

Ethical Dilemmas in Research Integrity

Janet Brigham, PhD

Arthur B. Chausmer, MD, PhD

Kendall S. Fraiser, DVM, PhD, ACVP

Claire E. Gutkin, PhD, MPH, MS

Gailen D. Marshall, MD, PhD

Shawn Spilman

Harry W. Tyrer, PhD

Copyright 2004

This publication was funded by the US Dept of Health and
Human Services, Office of Research Integrity.

ISBN 0-9628976-5-0

Contents

Data Acquisition, Management, Sharing and Ownership	
Independent Confirmation of a Colleague's Results.....	6
Sharing Data Prior to Publication	7
Commercially Valuable Research Results.....	8
Results Based on Proprietary Data	9
Incidental Results and Transient Data	10
Confidential Information that Might Affect Others.....	11
Ownership of and Responsibility for	
Research Materials.....	12
Data Integrity	13
Ownership of Data and Right of Use.....	14
Mentor / Trainee Responsibilities	
Staff Attendance and Working Hours.....	16
Advisor's Ownership of Mentored Work.....	17
Rights to Mentored Research Concepts and Results	18
Inside Knowledge and Equality of Opportunity	19
Recruiting Outside Resources.....	20
Romantic Relationships	21
Publication Practices and Responsible Authorship	
Use of Copyrighted Illustrations from Prior Publications .	24
Attribution of Mentored Research	25
Simultaneous Publication in Different Venues.....	26
Peer Review and Privileged Information	
Confidentiality of Material Being Reviewed.....	28
Protecting Information Provided Anonymously.....	29
Use of Anonymous Survey Data.....	30
Collaborations	
Collaborators Who Become Competitors	32
Spouses as Collaborators	34
Collaborating on the Review Process	36

Human Subject Research

Minority Representation that Confounds Data Analysis ...	38
Informed Consent that Confounds Data Analysis	40
Unexpected Changes in Sample Demographics	42
Unexpected Abnormal Test Results.....	44
Ending a Study Early	45
Informed Consent for Saving Research Data.....	47
Appropriate Use of Test Data	48
Scope and Venue Issues for Informed Consent	49
Selecting a Control Group	50
Selecting a Clinical Trial Site	51

Animal Subject Research

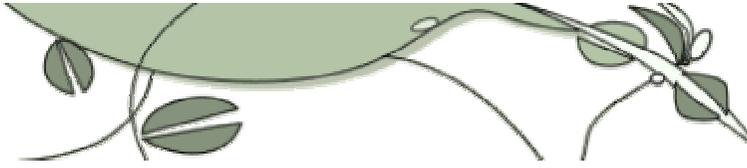
Choice of Animal Subject.....	54
Animals Used to Monitor Other Animals.....	55
Source of Animal Tissue Used in Research.....	56
Changing a Research Protocol that Uses Animals.....	57
Use of Animals after Research Ends	58
Unexpected Death of Animal Subjects.....	59
Research Use of Tissue from Livestock	60

Research Misconduct

Appropriate Use of Commercial Software	62
Research Use of Commercial Publications.....	63
Research Impact of Changes to Guidelines	65
Padding a Budget	66

Financial Conflicts of Interest

Divulging Information about Funding	68
Accepting Funding with Strings Attached.....	69
Evaluating Research Results for Commercial Applications	70
Working for a Competitor Company	71
Working for the Competitor of a Sponsor	72
Use of Proprietary Educational Material	73



Data Acquisition, Management, Sharing and Ownership

Independent Confirmation of a Colleague's Results

A graduate student brings her advisor experimental data that suggests a major breakthrough. The advisor asks another graduate student to repeat the experiment, in order to verify the accuracy and reproducibility of these results. He also asks the second student not to discuss this with anyone else, so as to ensure independent confirmation of the results. How should the second student proceed?

G9L says: It would seem that the investigator might engender better loyalty and integrity among his students if he discussed with the first student that he wanted independent confirmation of the results, then told the second student in to repeat the specific experiments in a blinded run, and then compared results. Since presumably the original data were generated by the student within the context of a mentor-trainee relationship, the investigator is responsible for confirming prior to dissemination. All three people should share in disseminating the information, with the first student as lead author and the investigator as senior author.

K5R says: I don't see a problem with either repeating the experiment or in not discussing it with others. However, the student should bring concerns to the investigator or at least question the investigator about an open discussion once the experimental results are independently confirmed. The first graduate student who found the important result should not be left out of the loop and should share recognition.

Sharing Data Prior to Publication

A researcher, speaking at a conference, presents two sets of results based on two related datasets. He references a paper that he published recently, describing in great detail the first set of results based on the first dataset. This paper mentions the second dataset but does not discuss the results based on it. A colleague attending the conference asks for a copy of both datasets. The researcher is pleased to deliver the first set of data, but does not want to turn over the second until he has had time to prepare another paper, describing results based on that dataset, and had it accepted for publication. Is the researcher justified in withholding the second dataset until he has published his results?

G9L says: Certainly, it is reasonable to withhold data until at least accepted for publication on the basis of competitive publication principles. However, it would likely be more satisfactory not to even mention the dataset publicly until the manuscript was at least prepared and submitted.

C4R says: The author should not have mentioned the second dataset unless results from its analysis are being used. It provides no additional information, and in fact, could provide contradictory results upon analysis. He does, however, have the right to withhold the second dataset, even if mentioned on the grounds provided.

Commercially Valuable Research Results

Your government-funded research at a university lab has produced results, published in a peer-reviewed journal, that have great potential for commercial application. A for-profit corporation requests a copy of your data, saying that they want this for use in their own research and that they have no intention of commercializing your results. You strongly believe that the potential for commercial application is compelling and unavoidable. How should you proceed?

