THEME 1: SCIENTIFIC MISCONDUCT

CASE 1

Adapted from: **Research Ethics: Cases and Materials**, **by Robin Levin Penslar**

Scientific Misconduct : by **Karen Muskavitch, Boston College**

Chapter 4 *What Is It and How Is It Investigated?*

This hypothetical case is loosely based on several scientific misconduct cases that have occurred in the last few years. It does not involve a whistle-blower and therefore does not involve such issues as whistleblower victimization, officials failing to heed warnings and take action, or the need to ensure accusers' confidentiality during an investigation while providing due process to the accused. While these are important issues which can be explored if time allows, the intended focus here is on three equally important topics:

1. Proper laboratory practices, particularly in the management of data and its manipulation as manuscripts are prepared.

2. The definition and identification of scientific misconduct.

3. The way in which investigations of alleged scientific misconduct are and should be carried out.

Part A (One Day in August)

David Dunbar, one of the postdocs in Professor Steve Grey's lab at Big Tech, has just finished presenting the results of his latest set of experiments to the lab group at the weekly lab meeting. Grey's lab is a large group, with 22 technicians, research associates, graduate students, and postdocs all working on the identification and mechanism of action of genes associated with cancer. Dunbar presented the results of a series of experiments investigating the expression of the *tnc* cancer gene in normal cells and a variety of cancer cell lines. (The *tnc* gene is associated with toenail cuticle cancer, a rare cancer usually seen only in certain at-risk families.) It was a nice presentation. For instance, his table of RNA levels was beautiful, as well it should be. It was the last figure in a manuscript he and Grey just submitted to the Prestigious Cancer Journal, Dunbar's fourth paper on which he was first author since joining the lab two and a half years ago.

Shortly after the meeting, Erik Larson, a graduate student, comes into Professor Grey's office, shutting the door behind him. "David couldn't possibly have done all the analyses he reported in group meeting," asserts Larson angrily. "Unless he's got a lab at home. In fact, I'll bet some of the cell lines he showed numbers for in that last table haven't even grown up enough yet for RNA isolation." "Have we ever had reason to doubt David's work?" asks Grey. "No," Grey continues, not waiting for Larson's response. "We have always been able to follow up on his results, to the benefit of many in the lab. Yes, I know he gets a lot done during his time in lab,

but he's just more experienced and better organized than most others. Now, how is that work of yours going on the search for tnc-related genes in yeast?". After a short discussion of his recent experimental results, Larson leaves Grey's office. Grey sits at his desk, reflecting on their conversation. "I guess Dunbar's success just makes others uncomfortable," concludes Grey, wishing that personnel management had been part of his training.

Questions for Discussion

1. Was Larson right to bring his concerns to Grey? Could Larson have presented his concerns in a better, more persuasive way? Should Larson do anything further now that he has spoken to Grey?

2. Was Grey's response to Larson appropriate? Is there some way in which you think it could be improved?

Part B (One Month Later)

Jeff Adams, a new postdoc who has just arrived in Grey's lab, pulls Larson aside. Adams is supposed to pick up the work on human tnc, since Dunbar will be leaving soon. "Hey, what's with these papers you guys have published?" Adams asks, waving a paper of which Dunbar, Larson, and Grey were authors. "What do you mean?" Larson responds. "Well, look at this autorad in figure 1. All the lanes are the same!" fumes Adams. "Sure," replies Larson, "that's the point of the paper. We see the same, odd rearrangement to give a new 7.2 kb band in all the cell lines from toenail cuticle tumors." "No, that's not what I mean," says Adams, shaking his head. "Look at the background dots on the film. The same dots are in each lane. These aren't the results from different tumor lines; these are copies of the same photograph!" "Oh, my heavens!" exclaims Larson. "I never noticed that before. I was a new student in the lab when this work was done and all I did was help on the cell growth and DNA isolations. I have no idea how Dunbar made this figure. We'd better talk to Steve right away."

