceptable because the child was asleep and needed to start treatment immediately.
19. This is acceptable because, based on the child’s poor grades in school, the child is unlikely to understand the information.
20. This is acceptable because the IRB allows assent to be waived in children less than 14 years of age.
21. A researcher is conducting a quality of life assessment clinical research study in a cohort of patients being treated for osteosarcoma. At least 30% of the patients are Spanish speaking. The researcher decides to exclude Spanish speaking patients. In which of the following scenarios is this acceptable?
22. The investigator does not speak Spanish.
23. The quality of life assessment questionnaire has not been validated in Spanish.
24. Less can be learned from studying Spanish speaking patients.
25. It is never acceptable to exclude Spanish speaking patients.
26. An investigator is writing a clinical trial protocol for a promising new alkylating agent in children that is known to cause hemorrhagic cystitis in 15% of adult patients treated at higher doses of the drug. Based on pharmacokinetic modeling, it is unlikely that that the adult maximum tolerated dose would be tolerable in children, thus decreasing the risk of hemorrhagic cystitis in children. The investigator therefore decides that it is not necessary for any specific monitoring for hemorrhagic cystitis or prevention measures. In doing so, the investigator is violating the research principal of
27. Respect
28. Beneficence
29. Justice
30. Protection of a vulnerable population
31. An investigator sets up a collaboration with a clinician in a different city to study a new marker of bacterial infection in patients who present with febrile neutropenia following treatment with chemotherapy. The researcher requests the clinician to provide him with leftover sample from a routine blood culture to test for this marker and requests the researcher to maintain a link to the specimen for later correlation of the biomarker and true infection. However, the researcher does not come in contact with any of the patients nor does the researcher receive any protected health information on the subjects. Based on this information
32. The institutional review board (IRB) can make the determination that the study is exempt from review.
33. The IRB cannot require that the clinician obtain written informed consent.
34. The IRB can waive informed consent because the researcher is receiving coded specimens with no protected health information and is using specimens that are left over and of no clinical use.
35. Only the researcher’s IRB of record needs to review the clinical trial because the researcher is investigating the new biomarker test.
36. A pharmaceutical company has developed a grape-flavored formulation of acetaminophen. The pharmaceutical company wants to find out whether the grape-flavored acetaminophen is more palatable than the existing strawberry-flavored acetaminophen. The two flavors are administered to all children with fever on the pediatric ward. The parents were given an anonymized survey at the time of discharge to complete their child’s preference of flavor. The pharmaceutical company collects this information to decide which flavor of acetaminophen to market. Based on this information
37. This study requires full IRB committee review because the children are being administered a drug.
38. Written informed consent is required because the children are subjects in a clinical trial.
39. The IRB can waive consent, but mandate that the patients be compensated for participating in this study.
40. The IRB may determine that this study is exempt review because acetaminophen is an approved drug, and the change in flavoring does not alter the safety of the drug and the survey is anonymized.
41. A group of institutions collaborate to conduct a Phase 2 clinical trial. An independent Data and Safety Monitoring Board (DSMB) is set up to monitor the conduct of the clinical trial. All of the following are responsibilities of the DSMB except
42. Review of interim and cumulative data on adverse events
43. Reviewing the roster of IRB members who approved the protocol.
44. Adherence to clinical trial protocol
45. Review of interim and cumulative data on efficacy according to predetermined statistical considerations.
46. A clinical trial offers $500 to a patient for participation in the optional pharmacokinetics component of the clinical trial that involves obtaining three blood samples drawn pre dose, at end of infusion, and 1 hour following infusion of the experimental agent. The IRB is likely to make the following determination
47. A payment of $500 will likely result in coercion of the patient to participate in the optional pharmacokinetic studies.
48. A payment of $500 is reasonable given that it is critically important to learn about the pharmacokinetics of the experimental agent.
49. A payment of $500 is a nice gesture to a patient for the hardship of suffering a relapse and enrolling on a clinical trial.
50. A payment of $500 is acceptable only if the patient’s annual family income is less than $30,000 per year.
51. Each of the following is considered a vulnerable population in clinical research except
52. Pregnant women
53. Native Americans
54. Prisoners
55. Children
56. A researcher requires a 1 mL blood for his research studies, which can be obtained by venipuncture at the time of a clinically indicated laboratory blood test. The IRB will determine that this procedure is
57. A minimal risk procedure
58. A slight increase over minimal risk procedure
59. A greater than minimal risk procedure
60. None of the above
61. The IRB is reviewing a clinical trial that randomizes an experimental regimen versus a standard of care regimen. The IRB should make the determination that the research can be approved under which of the following categories?
62. 45 CFR 46.404
63. 45 CFR 46.405
64. 45 CFR 46.406
65. 45 CFR 46.407
66. A leukemia investigator plans to obtain a bone marrow under general anesthesia at the end of consolidation therapy during the treatment of ALL following remission at the end of induction therapy to measure minimal residual disease (MRD) to see if this time point can predict early relapse, but the results are not shared with the treating oncologist, and no therapeutic interventions are decided on based on the results. The IRB rules that the procedure
67. Constitutes a minimal risk procedure because bone marrow assessments are considered routine for patients diagnosed with ALL
68. Constitutes a minor increase over minimal risk because it is a single additional procedure being performed during the course of treatment
69. Constitutes a greater than minimal risk procedure because it is being done under general anesthesia
70. Is justifiable because, if the bone marrow MRD status at the end of consolidation proves to be a predictor of early relapse, future patients may benefit from an early change in therapeutic intervention
71. The International Committee of Medical Journal Editors (ICGME) recommends authorship based on all of the following criteria except
72. Conception or design of work or acquisition, analysis, or interpretation of data of work
73. Providing funding to conduct the research
74. Drafting the work or revising it critically for intellectual content
75. Final approval of the version to be published
76. Agreement to be accountable for all aspects of the work