C4R says: Since this is government funded research, the data are required to be placed in a public repository and made available to others. The investigator must therefore comply with the request but can require that an intellectual property waiver be signed.

K5R says: This situation arises frequently, and is always a source of concern. Virtually every university has an intellectual property (IP) statement that is sent out simultaneously when either material or data are sent to other laboratories or to companies. Since this is government funded research, the investigator has the obligation to comply with the request, but he should also demand that the material waiver IP form be signed first.

Results Based on Proprietary Data

Using data mining technology to query her employer's extensive customer database, an economist at a Fortune-100 company develops a predictive model. She tests her model against real life events, as reflected by new entries into this same database. She tabulates impressive results and submits an article to your academic journal. During peer review, one reader comments that it would be impossible to reproduce the validity test results without having access to the proprietary corporate database, as no other comparable data is available, at least not in the public domain. Would you accept the paper for publication under these circumstances?

C4L says: Because the data belong to the employer, the employee should obtain permission from the owner to submit an article based on its use and the corporation should be cited or acknowledged in the article.

K5R says: I would not accept the paper without first discussing the matter with the author and asking for a letter from the corporate people giving permission for the data mining application. Otherwise, there is likely going to be a lawsuit at some point to contend with.

Incidental Results and Transient Data

The radiology department of a medical school has designed and programmed a data visualization program that reads a series of physiological test results and converts this data into a multi-colored scatter plot, which can expose anomalies that would not otherwise be apparent. They have copyrighted the software and applied for a patent on the process. A technician who works at the school has captured several hundred images, produced from patient data during the software testing process, and used them to make wall-sized collages. He is selling these at a local art gallery and on eBay. When confronted, he points out that neither the data nor the identity of the patients can be recovered from the images, nor can the images themselves even be recreated by the data visualization program, as the various settings and parameters would be impossible to reproduce. Is the student ethically correct in claiming sole ownership of these images?

C4L says: The data upon which the images are based belongs to the medical school and should not be used for any purpose other than that for which it was collected. Under federal human subjects protections, previously existing data, collected for one purpose and presumably with consent given for that purpose, cannot be used unless the original consent allowed other uses. Even though confidentiality and anonymity will be maintained, these data should not be used to construct the images.

K5R says: In this situation, the technician is using proprietary material from their job for their own personal gain. I don't think it matters that the source of the data cannot be established or that this is artistic rather than scientific. This is still stealing from the company unless prior approval is received.

Confidential Information that Might Affect Others

Your employer is developing a diagnostic machine that performs genetic screening to identify inherited diseases. While testing the device using samples provided by co-workers, you discover that one of your fellow employees has a treatable inherited disease. You inform him about this and he tells you that he was not previously aware of it. Do you have any obligation to inform his family? If so, must you first obtain his consent for this? What if he withholds consent? What difference would it make if, instead of being affected with this disease, your co-worker were merely a carrier whose offspring would be predisposed to the disease?

C4L says: The samples provided by the co-workers were presumably collected subsequent to the signing of a human subjects consent form. The consent probably included a confidentiality clause and therefore disclosure of the results to anyone would be a breach of this consent.

K5R says: The obligation is his, not yours, to tell his family, and nothing can or should be done without his consent, regardless of whether he has a clinical condition or is a carrier for a disease.

Ownership of and Responsibility for Research Materials

A graduate student gathers dissertation data while working on her advisor's federally funded research project. Following a disagreement, the student finds a new advisor and leaves the project, taking her laboratory notebooks, microscope slides, and copies of data on computer diskette. Is she justified in taking her notebooks? The slides she made? A copy of the data she collected? What if there had been no disagreement and, instead, the advisor told the student to take these materials with her, after graduation, explaining that they would be safer in her possession and she would need them to prepare presentations and articles for publication?

K5R says: It is my opinion that the laboratory notebooks, data and microscope slides belong to the lab, not to the graduate student, and therefore they should stay with the advisor. Certainly, the situation would change if there was no disagreement and the advisor said it was OK to take them. I think the originals should stay with the laboratory, however, and the graduate student should take only copies.

Data Integrity

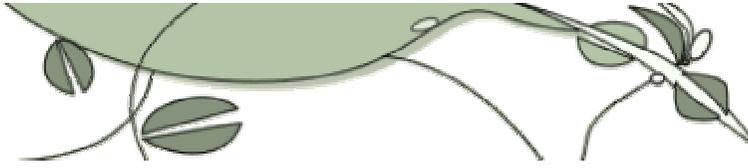
When it is learned that the experimental results reported by a graduate student cannot be reproduced, after further investigation the student is charged with misconduct and dismissed. The student had earlier presented these questionable results at a meeting where, although no proceedings were published, written abstracts were handed out. The student also exchanged email with staff at other research facilities, discussing these results and forwarding a small part of the data. What action should the university take, if any, after discovering that this questionable data was discussed prematurely and perhaps even partly released? Does the university have any obligation to protect the privacy and reputation of this student?

W8Y says: When the student was charged with misconduct and dismissed, presumably this occurred through a formal process and the evidence indicated that the student was indeed guilty. The university has no obligation to correct the dissemination of questionable results, since it was of an informal nature. Publishing retractions to unpublished results would only confuse the issue. There is no reference, and others who might mention that work would do so without citation. The university has expelled the student and has no further obligation to the student. Given that the courts have determined the right to privacy of students, the university must not publicize the issue, although leakage to local papers might occur and the university might not be able to stop it.