After talking with Adams and Larson and seeing the published figure in a whole new way, Grey calls in Dunbar and angrily accuses him of fabricating data. Dunbar appears genuinely shocked. "I didn't make up any data!" he asserts. "I did all those analyses and got those results; I can show you the autorads. I was just trying to make the nicest-looking figure for publication." "But these aren't the results for the cell lines indicated in the figure. It's all copies of one of them. You can't do that," replies Grey. "Why not? It's the same thing as cutting up the autorad to make figure 4. I didn't try to deceive anyone," says Dunbar. "And besides, no one said anything. Not people in the lab, not you, not the reviewers. I thought that was how it was done."

Questions for Discussion

1. At the end of the case are drawings of the two figures from the published paper (figures 1 and 4), as well as the two original autoradiograms from which they were derived (figures 2 and 3). Did Dunbar fabricate data in his production of figure 4? In the production of figure 1? Explain your criteria for determining fabrlcation.

2. Does it matter that the primary data show that the results are the same as shown in figure 1? Does it matter that the avowed intent was to produce a prettier picture, not to deceive?

3. Should Larson have been a coauthor on the paper if all he contributed were some routine

laboratory manipulations?

4. What are the responsibilities of coauthors for the authenticity of the contents of a paper? What are the responsibilities of reviewers in this area?

5. How could Grey change the practices in his laboratory to minimize the possible recurrence of a problem of this sort?

Part C

Although somewhat relieved that the autorads Dunbar produced verified that his creative graphic artistry did not alter the basic results or conclusions of the published paper, Grey is still shaken and worried. He decides to check all of the work Dunbar did while in the lab. Grey asks three senior postdocs in the lab, Xavier, Yates, and Zimm, to begin a review of Dunbar's notebooks and published work. Grey then heads for the department chair's office to inform him of what has been discovered and what is being done.

Questions for Discussion

1. Should Grey have contacted the departmental chair at this point?

2. Are there any other interested parties who should be informed?

Part D

Dunbar returns to the lab after lunch to discover Xavier, Yates, and Zimm looking through his notebooks. Dunbar is furious, asserting that notebooks are, like diaries, private. "I thought I made it clear to the lab last year, when that new student was pawing through my notebooks, that no one was to touch them without my permission," says Dunbar.

Yates can't believe what he's hearing. "It was Steve who asked us to check over your work," Yates says, "and I think you know why. Besides, where do you get these ideas about notebooks? When I was a grad student my Ph.D. advisor routinely checked each student's notebook every evening, and anyone in the lab was free to look up any information needed for their work."

"Actually, it's a good thing you're back. We have a couple questions," interjects Zimm. "Where are the data for the first paper you published from this lab? We can only find this box of autorads."

"I threw those notebooks out a few months ago. I figured the work was all published long ago, and I needed more space on my bookshelves," replies Dunbar.

"\Vell, then, what about the instrument printouts for the analyses you presented in the second paper? We can only find tables recording mean values. There doesn't seem to be any record of the actual, individual determinations," says Xavier, jumping into the discussion.

"I never keep instrument printouts," replies Dunbar, getting angrier by the second. "Who does? I don't need all that useless paper cluttering up my desk. I just analyze the data and ditch that

stuff. I've got better things to do than play filing clerk."

Questions for Discussion

1. To whom do laboratory notebooks belong? The individual? The principal investigator (PI)? The department? The laboratory? The university? The funding agency? The NIH?

2. Who should have access to laboratory notebooks and other experimental data? Are there only certain circumstances under which some people should have access?

3. What types of data should be retained, in what form, and for how long? Whose responsibility is it to see that data are appropriately retained?

4. Where should the data be retained? For instance, do the notebooks go with a finishing student or should they stay in the lab?