**Research Ethics: Answers**

Question 1

**Answer:** C

**Explanation:** A financial conflict of interest exists when two or more contradictory interests relate to an activity by an individual or an institution. The conflict lies in the situation, not in any behavior or lack of behavior of the individual. Conflicts of interest are situations in which financial or other personal considerations may compromise, or have the appearance of compromising, an investigator’s judgment in conducting or reporting research, or a conflict of interest in research exists when the individual has interests in the outcome of the research that may lead to a personal advantage and that might, in actuality or appearance, compromise the integrity of the research. Financial interest by an investigator’s spouse or children is considered a conflict and must be disclosed by U.S. Department of Health and Human Services guidelines. The National Institutes of Health (NIH) minimum threshold for disclosure is $5,000 in the previous 12 months when aggregated or when the investigator (including the investigator’s spouse or dependent children) have any equity interest in the entity*.*

Question 2

**Answer:** A

**Explanation:** Conflict of commitment is a situation in which an individual has substantial professional activities and business interests outside his or her regular employment. Such external interest may vary from consulting, lecturing, acting as an expert witness, public service, or service on a professional board or committee. Supervision of graduate students is a faculty teaching responsibility, and it is inappropriate to use student effort to financially benefit a non-university entity. Because the professor is on university payroll for full-time effort, effort beyond permissible allowance according to university regulations even if there is no financial benefit to the professor is a conflict of commitment. The same holds true if the faculty member is planning a departure as the individual is still employed by the university.

**Question 3**

**Answer:** D

**Explanation:** Research misconduct means fabrication, falsification, or plagiarism in proposing, performing, or reviewing research, or in reporting research results. Fabrication is making up data or results and recording or reporting them. Falsification is manipulating research materials, equipment, or processes, or changing or omitting data or results such that the research is not accurately represented in the research record. Plagiarism is the appropriation of another person's ideas, processes, results, or words without giving appropriate credit. Research misconduct does not include honest error or differences of opinion. In this case, the fellow did not manipulate the conditioning medium and, therefore, is considered to have committed an honest error.

**Question 4**

**Answer:** D

**Explanatio**n: Legally, children are not able to give true informed consent until they turn 18 years of age. So, before taking part in a clinical trial, they are asked for their assent. Assent means that they agree to take part. To take part in the assent process, children must be mature enough to understand the trial and what they are expected to do. Assent must be obtained from children unless the child is not capable of assenting, the child might benefit from the treatment or procedure being studied in the trial, or the treatment or procedure that may benefit the child is only available in clinical trials*.*

**Question 5**

**Answer:** B

**Explanation:** The Belmont Report outlines the research principles of Respect, Beneficence, and Justice. Respect for persons involves recognition of the personal dignity and autonomy of individuals as well as special protection of those persons with diminished autonomy. Beneficence entails an obligation to protect persons from harm by maximizing anticipated benefits and minimizing possible risks of harm. Justice requires that the benefits and burdens of research be distributed fairly. The case vignette described above is in reference to the research principle of Justice.

**Question 6**

**Answer:** B

**Explanation:** Please refer to answer explanation for question 5.

**Question 7**

**Answer:** C

**Explanation:** The U.S. Department of Health and Human Services regulations allow the IRB to waive the requirement for obtaining informed consent or parental permission or to approve a consent procedure that leaves out or alters some or all of the elements of informed consent otherwise required under [45 CFR 46.116(a) and (b)](http://www.hhs.gov/ohrp/regulations-and-policy/regulations/45-cfr-46/index.html#46.116). Waiving the requirement for obtaining informed consent or parental permission means that the IRB has determined that investigators need not obtain the subjects’ informed consent to participate in research. In the above scenario, because no protected health information is being transmitted and the study is minimal risk and dependent on leftover sample being used, IRB may waive obtaining informed consent. However, because patients can be potentially identified through a code, it is considered human subject research and the study cannot be exempt from IRB review. Lastly, both the clinician and investigator are participating in the research, and, therefore, both institution’s review boards will need to review the study and determine whether or not informed consent can be waived.