Ownership of Data and Right of Use

Your research project has leased a new, state-of-the-art piece of laboratory equipment that prints graphical displays in full color. The manufacturer has posted a technician on site at your lab for several weeks to get the equipment up and running. At the end of his last day, the technician asks to take about twenty printouts, created with data from your project while he was monitoring your analysis and calibrating the equipment. He wants these for use in sales presentations and possibly in a brochure. He explains that your data was incidental to obtaining the output and it was his machine which produced the printouts. Should you permit this?

K5R says: Data derived from leased laboratory equipment does not belong to the equipment manufacturer. Material for brochures must be derived from in-house experiments, not from those taken from investigators using the equipment. This could pose problems with copyright later when data is to be published in journals and there is an issue of prior publication in a brochure.



Mentor / Trainee Responsibilities

Staff Attendance and Working Hours

A graduate student works increasingly late night hours after other lab staff have gone home, and is less often present during the day. His advisor asks the student to spend more time in the lab during the work day, when others are present, to enhance interaction with other researchers. The student refuses, insisting that equipment he needs is rarely available during regular working hours and he is more productive at night when fewer people are around. How can this conflict best be resolved?

K5R says: This situation requires compromise by both parties. The laboratory director has to have flexibility in allowing students and staff to work later if that is when they will be most productive, but the director is under no obligation to cave into the demands of students and staff who do not want to be present during the day to be properly supervised. It would not be difficult to set up a schedule where the student spent half time present during the day (afternoons or perhaps alternating one day and one evening).

Advisor's Ownership of Mentored Work

A graduate student prepares a research proposal as part of her dissertation requirements. Her faculty advisor reviews the proposal but otherwise provides only minimal assistance in developing the concept. The student later learns that her advisor has paraphrased sections of her proposal and incorporated them into his own application to a different funding agency. How should the student respond?

J1G says: This happened to me in graduate school. I tried to bring this to the attention of the dean of the college, who "investigated" it and wrote me back a scathing letter in which he chastised me for daring to criticize one of their sterling faculty members. So my advice is: Let it go, get on with your life, and recognize that students are treated like germ entities at many institutions. It's just a fact of life, and no student is going to be able to change it.

K5R says: This situation is unfortunately all too common, and I don't see much recourse for the student. I do think the student should make sure that his or her name is included as a participant in the advisor's grant application, with funding requests. The student will therefore be able to gain some mileage out of the advisor's grant application, even if their own grant is not funded.

Rights to Mentored Research Concepts and Results

A postdoctoral student working in a lab for several years is offered a faculty position at another university. He asks his advisor to write a summary of his accomplishments. The advisor appends to this a list of research materials that the student may not take with him when leaving the lab, as well as a list of research areas--some not yet under investigation--and a statement that the student agrees not to work in these areas. The advisor asks the student to sign a copy of this document. How should the student respond?

W8Y says: The postdoctoral student should not sign the paper. And, indeed, the student is a better judge of his own accomplishments and should provide the information himself under these circumstances. The student must respect the mentor's wish that research materials not be taken from the lab. The student should copy whatever data he produced, however, and then hurry up and write the papers. The case of the patent rights to lasers provides instruction here. Gould had the presence of mind to get his notebook notarized. The laser patent was granted to Townes and Schawlow, and Gould's application was turned down. Gould fought, however, and a decade and a half later he was given a window of opportunity so that he received his fourth and final laser patent nearly three decades after Townes and Schawlow received their award.

Returning to the issue of rights to mentored research, it seems clear that the patent courts recognize the worker, as is generally true in competing claims to intellectual contributions. The student must protect himself and, in the absence of a contractual arrangement, he has first right to the data and its eventual disposition.

Inside Knowledge and Equality of Opportunity

A professor is mentoring two postdoctoral fellows. The professor hears about a desirable job opening at another institution, and strongly believes that one of his postdoctoral candidates is significantly better suited to this particular job than the other. How should the professor respond?

K5R says: The professor should mention the job opportunity to both of his post-docs and let them decide if they are interested. His letters of reference for the job can be weighted towards the suitability of the other candidate, and if asked pointedly by the hiring researcher, he may rightfully give his opinion of which one would be better suited for the job.

Recruiting Outside Resources

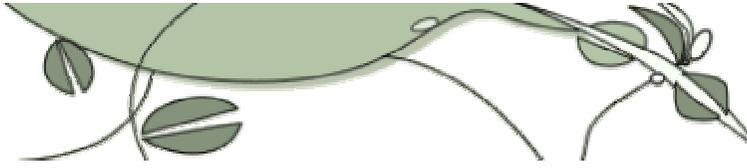
A graduate student working in a government funded lab has made an important discovery, on his own initiative, which his advisor believes to warrant further analysis. The student wants to perform this analysis himself because it would give him an opportunity to learn the techniques involved. A commercial lab can perform the analysis much more quickly, however, and at low cost. Besides, the advisor does not consider it particularly worthwhile for the student to learn these analytical techniques. How should the advisor have the analysis performed?

Romantic Relationships

Romantic relationships have developed among doctoral candidates working in a large university laboratory on several occasions. Invariably these relationships have led to bad feelings, either among those involved or among their colleagues in the lab, and productivity has suffered as a result. The director seeks to establish a policy that would sustain morale in such cases, preferably by requiring that at least one party to any such relationship must leave the lab. Is this appropriate? How should the director proceed?

J1G says: What is this, a third-world country where marriages are arranged? Geez--live and let live! If romance between students were the only source of conflict (or conflict of interest) we would have nearly a perfect world. Any lab director who thinks that love among equals is the source of trouble needs to get a life.