Part E

Larson, rather shaken by the revelations of the day, wonders about the effect that this business will have on his career. He was so pleased to have his name on a paper published in his first year in the lab; now he's not so sure it will be to his advantage at all. In the cell culture facility, Larson, remembering Dunbar's lab meeting last month, decides to take a look at the culture logs and compare them with the lines listed in Dunbar's RNA level table in the submitted manuscript. Unfortunately, his unease was justified. Two of the lines listed in the table were not even in the lab at the time of the meeting. They arrived since then from the stock center and are being grown, but Dunbar couldn't have obtained data from them when he said he did. Larson makes a copy of the log and goes to look for Grey.

When Grey and Larson confront Dunbar with the cell culture log the next day, Dunbar admits that the numbers reported in the table were not derived from RNA analyses but were his best estimates of what the results would be. "Look," says Dunbar, "I knew what the results would be. You know how long it takes to go through the review process for the Prestigious Cancer Journal. It's been more than a month, and we haven't heard a thing. If I had waited for the cells to come in and grow up and for the review, it would have been a year, and I could have gotten scooped! Don't worry, I didn't do anything wrong. When the paper was accepted pending a few requested revisions, I planned to just put the real data in the table and everything would be fine."

"Sure," says Larson. "How can I believe that you really would put in the real data?

"Easily," replies Dunbar, "because that's just what I've done before."

"What! When else have you submitted 'estimated data' for review?" asks an astonished Grey.

"Lots of times. Like in that first paper with the figure you're so upset about. What's the big deal? I've never tried to deceive anyone. I've never had to change the conclusions of a paper."

Grey searches for and finally finds a disk with the file of the two-year-old manuscript (in the form in which it was submitted), calls it up on his computer, and compares it with the reprint he keeps in his top desk drawer. Sure enough, the numbers listed in the table show the same basic trend

in the two versions, but are not the same.

Questions for Discussion

1. Does Dunbar's method of preparing his manuscripts for publication constitute fabrication or falsification? Is it, rather, a questionable research practice? Or is it simply a novel way to speed the progress of science?

2. Is it important to consider that the conclusions drawn in the submitted and final versions are the same?

3. Is it important to consider that, as Dunbar asserts, he did not intend to deceive anyone?

4. Is it important to consider that, in the end, only the real data were actually published?

5. What are the consequences to science of this approach to publishing?

6. Suppose that, in his fury, Larson threatens to call the editor of the Prestigious Cancer Journal and tell all. Should he do this? Is it warranted and proper, is it premature, or is it unwarranted and inappropriate?

Part F

While all this was going on in the Grey lab, the departmental chairman, Jack Washington, was also busy. After Grey informed him of the problematic figure, Washington consulted with the dean for research at Big Tech to see what was expected of him. He was told that he was to see that an initial inquiry was undertaken to determine whether an investigation was in order. It was up to Washington to appoint those who would conduct the inquiry. Above all, the dean cautioned, keep this quiet. "Well, if all we have to do is gather information while keeping a lid on this, the people Grey has got looking into it will make a perfect inquiry committee," he decides. "No one else need be involved." So Washington calls Grey to request that Grey send him a written report when Xavier, Yates, and Zimm finish.

Within three weeks, the three postdocs give Grey a written summary of their findings which mentions the figure produced by creative graphic artistry and the "estimated data" submitted for review, as well as the missing laboratory notebooks and primary data. Grey reads it over, edits it a bit, and sends it to Washington. Washington then forwards it to the dean for research as the report of the inquiry committee he was told to appoint.

Questions for Discussion

1. Are other members of the same lab the best people to review Dunbar's work? If not, who would be a better choice and why?

2. Should the head of the laboratory, who is also a coauthor, be involved in the initial inquiry in the manner described here? What arguments for and against his involvement can you make?

3. Has Washington fulfilled his obligations to the institution and the accused?

Part G

After reviewing the inquiry report, the dean for research and other administrators at Big Tech decide that a full misconduct investigation of Dunbar is required. They further conclude that no investigation need be carried out for Grey or the other coauthors, as the suspect conduct seems to be Dunbar's alone. They so inform Dunbar, Grey, Washington, and the National Institutes of Health (NIH) which funded this research.