**Question 8**

**Answer:** D

**Explanation:** Research activities in which the only involvement of human subjects will be in one or more of the following categories are exempt from IRB review.

1. Research conducted in established or commonly accepted educational settings, involving normal educational practices
2. Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior
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
4. Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects
5. Research and demonstration projects that are conducted by or subject to the approval of department or agency heads, and which are designed to study, evaluate, or otherwise examine: (i) public benefit or service programs, (ii) procedures for obtaining benefits or services under those programs, (iii) possible changes in or alternatives to those programs or procedures, or (iv) possible changes in methods or levels of payment for benefits or services under those programs
6. Taste and food quality evaluation and consumer acceptance studies.

It is best that the IRB makes the determination that a clinical study is exempt review.

**Question 9**

**Answer:** B

**Explanation:** The DSMB is an independent group of experts that advises the study investigators. The primary responsibilities of the DSMB are to (1) periodically review and evaluate the accumulated study data for participant safety, study conduct and progress, and, when appropriate, efficacy; and (2) make recommendations concerning the continuation, modification, or termination of the trial. Items reviewed by the DSMB include: (i) interim/cumulative data for evidence of study-related adverse events; (ii) interim/cumulative data for evidence of efficacy according to pre-established statistical guidelines, if appropriate; (iii) data quality, completeness, and timeliness; (iv) performance of individual centers; (v) adequacy of compliance with goals for recruitment and retention, including those related to the participation of women and minorities; (vi) adherence to the protocol; (vii) factors that might affect the study outcome or compromise the confidentiality of the trial data (such as protocol violations, unmasking, etc.); and (viii) factors external to the study such as scientific or therapeutic developments that may impact participant safety or the ethics of the study. The DSMB should conclude each review with their recommendations as to whether the study should continue without change, be modified, or terminated.

**Question 10**

**Answer:** A

**Explanation:** The IRB should determine that the risks to subjects are reasonable in relation to anticipated benefits and that the consent document contains an adequate description of the study procedures as well as the risks and benefits. It is not uncommon for subjects to be paid for their participation in research, especially in the early phases of investigational drug, biologic, or device development. Payment to research subjects for participation in studies is not considered a benefit; it is a recruitment incentive. The amount and schedule of all payments should be presented to the IRB at the time of initial review. The IRB should review both the amount of payment and the proposed method and timing of disbursement to ensure that neither are coercive nor present undue influence. All information concerning payment, including the amount and schedule of payment(s), should be set forth in the informed consent document.

**Question 11**

**Answer:** B

**Explanation:** Certain groups including pregnant women, children, fetuses and neonates, decisionally impaired individuals, prisoners, and students are considered vulnerable as determined by the U.S. Department of Health and Human Services and have special rules regarding their participation in clinical research.

**Question 12**

**Answer:** A

**Explanation:** The regulatory definition of “minimal” risk is: The probability and magnitude of harm or discomfort anticipated in the research are not greater than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

**Question 13**

**Answer:** B

**Explanation:** The Code of Federal Regulations Subpart D includes additional protection of children involved as subjects in research. As such, research in children can be approved only under four categories:

* [46.404](http://www.hhs.gov/ohrp/regulations-and-policy/regulations/45-cfr-46/#46.404) Research not involving greater than minimal risk
* [46.405](http://www.hhs.gov/ohrp/regulations-and-policy/regulations/45-cfr-46/#46.405) Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual subjects
* [46.406](http://www.hhs.gov/ohrp/regulations-and-policy/regulations/45-cfr-46/#46.406) Research involving greater than minimal risk and no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subject's disorder or condition
* [46.407](http://www.hhs.gov/ohrp/regulations-and-policy/regulations/45-cfr-46/#46.407) Research not otherwise approvable, which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children.

The IRB can grant approval for research in the first three categories, while all those that fall into the 46.407 category are referred to the Office of Human Research Protections (OHRP) for final determination.

**Question 14**

**Answer:** C

**Explanation:** Please refer to explanation under Question 12.

**Question 15**

**Answer:** B

**Explanation:** Authorship confers credit and has important academic, social, and financial implications. Authorship also implies responsibility and accountability for published work. The ICGME recommendations are intended to ensure that contributors who have made substantive intellectual contributions to a paper are given credit as authors, but also that contributors credited as authors understand their role in taking responsibility and being accountable for what is published. These recommendations include: (i) substantial contributions to the conception or design of the work or the acquisition, analysis, or interpretation of data for the work; (ii) drafting the work or revising it critically for important intellectual content; (iii) final approval of the version to be published; and (iv) agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.