K5R says: I disagree with a policy that would make one of two parties in a relationship leave the laboratory. I think it is unfair and impossible to control (people would tend to be discreet rather than aboveboard) and in the end, bitter feelings could turn even more bitter. On the other hand, I do agree with a policy in which supervisors should not be allowed to become romantically involved with those they supervise (eg, there should not be romantic relationships between an advisor and a student or advisor and staff). This is written into most human resource policies at companies and universities, and is probably sufficient.



Publication Practices and Responsible Authorship

Use of Copyrighted Illustrations from Prior Publications

Two researchers have co-authored a paper, describing their results, which has appeared as a preliminary report in a copyrighted monograph. One illustration in this paper is a computer-generated scatter plot of research data. Both researchers are preparing more substantial papers for submission to peer-reviewed journals. They both agree that the scatter plot in the monograph article is crucial to their presentations. Deciding that this illustration must be included in both new papers, they alter their computer program to generate the exact same figure using different fonts and different line thicknesses. Is it necessary to say in their papers that these figures were adapted from the monograph article? If so, is that sufficient, or must permissions be obtained?

K5R says: It would be appropriate to mention that the illustration came from a prior publication, but I don't think permission is required from the previous publication since an illustration itself is not copyrighted.

5S says: An acknowledgement would be polite, but is not necessary, nor must permission be obtained. The illustration is not a work of authorship, and is not by itself copyrightable, and is small enough that reproducing it can be considered fair use.

J1G says: I disagree with the previous comment. Better to be safe than sued -- it is usually very easy to get permission to reprint any part of an article, or even an entire article. Just write and ask. It's more burdensome to come up with a workaround than to do the ethical thing and honor the copyright.

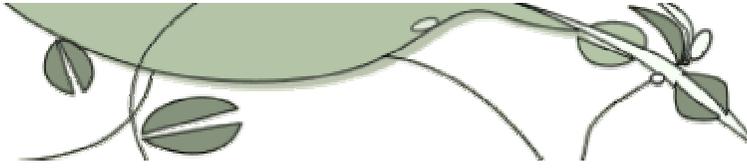
Attribution of Mentored Research

You are writing a book chapter describing recent advances in your field. One of your graduate students made significant progress. Using ideas that you conceived, he designed and ran experiments without supervision, interpreted the results without assistance, and wrote several important papers that were published citing him as the primary author and you as the only coauthor. In your book, should you attribute these advances to you first and then him? To him first and then you? Or to him and unnamed associates?

K5R says: In most book chapters that I am familiar with, the authors use "we" or "in our laboratory" or "in collaboration with X, we found...." rather than using one person's name or the author's own name. Research is always a plural rather than singular effort.

Simultaneous Publication in Different Venues

You are the editor of a yearbook summarizing recent research in your field. One of the main articles was submitted by a colleague, who is cited among your coauthors. Several months after your book was published, you see an article by that colleague in a peer-reviewed journal. Although dealing with the same subject matter, this article is entirely different from the chapter in your book. You notice, however, that two illustrations--a graph and a diagram--are identical in both. Neither publication acknowledges the other. You later learn that the article was prepared and submitted to the journal before your book was written, although it did not appear in print until after the book was published. What, if anything, should you do?



Peer Review and Privileged Information

Confidentiality of Material Being Reviewed

Having been asked to review an article for a journal, you give a copy of it to one of your graduate students, asking her to read it and prepare a 1-page written critique. She later gives you a page of comments and also discusses the paper with you in detail during an hour-long meeting. After reading the article yourself, you use the graduate student's written and verbal comments as part of the basis for your review. You later learn that the graduate student kept a copy of the article in her files. Was any of this inappropriate?

C4L says: Permission to do so should probably be obtained from the journal prior to sharing the document with the student. If the student provided substantial input, he or she might be also be listed as a reviewer, which would be advantageous to the student.

K5R says: Most journals have policies against circulation of unpublished manuscripts. Therefore, making extra copies for graduate students is probably inappropriate, as is the graduate student keeping a copy. However, I think it is entirely appropriate for an advisor to allow a mature grad student, post-doc or another close colleague to simultaneously review a manuscript, discuss it, and to incorporate some of those comments into an editorial review. Such a procedure only enhances the accuracy, fairness and thoughtfulness of the review process.

Protecting Information Provided Anonymously

You have a grant to develop a Web-based program of genetic counseling. Clients who navigate to your Web site and use the program do not identify themselves by name. Nonetheless, insurers, prospective employers, and others would place a high value on the identities of clients and might use this information in discriminatory ways. Should you warn clients about this? What level of security should you provide to protect the identity of clients?

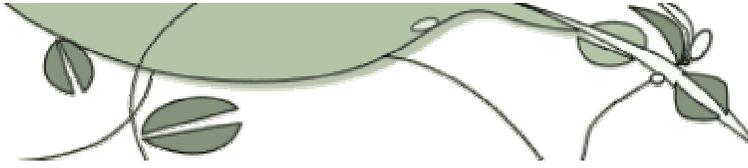
K5R says: A published privacy policy should be readily available to the participants, and a strict level of security with a mandatory firewall and/or encryption should be in place to protect the public in this situation, as extraction programs might still be able to glean email addresses for those giving information.