Grey contemplates what he should do. Concluding that the best way is full disclosure and a clean break with Dunbar, he dismisses Dunbar from the laboratory and terminates his salary, which had been drawn from an NIH grant awarded to Grey. Then, after consulting with the other coauthors but not with Dunbar, Grey writes to the journals retracting all the published papers on which Dunbar was an author and withdrawing the manuscript still in review.

Questions for Discussion

1. Do you also conclude that an investigation of Dunbar is warranted? If so, what would be the components of scientific misconduct of which you would accuse Dunbar?

2. Do you conclude as well that only Dunbar should be subject to a misconduct investigation?

3. Are Grey's actions proper and warranted? Which, if any, are inappropriate and why?

Part H

All of this couldn't have happened at a worse time for Dunbar. After a series of successful interviews, he was looking forward to starting his own lab at another university. With the research he had done in Grey's lab and previous publications from his Ph.D. research, Dunbar figured he had a pretty good shot at a good job. Now getting a good job looked impossible because, in addition to everything that had already happened, Grey sent letters to each of the universities to which Dunbar applied telling them of the accusations against Dunbar and the planned investigation and retracting what had been very strong letters of recommendation. In response, the one university that had already offered Dunbar a position withdrew its offer.

Questions for Discussion

1. At the time the concerns about Dunbar's work were raised, Grey had already sent letters of recommendation in support of Dunbar's job applications. Was he under any obligation to inform the institutions to which Dunbar had applied of changes in his evaluation of Dunbar since writing his letters?

2. Suppose Grey has not yet written his recommendation letters when these matters come to light. Is he under any obligation to inform potential employers of the pending investigations?

Part I

The dean for research appointed a five-member committee to conduct the investigation. All five members were from the Biological Sciences Division of Big Tech. They reviewed the evidence and interviewed people at Big Tech and other universities.

When Dunbar was interviewed, he did not deny any of the actions of which he was accused, but he did deny that he was guilty of scientific misconduct. He asserted that it was never his intent to deceive and that all of the data presented in his papers were derived from actual primary data. He denied ever fabricating anything.

"I thought that was how you prepared a paper for publication," Dunbar said. "No one told me any differently. In fact, the first manuscript I ever prepared was when I came to Grey's laboratory. When I was a graduate student at Enormous State University, my advisor wrote all the papers that came out of the lab. Yes, some of my original data are gone. I didn't know that I was expected to keep them even after they were published, or that people thought instrument printouts were important. So I'm a poor document clerk; that's no crime!"

Questions for Discussion

1. Was the composition of the investigating committee appropriate?

2. Should naivete be an adequate defense in a situation like this?

3. How can the scientific community ensure that others in the future will not also be able to say, "But I didn't know."

Part J

The Big Tech investigating committee concluded that Dunbar was guilty of scientific misconduct, having found the multicopied lanes on the autoradiogram and the submission of 'estimated data" for review to be examples of fabrication. In addition, they concluded that Dunbar had engaged in many questionable research practices, such as prematurely destroying data, failing to record or keep primary data, and denying other scientists access to his data.

The findings of the investigating committee then went to Big Tech's administration for action. As required, a report was sent to NIH, but no further action was taken to punish Dunbar because he was no longer associated with Big Tech and was no longer engaged in scientific research. When last contacted, Dunbar had enrolled in an MBA program and was trying to put his life together again.

