Teaching the Responsible Conduct of Research through a Case Study Approach

A Handbook for Instructors

Prepared for the Association of American Medical Colleges by

Stanley G. Korenman, M.D.
Associate Dean for Ethics and Medical Scientist Training
University of California, Los Angeles, School of Medicine

and

Allan C. Shipp
Senior Staff Associate
Association of American Medical Colleges

with the oversight and contributions of the

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CASE C2

Anne Baldwin is a postdoctoral fellow working in a highly specialized area of research on lentiviruses and prions. Her boss, Dr. Sam Richardson, recognizes Anne’s talents and believes that she is the most promising postdoctoral fellow in his lab.

Anne’s contributions have included aiding Dr. Richardson in identifying a rather obscure pathway by which the prion responsible for Creutzfeldt-Jacob disease, a degenerative brain disorder, emerges from years of latency to initiate active infection.

When Dr. Richardson is asked by a leading neurobiology journal to review an article on the pathology of Creutzfeldt-Jacob disease, he decides to involve Anne because of her skills and specialized experience. He makes a copy of the manuscript and asks Anne to write her own critical review of the piece, just as if she were the actual reviewer. This exercise, he reasons, would afford Anne a good opportunity for exposure to the process of peer review, while putting her in touch with the latest literature on her primary field of research.

As Dr. R's request ethically permissible?
CASE C2

Questions

1. Is Dr. Richardson's idea a good one? Why or why not? Are there other ways for him to involve Anne in reviewing the article?

2. Dr. Richardson's motives for having Anne participate in this manner seem well-intended. What might be some negative reasons for involving Anne in this way?

3. What concerns might Dr. Richardson's approach pose for the author of the article? What issues are posed for the journal in which the article may appear?

4. If Anne feels uncomfortable about Dr. Richardson's request, how might she respond?

5. Assume that rather than sharing the paper with Anne, Dr. Richardson distributed it to the laboratory's "journal club" for discussion. What kinds of problems does this scenario pose?
Use of Confidential or Proprietary Information

CASE D3

While quietly sipping a soda and looking over the landscape at his departmental retreat, Professor Aaron Chen inadvertently focuses in on the conversation at the next bench. Joe, a young faculty member, is talking to his graduate student, Yolanda.

Joe I know that reviewing papers for publication is part of our job, but this steady influx is exhausting me. The only saving grace is that I get to learn about some pretty exciting science.

Yolanda That's a pretty desirable burden compared with what I have to put up with as a teaching assistant. At least you get to learn something in the process. Come across anything particularly interesting?

Joe Well, since we don’t work in this immediate area, I guess it’s okay to talk about it. There’s a report of a new cellular transcription factor that plays a powerful role in expression in virus-infected cells. It’s been messing up everyone’s in-vitro transcription systems. It’s easy to purify because it binds to the DNA binding region of the estrogen receptor and can be affinity-purified from columns containing that region specifically. The paper is well-written and I am recommending publication with only minor corrections so it should be out soon.

Yolanda Fascinating! I can’t wait until I see that in print.

Prof. Chen has been having great difficulty carrying out in vitro transcription with DNA from virus infected cells and has been wondering where to turn next. The overheard remark is like a gift from heaven. He then unexpectedly runs into his graduate student Paul Louden.

Prof. Chen Paul, have you been thinking how to get our in vitro transcription process to work better? Maybe the viruses induce new cellular transcription factors that are not present in normal cells.

Paul That’s a great idea. We’ve been looking for technical problems for much too long. Why don’t we try to find out.

Prof. Chen Let me tell you about what I overheard. I think we could get this project done in time to submit it just about when the other group publishes their finding. It surely makes science more efficient for us to get on the right track, and our study will validate their result if we can confirm its validity in our system.
CASE D3

Questions

1. How would you assess the behavior of the following individuals in this case (where appropriate, explain what was troublesome or unethical about the behavior of the individual identified):
   a. Yolanda?
   b. Joe?
   c. Professor Chen?
   d. Paul?

2. If you were an author of the paper under discussion, with whom would you be upset?

3. How should Professor Chen have reacted to Joe’s conversation with Yolanda?

4. What is an appropriate way for Joe to respond when he learns that Professor Chen has overheard and acted on the information that Joe and Yolanda exchanged informally? If Yolanda were to learn of Professor Chen’s actions, how might she respond?
Conflicts of Interest

CASE G1

Cynthia Walsh, M.D., an associate professor of medicine, is a prominent academic cardiologist. Her personal financial investments include significant stock holdings in three publicly traded biotechnology firms. She is approached by one of these firms to be a lead investigator in a therapeutic trial of a novel agent for preventing tissue damage from myocardial infarction (MI). This will be a randomized double-blinded, placebo-controlled clinical trial (neither patient nor physician will know whether the drug under investigation or a placebo is being used in a given patient). Dr. Walsh is quite familiar with the preliminary animal and cell biology work in the area and believes that there is an excellent chance that this new drug will result in a significant improvement in survival and reduce damage to the heart muscle. She even thinks this novel agent may reduce the risk of heart failure and irregular beats.

Dr. Walsh’s group is one of the few cardiology groups fully prepared to carry out this investigation, which is why she was contacted, and a clinical fellow suited to manage the study is available. She cares for a large number of patients with MI and believes that she could enroll numerous patients efficiently. The drug will only be available to her patients if her group participates in the trial. The company is offering $5,000 for each patient enrolled and the money would really help both her salary and the division budget. As a lead investigator, she will become much better known and will likely experience an increase in referrals if the trial succeeds.