Use of Anonymous Survey Data

Every semester, a psychology professor asks his undergraduate class to fill out an anonymous survey form that asks many general questions about their beliefs and attitudes. Some of the questions deal with such issues as drug use, sexuality, and criminal behavior. The professor tabulates their responses and uses this information when preparing and presenting his lectures. While preparing an article that he will submit for publication, the professor decides to cite some of this data, data which reflects poorly on the students. The chairman of his department prohibits this, ostensibly on the grounds that neither institutional review board approval nor informed consent was obtained. It is obvious that, in reality, the chairman's purpose is to protect the reputation of the school. How should the professor respond?

C4L says: Regardless of how the data represent the students or the school, it cannot be used for these purposes since no consent to do so was obtained prior to its collection. The chairman is correct.

J1G says: The larger problem is with the sample's generalizability. The anonymity issue is secondary to the fact that the data probably aren't meaningful outside the narrow community of students of that demographic. No good journal would want the paper anyway.



Collaborations

Collaborators Who Become Competitors

Two senior scientists at a biotechnology company collaborate in preparing a grant application that they submit under the Small Business Innovative Research (SBIR) program. Before the application is reviewed, one of these scientists accepts a job at another firm. The application receives a good score, at the review meeting, although not good enough to be funded. Nine months later, at a subsequent SBIR review meeting, the reviewers notice that the original application has been resubmitted with changes reflecting their earlier critique. They also note a remarkably similar new application, from the scientist who changed jobs and on behalf of his new employer. The new proposal makes no mention of the original, although it contains much of the same language and the summary is nearly identical. Is this plagiarism? Does the new proposal have the same standing as the revised original? How should the reviewers respond to similarities in the two proposals?

C4L says: The application belongs to the submitting institution. The revised submission should have indicated that one of the co-investigators is no longer participating in the proposed research. The second application would not have been accepted for scientific review, had it been possible to have identified it as too similar, prior to review. Both applications can be reviewed, and scored, at the initial review group meeting, but if the reviewers of the two applications believe them to be substantially identical, they can request that final review decisions on both be deferred. This is normally handled by an administrative note and allows program staff to address the concerns. Since both investigators presumably contributed to the initial application, they are both authors of the original work and

plagiarism should not be an issue. The two investigators should have agreed on the future of the proposed work, however, and highly similar applications should not have been submitted.

Spouses as Collaborators

During her first year as a graduate student in pharmacology, Susan meets John, a salaried software engineer working in the university computer center, whom she marries that summer. During her second year, Susan works closely with John on several projects, relying on him for computer expertise. Susan achieves impressive results based on computer simulation and sophisticated data analysis. She publishes several papers in which she acknowledges the "help and support" of her husband, John, but does not name him as a co-author. Other graduate students complain that Susan had, in John, a valuable university resource that was not available to them and that her publication record unfairly conceals the impact of John's help. Is Susan's behavior appropriate? Is John's? Would it matter if they were not married? If John were not employed by the university?

J1G says: The inappropriate behavior is on the part of the whining students who complain that Susan has the "advantage." Nothing is stopping them from collaborating with someone who could give them an advantage, as well. Susan just happens to be married to her collaborator. As for naming him as a co-author, that is between the two of them, and depends on the rules and expectations of the publication.

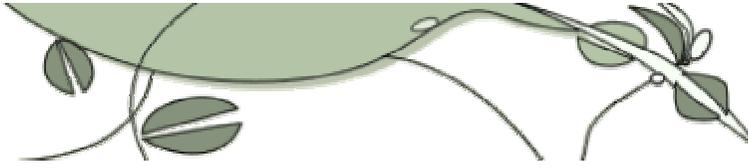
K5R says: As long as she gave John an acknowledgement, there is nothing inappropriate here in their collaboration. If his contributions were great, however, a co-authorship may have been more appropriate than a simple acknowledgement. Complaints of other students are unfounded unless John refused to provide any help or guidance to other students when asked. In his capacity with the university he could help anyone with their research as

part of the collegial environment and within time and resource constraints. If he did not work for the university then he could refuse anyone at any time.

Collaborating on the Review Process

Your supervisor, the principal scientist at a R&D firm, reviews grant applications for the Small Business Innovative Research (SBIR) program. He gives you an SBIR application, asking you to read it and email him your comments. Portions that identify the company which submitted the application have been blacked out. When you ask whether the funding agency knows that you are helping to review this grant application, he says, no, but it is common practice. Should you review the application? Should you notify the funding agency? What if it were not a grant proposal but, rather, an article being reviewed for publication in a journal?

JIG says: This practice might be commonplace; however, it is not only unethical, but perhaps also illegal. The supervisor is at fault. If I were the person being asked to do the review, I would politely decline unless the supervisor clears it first. This situation requires sunshine.



Human Subject Research

Minority Representation that Confounds Data Analysis

Your research project will study the impact of a new method for prophylactic treatment to reduce hypertension in elderly nursing home residents. Guidelines for research with human subjects require a minimum threshold level of minority group representation. Earlier studies have shown that the incidence of hypertension varies markedly among racial groups, with black Americans having a higher incidence of hypertension, proportionally, and Americans of Asian decent having a lower incidence. If the study sample were to include minorities, this variation in the incidence of hypertension would confound the analysis and complicate the interpretation of results. Do you:

1. Request an exemption from the requirement for minority representation.
2. Increase the sample size sufficiently that each minority group can be analyzed separately.
3. Increase the sample size sufficiently that minority subjects can be disregarded.
4. Ignore the confounding effect of race when analyzing the study data.

J1G says: None of the above. Over-sample the under-represented groups that need to be represented in the analyses.