Questions for Discussion

1. Is this an appropriate conclusion for this tale?

2. What, if anything, could and should Big Tech or NIH do to punish Dunbar?

FIGURE 1

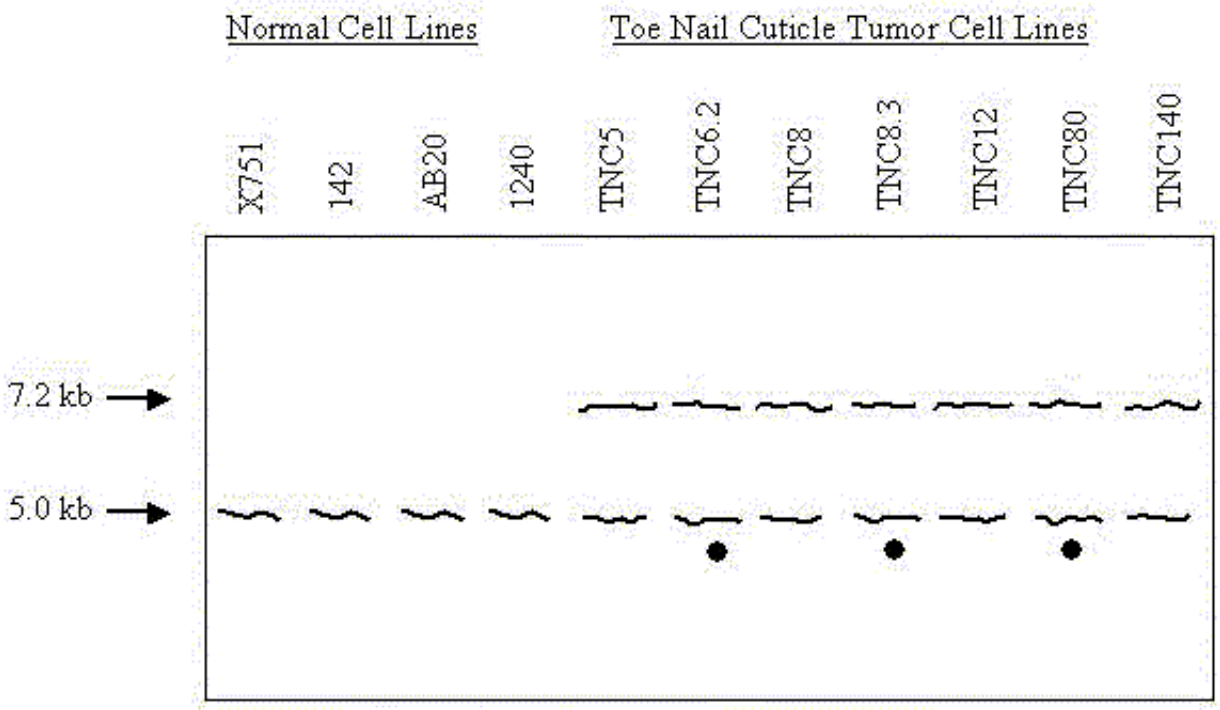

Figure 1.

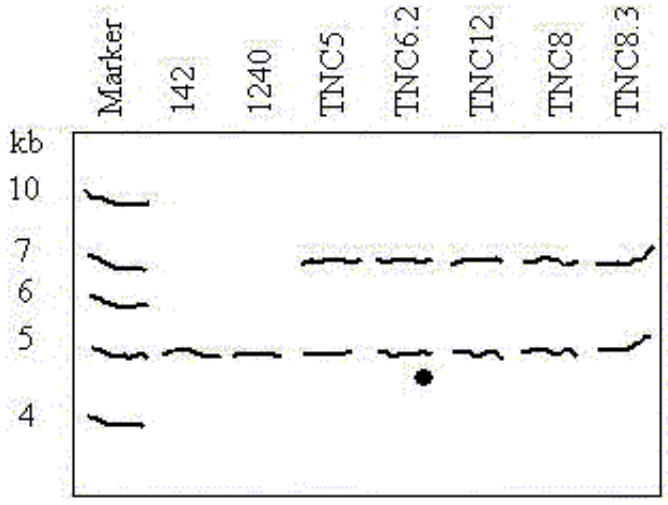

Figure 2.