Should Dr. Walsh accept the offer?

133
CASE G1

Questions

1. Is Dr. Walsh’s participation in this study appropriate? Justify your position.

2. Does Dr. Walsh have a conflict of interest? If so, what is the nature of the conflict? How could it be mitigated? Would the nature of the conflict of interest be different had she not already owned stock, but instead had been offered stock as a form of compensation for conducting the study?

3. If Dr. Walsh already believes the drug is an improvement based on the literature emanating from animal experiments, can she honestly assign patients randomly to treatment or placebo? What if she believes the drug is deleterious because of its adverse effects on the kidney late in the course of treatment?

4. What should the role of the university be in this case?

5. During study of the first few patients, it becomes apparent to Dr. Walsh that she can tell who is on the active drug because the patients get a facial flush. Might that further influence her ability to remain objective? What considerations apply in answering that question?
Dr. Simon Goldberg is a dermatologist and a tenured faculty member at a research-intensive medical school. When not attending to his clinical and educational responsibilities, he conducts research into the mechanisms by which skin tissue heals and repairs itself. Recently, Dr. Goldberg received a contract from Vanité, a large cosmetics company whose products are sold worldwide. The U.S. Food and Drug Administration (FDA) has questioned claims the company makes concerning one of its leading products, Crème de Jouvence, which Vanité asserts can repair damage to the skin caused by aging and exposure to the sun. Vanité stands by this claim, although it is uncertain which of the many ingredients in the product actually produces the rejuvenating effect. Therefore, it would like to hire Dr. Goldberg to investigate this matter. Dr. Goldberg’s findings will be used in Vanité’s response to the FDA. As it is under some pressure to respond in a timely manner, Vanité would like to have the results of this study as quickly as possible. Whatever Dr. Goldberg finds, he will receive $250,000 to cover the expenses and salary associated with the project. However, if he can identify an ingredient that proves active within nine months, a company representative has assured Dr. Goldberg that Vanité will hire him again to study the safety of a new cosmetic ingredient the firm has developed.
CASE G2

Questions

1. What kinds of incentives are created by the promise of future employment?

2. Assume that in order to make the deadline, Dr. Goldberg enlisted two predoctoral students to assist with the project. To recruit them for this effort, he told the students that they would gain valuable exposure and experience from their participation. What problems might be posed by this situation?

3. Vanité is clearly under pressure to support its claims and Dr. Goldberg is conscious of Vanité’s desire to acquire data to help the company make its case. If you were Dr. Goldberg, what would you do to retain your objectivity in this study?

4. The FDA will scrutinize Dr. Goldberg’s research findings. What impact does this independent review by a government agency have on your concerns about this contract?

5. Assume that Dr. Goldberg has been offered equity holdings in the company as part of his compensation package. In what ways might that arrangement influence Dr. Goldberg’s objectivity? By what mechanisms might his objectivity be preserved in spite of that form of compensation?

6. Assume that Dr. Goldberg’s university has a rule that precludes faculty from accepting an equity interest in a company that supports the faculty member’s research. Dr. Goldberg wishes to accept equity as a form of compensation and opposes the university’s policy. What do you think about this policy? Support either Dr. Goldberg’s position or that of the university.

7. Society as a whole has many concerns about the relation between scientists in academic research institutions and industry. What are some of the concerns as you understand them and what principles should be applied to regulate that relationship?
It is several years into the future. Professor Ken Tanaka’s studies generalizing the ligand specific polymerase chain reaction, in combination with the wide variety of gene segments now available, have allowed him to develop a ligand-specific chain reaction (LCR) assay that can detect in utero genetic predisposition to almost 200 genetic and congenital conditions. These include:

- Tay-Sachs disease
- Phenylketonuria
- Huntington’s disease
- Cystic fibrosis
- LDL receptor defects
- Congenital adrenal hyperplasia
- Essential hypertension
- Early onset Alzheimer’s disease
- Diabetes mellitus (types I and II)
- Autoimmune diseases
- Asthma
- Sickle cell disease

Prof. Tanaka has been approached by a major clinical laboratory company to license the method. They promise to create a prenatal diagnostic package that for $1,000 will provide information about all of these conditions during the 14th week of gestation from a placental biopsy. The test would provide similar information about newborns using a blood sample.

The company wishes to take advantage of developments in genetics to extend the profile by at least 200 conditions each year. Prof. Tanaka can anticipate testing for 1,000 genes within four years or so.

The financial return to him and the university promises to be enormous, but he has misgivings.
CASE J3

Questions

1. What might be some of Dr. Tanaka’s misgivings?

2. Would your opinion of Dr. Tanaka’s assay be different if the test were restricted to newborns?

3. Does your level of concern with regard to the diagnostic package depend in any way on the conditions for which it would test? If so, why do you feel differently about testing for some genetic or congenital conditions as compared to others? The conditions listed in the case are all diseases and disabilities. What concerns, if any, would you have about using these tests to ascertain gender, sexual orientation, or constitutional short stature?

4. Assuming the technology is available to do so, do you believe that there are any conditions for which one should not test? On what basis?

5. What would be your criteria for determining whether it is ethically or otherwise acceptable to test for a given condition?

Further Discussion:

1. As the Human Genome Project progresses, much concern has been generated with regard to the potential uses of the genetic information that will inevitably become available. The potential for abuse of genetic information has led some to question whether the Human Genome Project should continue. Discuss whether the potential applications of the knowledge gained through any course of research should serve as grounds for arresting research efforts.

2. Someone else will shortly develop technologies with a similar capacity to Dr. Tanaka’s. How does that affect your thinking?