R3H says: There are several options here. An IRB can always grant an exemption if such an exemption is justified. If the study is sufficiently defined as to the target group, ie a study of risk factors for hypertension in a black population or a study of risk factors for hypertension in a

white population, then by definition the study group is defined and non members of the study group would automatically be excluded. The conclusions, of course, are not generalizable. Alternatively, the study group can be skewed to include sufficient numbers for individual sub set as well as total group analysis.

Knowingly accepting a biased sample is, under no circumstances, acceptable. Analysis of a larger group, so that minorities can be excluded, is likewise unacceptable, since the target group must be larger than necessary to expose the minimum number of target population members. The excess target group members and all of the members of the group to be excluded would be exposed to potential risks of the study, even if such risks are minimal.

Informed Consent that Confounds Data Analysis

Your research project will study the impact of a new way to care for patients with Alzheimer's disease. Guidelines for research with human subjects require obtaining informed consent from each subject. For most Alzheimer's patients, a family member or other authorized person must provide this consent. You suspect that Alzheimer's patients who have family or a health care proxy will respond differently from those who lack such support. Do you:

- 1. Request an exemption from the requirement for informed consent.**
- 2. Increase the sample size sufficiently that data on subjects who provided informed consent can be analyzed separately from any available data on subjects who did not provide informed consent.**
- 3. Remove individual identifiers from data on subjects who did not provide informed consent and analyze this data anonymously.**
- 4. Exclude subjects who did not provide informed consent from the study and ignore the confounding effect of having informed consent.**

J1G says: Work the dilemma into the research design and analyses. Consider covariance, crossover, counterbalancing, etc.

R3H says: This is not an uncommon problem. There is a mechanism in the institutional review process for dealing with exactly this problem. An approved IRB can grant approval for a research project under particular circumstances (minimal risk, no individually identifiable data) without the requirement for prior informed consent if

the IRB concurs that prior consent would taint the data. In some cases, consent may be required after the data has been acquired but before it can be used as part of the study database. All of this is included in the purview of an appropriate IRB.

Unexpected Changes in Sample Demographics

Your study sample contains adequate representation of minorities. During the course of data collection, however, an unexpectedly large number of minority subjects must be dropped for various reasons, leaving insufficient representation of one minority group. It is too late to recruit additional study subjects. Do you:

- 1. Request an exemption from the requirement for minority representation.**
- 2. Discard the study data and start again.**
- 3. Proceed as though all minorities were represented adequately, ignoring the attrition in study subjects.**
- 4. Perform a second study using only subjects from the under-represented minority.**

J1G says: None of the above. Subject recruitment is part of the study, not a preliminary step. Report the difficulty with minority subjects' completion of the protocol. It's a finding.

R3H says: None of the proposed alternatives is acceptable. Subject selection was part of the study design which cannot be changed after the fact. The study result is the study result and the fact that particular groups had difficulty with the study is part of the result. It is not ethical to delete or ignore data under these circumstances. There are statistical techniques, such as intention to treat analysis, that may be helpful and consultation with a statistician may be considered, even after the fact.

The data must be presented "as is," or as some would say, "warts and all" with care being made not to overdraw the

conclusions and with some discussion of the problems and implications. This should be a fairly standard approach in the honest presentation of data.

Unexpected Abnormal Test Results

As a laboratory exercise, your graduate students prepare slides with smears of their own blood. You then randomize the slides and ask each student to run various tests on an anonymous slide from a classmate. One of the slides shows very low values on some tests, low enough to suggest HIV infection. What action should you take?

R3H says: Because of the implications of this finding to the subject who would benefit from early intervention and the risk to partners who may be exposed without choice, it is not acceptable to do nothing. What should be done provides a challenge to the professor. One possible and acceptable option is to alert the class that one of the slides had some abnormal values which might be a true positive or might be a false positive for an abnormality without necessarily stating the nature of the abnormality, although for an educated group such as this, revealing the possibility of HIV may be preferable. All of the students should be encouraged to see their own physicians for a complete blood work up and HIV testing.

Ending a Study Early

An assisted living facility has increasingly high levels of infection among residents admitted to its two intensive care nursing wards. The facility obtains funding for a 1-year study of techniques that might reduce the risk of infection in such an environment. Researchers enroll every patient in one of the wards, obtain informed consent from them, and begin applying the study protocols in that ward. A few months later, they see a thirty per cent decrease in infections on the study ward. Infections in the other, control ward continue at a high level, meanwhile, and several patients from that ward must be hospitalized. At the end of the year, comparison of rates of infection in the study and control wards supports use of the clinical interventions. Should the study have been ended early? Should patients in the control ward have been asked for informed consent?

J1G says: Control subjects are subjects. They should've been consented. As for ending the study early -- hard to say, since the study wasn't conducted correctly anyway.

R3H says: Without knowing the details of the study it is difficult to have a definitive answer. Most studies of this type have a data review panel which can suggest early termination. This was the case, for example, with the laser treatment of diabetic retinopathy.

If there is no interim analysis, it is hard to really assess if there is an actual difference. In this example, however, one must conclude that there are interim analyses else how would one know there was a difference. If a clear medically and statistically significant difference is demonstrated, as it appears to be in this case, it is ethically required that the study be stopped and intervention done in the control group. The study at that point has been concluded, a benefit or increased risk has been

Human Subject Research

demonstrated and there is no longer any justification for increased exposure to risk.

Informed Consent for Saving Research Data

In a laboratory exercise, graduate students draw samples of their own blood and use these to perform various tests. Afterward, the instructor tells the class that he wishes to collect their test results for use as baseline data in a clinical study. Anyone may decline to participate, he says. Is informed consent from the students needed? What if, instead of their test results, the instructor also asked for the leftover blood samples? Would it matter if the data and/or samples were unlabelled and anonymous?