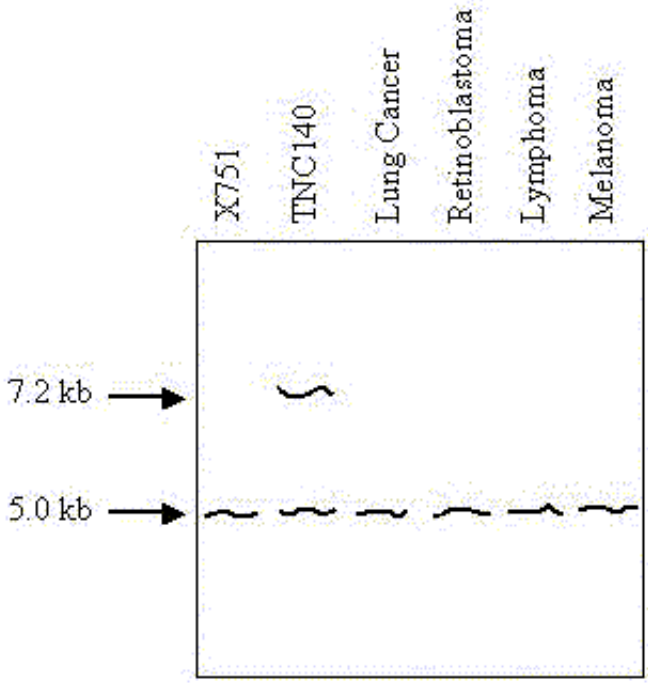

Figure 4.

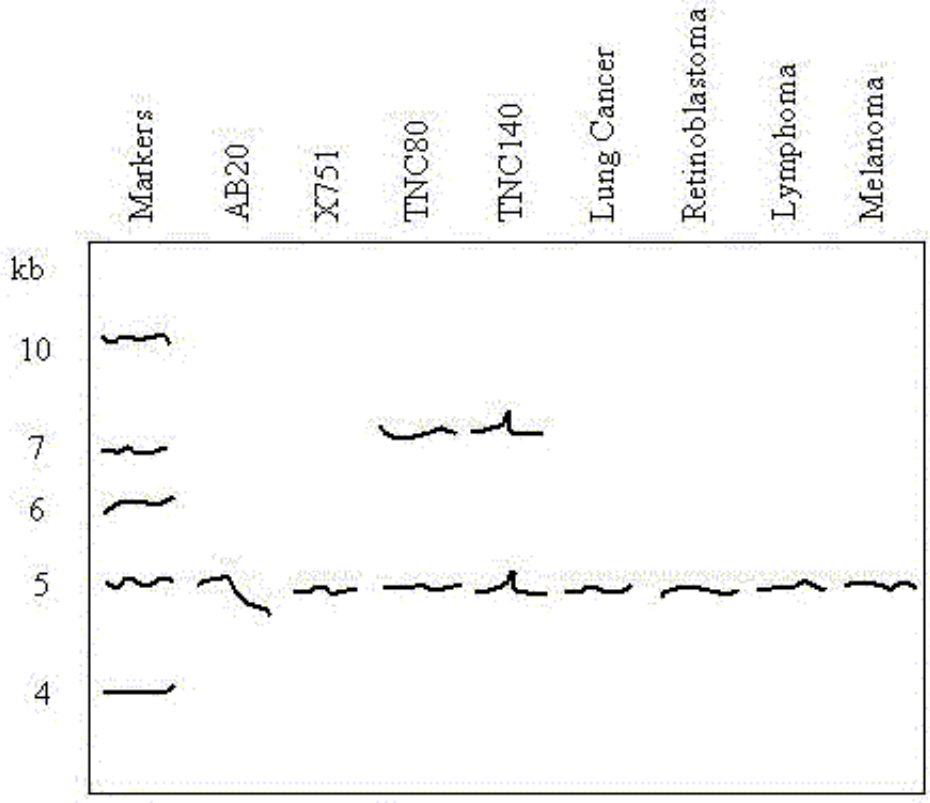

Figure 3.