R3H says: Informed consent cannot be obtained in this circumstance and the data/samples may not be used. Consent cannot be obtained since the consent cannot be considered free. This is roughly analogous to general rule that a prisoner may not give informed consent because of the expectation of some benefit, even it is explicitly stated that no favoritism will be granted. In this case there may be an element of coercion here since the perception may be that a grade will be affected, positively or negatively, as it relates to participation. Even more particularly, in the context of a required class in which the grade is an important outcome with long term ramifications, the element of potential coercion is even stronger. The grade depends on the good will of the instructor at some level. There is potential for a real conflict of interest here, even if it is not perceived as such by the instructor.

Appropriate Use of Test Data

A government agency is training students from local law enforcement agencies in use of a new device for matching DNA samples. Trainees collect specimens of their own DNA in various ways and then analyze these to learn how the mode of collection influences the likelihood and reliability of a match. At the end of the course, and unbeknownst to participants, everyone's DNA profile is entered into the agency database. Is this appropriate? Would it be more appropriate if consent were obtained? Would it be more appropriate if the data were fingerprints, rather than DNA samples?

R3H says: Under no circumstance can personal information be taken and incorporated into a database, government or otherwise, without knowledge and consent. This is not only unethical on its face, it is illegal and the government itself is not exempt under its own US code. It does not make any difference if it is DNA or fingerprints. If consent is not knowingly and freely given, it cannot be ethically done. If consent were obtained, this might be permissible, although there are concerns about implied or actual coercion. This would depend on the specifics of the situation and consent.

Scope and Venue Issues for Informed Consent

A researcher who is studying intestinal bacteria has designed an innovative, non-invasive probe for collecting samples during a routine colonoscopy procedure. Must she explain the risks of colonoscopy when obtaining informed consent to use this probe? Can she assume that no colonoscopy will ever be performed solely for the purpose of using her probe to obtain a sample?

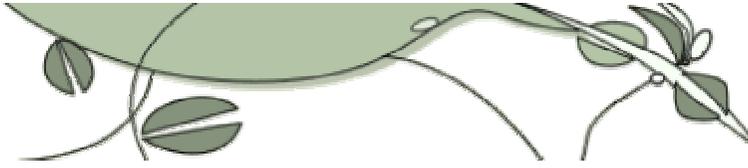
Selecting a Control Group

A private corporation has obtained government funding to test dramatic enhancements in a program that treats addiction to painkillers. Owing to the nature of the psychological interventions used, subjects who were exposed to the older program might or might not respond well to the enhancements. Is it appropriate to use the old program with a control group, when testing effectiveness of the new program? Would it be appropriate to use the old program with a control group, when testing whether exposure to the old program reduces effectiveness of the new program?

Selecting a Clinical Trial Site

You are designing the clinical trial for a prosthetic device used when a young child has lost a lower limb. You wish to conduct the trial overseas, in a region where victims of line mines can be recruited as subjects. The prosthesis will be very expensive, however, and apart from the high cost of purchase, it will be costly to maintain. For these reasons, it will almost certainly not be available outside the US. Is it appropriate to recruit clinical trial subjects from a population that will not benefit from the product? Is there an obligation to support study participants after the trial ends?

K5R says: In this situation, although it might be preferable to do the study overseas, logistics prevent it from being performed outside of the US, and so it should be done in the US. The selection of site for a clinical trial is based on the total sum of information, and benefit by the local population can only be one part of this equation. There is likely a moral obligation, if not a legal one, to provide some sort of ongoing support for the participants, and this information should be included in the study protocol.



Animal Subject Research

Choice of Animal Subject

A program of research will study the effects of a new psychotropic substance on human brain chemistry. After the substance is administered, the animal subjects will be immobilized and electrodes will be attached. Then, once encephalography data has been obtained, the animals will be sacrificed and dissected to examine for changes in brain physiology. Although dogs are deemed adequate subjects, use of primates, such as monkeys, would produce more persuasive results that would generalize to humans with greater validity. Should the project use dogs or monkeys?

J1G says: Whatever happened to mice and rats? We have learned a lot about human neural function by studying it in little bitty critters with short lifespans and less pet-appeal.

K5R says: There are strict laboratory animal scientific guidelines for the use of non-human primates in experiments. "Greater validity or easier generalization of results to human subjects" is definitely not an appropriate or valid reason for using primate subjects. Rather, there has to be a valid reason for exclusion of other routine laboratory animal species. If the dog is termed adequate, it should be the default for this experiment, and if the experiment could be performed equally as well with rodents, then they should be the default choice. The choice of primate in this case would be declined by any Animal Care & Use Committee at any research institution in the US.

Animals Used to Monitor Other Animals

You have a colony of laboratory animals that must be kept isolated from all other animals. Every few weeks, you sacrifice one or two animals in order to verify that they have not become contaminated by outside contact. How are these “monitor” animals different from the other animals actually used for research?

K5R says: Guidelines have been established by the Association for Assessment of Laboratory Animal Care (AALAC) for keeping and maintaining sentinel animals within a facility. In theory and practice, sentinel animals should be housed, manipulated and treated in all respects like the other study animals within the same environment.

Source of Animal Tissue Used in Research

Your research project seeks to isolate substantial quantities of a substance that occurs in trace amounts in the glands of codfish. Your technician will collect fish entrails at a local wharf, where fishermen's catch is cleaned for market. Do the usual guidelines for animal subjects apply? Suppose it were chickens at a poultry ranch? Cows or pigs at a slaughter house?