THEME 1: SCIENTIFIC MISCONDUCT

CASE 2

From: ***Teaching the Responsible Conduct of Research Through a Case Study Approach: A Handbook for Instructors:*** With permission from the Association of American Medical Colleges

Dealing with Suspicions of Misconduct

CASE FI

Eric Woodworth is an oncology nurse working in a clinical research center (CRC) at a large academic medical center. Dr. Philip Thomas is an oncologist and clinician researcher who conducted a trial in the CRC of a drug being evaluated for its safety and efficacy in alleviating the nausea and discomfort associated with cancer chemotherapy. Eric assisted on Dr. Thomas's project in several ways. He attended to the patients' routine clinical needs and administered their cancer chemotherapy by I.V. He also gave the patients participating in Dr. Thomas' protocol oral doses of what may have been either the experimental drug or a placebo. The vials were numerically coded, so Eric did not know which he was providing. Finally, he interviewed patients concerning their symptoms, following a standardized questionnaire prepared by Dr. Thomas.

At times, Eric tried to guess, based on their responses, which patients were getting the placebo, and which were getting the real drug. In fact, he did not observe much difference in any of his patients and was convinced that the experimental drug was ineffective. He conveyed his opinion to Dr. Thomas, who merely shrugged and said, "We'll see."

After Eric's role in this protocol concluded, he was quickly engaged in other responsibilities. Meanwhile, Dr. Thomas compiled and analyzed the data that Eric collected and wrote up the results. Months passed, and the research ultimately was published in a well-known oncology journal. Eric was curious to read the results of this project, particularly since he was to be acknowledged for his contributions to the effort. Upon locating a copy of the journal, Eric read with astonishment Dr. Thomas's conclusion that the experimental compound was highly effective in alleviating the physical distress precipitated by chemotherapy. Eric read the article closely and decided that Dr. Thomas's recounting of the survey results was inaccurate, describing alleviations of discomfort that Eric never observed or recorded.

Questions for Discussion

1. If you were Eric, what would you do at this point to address these concerns?

2. Does Eric have a responsibility to take action toward correcting what he believes is an erroneous report?

Eric wondered what he should do in response. He hesitated to tell his supervisor, the head CRC nurse, because they did not have a very good relationship. Although Eric thought of himself as assertive and conscientious -- never hesitating to point out ideas for improving the operations within the CRC -- he understood that his boss viewed him more as a thorn in her side. He reported his concerns to her, nonetheless, figuring that, at worst, she would discount his report as another in a long list of complaints. As he predicted, his supervisor advised Eric that it would be in his best interest to focus on his current responsibilities and to stop looking for problems. That earlier project was so subjective, she added, that differing opinions on the results were not surprising in any case. Eric indeed recognized a certain subjective quality to the study, having wondered at times if he was recording patient reports consistently.

Questions for Discussion

3. Did Eric's supervisor respond appropriately to Eric's concern? How might you have responded were you in her position?

4. Having received such a response, what might Eric do next?

One day, when crossing the medical center complex, Eric ran into Dr. Thomas and expressed his surprise at the paper's findings. Dr. Thomas stated that once the survey results were decoded, a significant difference between patients receiving the placebo and the experimental drug became evident. Eric then stated that he would be fascinated to learn which patients were getting the drug and which weren't; he asked if he could take a look at the completed surveys now that they were unblinded. Acting hurried, Dr. Thomas stated that they had been sent to storage and that it would be too much trouble to retrieve them. He then dashed off. This behavior seemed suspicious to Eric and made him inclined to believe that some deliberate misrepresentation had taken place.

Questions for Discussion

5. Eric suspects that Dr. Thomas misrepresented the findings of the survey, but he cannot empirically support his suspicions without access to the surveys. Does he have a right to those materials since he is acknowledged in the paper?

6. Given Eric's lack of access to the surveys, how should he follow up on his suspicions?

7. Does Eric have an appropriate basis for lodging an allegation of scientific

misconduct? Is there a distinction to be made between an "allegation" and an "expression of concern"?

Eric tried on several more occasions to get the survey data from Dr. Thomas, without success. Knowing his supervisor was unsympathetic to his concerns, and upon the advice of a trusted

colleague, he decided to approach the administrator of the medical center's institutional review board (IRB). The IRB reviews the ethical and legal ramifications of proposed clinical research and its administrator would certainly be interested in his suspicions, he reasoned.

Questions for Discussion

8. Does the IRB or its administrator have authority to deal with instances of scientific misconduct?

9. Whom would you approach at your institution if you suspected research misconduct?

Upon meeting with the IRB administrator, Eric explained his belief that Dr. Thomas had misrepresented the findings of his research. In response, the IRB administrator informed Eric that complaints of that nature should be taken to Dr. Holly Baird, the associate vice president for research and the institutional Research Integrity Officer. The IRB administrator counseled Eric that he should not take his concerns any further, though, unless he were fairly certain of them. His allegations seemed to be based on sketchy recollections of data collected long ago, she said, adding that, in her opinion, he did not have sufficient basis for a complaint.

Questions for Discussion

10. How should one decide whether a suspicion of wrongdoing is sufficiently significant to warrant lodging a formal complaint?

11. What are some considerations Eric might take into account in weighing whether to lodge a formal complaint?

12. In your opinion, does Eric have sufficient cause to register a complaint with the Research Integrity Officer?

After the conversation, Eric pondered different ways to handle this situation. One approach would be to lodge an anonymous complaint with Dr. Baird and simply let events run their course. Alternatively, he could present his concerns in person, but rather than focus on the inaccuracy of Dr. Thomas's work, he would simply assert a right to access the surveys. Both approaches seemed loaded with pitfalls.

Questions for Discussion

13. Should institutions encourage or discourage the practice of lodging anonymous complaints when individuals suspect misconduct? What problems might anonymous complaints pose for the institution? What issues of fairness might anonymous complaints pose for the accused? What advantages and disadvantages are posed by this approach for Eric?

14. If you were Dr. Baird, the institution's Research Integrity Officer, how would you handle an anonymous complaint?

15. Why might Eric's second idea, to focus on his desire to access the surveys, prove risky?

16. Would it be better for Eric or for someone else to examine the surveys? Why?

In the end, Eric approached Dr. Baird with the observation that Dr. Thomas's findings seemed inconsistent with Eric's knowledge of the surveys. He framed his concern as much as possible as an observation of fact, without suggesting that any deliberate misrepresentation had taken place. Eric was also quick to note that he repeatedly tried to access the original surveys without success.

Dr. Baird listened to Eric's report and told him that because he had questioned the integrity of Dr. Thomas' research, the institution would be compelled to explore the legitimacy of Eric's statements. This initial phase is termed an "inquiry" she said and would involve an initial review to determine whether a formal investigation would need to take place. Although the complaint might be resolved after reviewing the original survey instruments, it is possible, she explained, that an investigation might ensue, at which point Eric might need to become involved. Eric suddenly felt very queasy. Reflecting upon the prospect of having a face-to-face confrontation with Dr. Thomas, Eric wished that he had never raised the issue at all. The drug in question wasn't even that important, he thought. It's not as though patients would be harmed by it, he considered, wondering why should he take the risk of becoming further involved.

Questions for Discussion

17. Even if an investigation takes place, is it necessary for Eric to become involved in the process? Under what circumstances might his involvement be essential to permitting those conducting the investigation to arrive at a determination of what happened? Under what circumstances might his involvement not be required?

18. If Eric does become involved in the process, is it necessary for him to confront Dr. Thomas directly, as he envisions?

19. Should the clinical importance of the research weigh in the decision to pursue the allegation?

20. Eric might have wrongly accused Dr. Thomas. What should the consequences of that error be, if any?

21. If misconduct is found, what steps should the institution take?

22. If misconduct is ruled out, what steps should the institution take?

23. If Dr. Thomas is exonerated, but Eric feels certain that he misrepresented the data, what recourse does he have?