K5R says: The usual guidelines for animal subjects do not apply to tissue from fish, pigs, cows or chickens procured at slaughter plants or at the fish market. If live animals were used, then Laboratory Animal Services (LAS) or US Department of Agriculture (USDA) guidelines would apply to their maintenance. Typically, however, a specific protocol for obtaining such tissues would have to be presented to--and approved by--a biohazard committee at a university prior to submitting a proposal for, or initiating, such studies.

Changing a Research Protocol that Uses Animals

A research project was designed to collect encephalographic data from animal subjects using surface electrodes. Problems have developed, however, and you now suspect that surgically implanted electrodes would give significantly better results. Is it appropriate to try this technique once or twice before incurring the administrative burden of altering the research protocol, which does not provide for any surgery?

K3R says: Before switching from surface electrodes to a surgical procedure involving animals, approval would have to be obtained from the animal care and use committee and an amendment to the prior animal use protocol would have to be obtained. It is not ethical (or legal) to perform invasive surgical procedures on animals without approval from an animal care committee, even if this involves only once or twice for practice.

Use of Animals after Research Ends

You are asked to design a laboratory protocol for harvesting serum from animals by bleeding the animals at regular intervals. The nature of the process makes these animals unsuitable for any other laboratory purpose, afterwards, although they might have some slight commercial value. Is it better to end the procedure by sacrificing the animals to extract all their blood? Or by performing several additional bleedings to obtain the same amount of blood, at additional cost in ongoing maintenance, and with a live animal of little commercial value at the end? If the procedure calls for sacrificing the animals, would this preclude keeping one or two as pets?

K3R says: The endpoints to any animal experiment should be evaluated and addressed ahead of time so that the decision of when to end the experiment is already established in the protocol. Both options in this case (ending the experiment with exsanguination or continuing multiple bleeds) are viable alternatives and the correct choice would depend on circumstances. If experimental treatment was given to livestock, it might not be legal to sell them commercially, as drug withdrawal periods might be unknown. In a non-terminal experiment, it is justifiable to allow adoption of animals at the end of the study, although at every institution I know of, this requires approval of the animal care and use committee and of the investigators involved.

Unexpected Death of Animal Subjects

Your experiment on dogs involves surgically implanting a drug delivery device, monitoring the dogs for a time, and then removing the device and monitoring for a while longer. Early on, some dogs unexpectedly die. It is not clear whether this resulted from the surgical procedure or the drug. Should you stop the experiments and refine the surgical procedure without administering any of the drug, even though this might ultimately sacrifice more animals? Or should you continue the experiment in hope that results might improve as the surgical procedure becomes more practiced, but with no guarantee of this? Or should you revisit the entire protocol design?

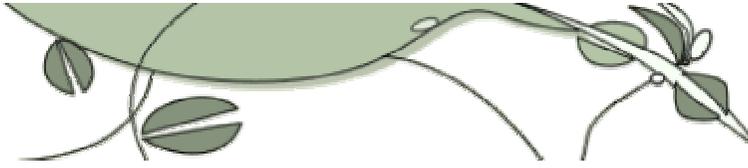
K3R says: Since it has not been established whether the problem is the drug or the drug delivery device, it would be appropriate to halt drug administration and see if any other animals die from the delivery system alone. This would establish whether the surgical procedure and/or delivery device was responsible. Once this is established, the drug could be given again to see if it was inducing death. If mortalities recurred, the experiment should be halted as a non-tolerated drug dose is achieved.

Research Use of Tissue from Livestock

In your government funded research involving farm animals, you collaborate with a local veterinarian who occasionally sends you tissue samples. The veterinarian receives no government funding and does not sacrifice any animals. Are the farm animals whose samples come in from the field subject to the same standards and concerns as those in your laboratory?

K3R says: If the veterinarian is routinely obtaining tissues in the normal day-to-day activities of his practice, but is simply supplying the investigator with the material periodically (with no history or background on the patients involved), there are probably no guidelines or controls on this material that are required for this tissue source.

However, if the veterinarian is recruited prospectively to obtain tissues and/or to do a procedure specifically as part of an ongoing study that he would otherwise not be performing on a specific animal, this probably would fall under animal care and use guidelines. Under these circumstances, a specific protocol would have to be approved by an Institutional Animal Care & Use committee ahead of time and relevant guidelines would apply.



Research Misconduct

Appropriate Use of Commercial Software

A newly appointed assistant professor is unpacking her new computer and preparing to install a dozen software packages, all recently purchased for her use with grant funds. A colleague in the next office tells her that he makes a practice of copying entire software installation CDs into folders in an install directory on his hard disk, before installing the software from this hard disk copy. He suggests that she simply install each software package she has purchased from his computer, over the network. This will be much faster, also easier, and will not require opening the shrink-wrapped software packaging. He also suggests she install several programs that she has not yet purchased and try them out. If she likes them, she can purchase them online, and if not, she can uninstall them. What, if anything, might be unethical about this practice?

K5F says: This violates the licensing agreement included with virtually every piece of software that an investigator is likely to have access to, and is contrary to the software sharing policy of most institutions including industry, government or universities.

C4R says: Where is the license number for the new software? If it is visible, then install the software over the network and use the provided license number. If it is not visible, open the package. Provided that you use your license number, this is fine. Media is often available online. As for that software for which the new user does not have a license, no go.

Research Use of Commercial Publications

A research consortium subscribes to many publications that are available both in printed form and as PDF files on the Internet. Instead of circulating printed copies of these newspapers, magazines and journals, the consortium posts a list of user names and passwords, so that members can access the materials for themselves online. Rather than copying portions of publications that they want to save on a copier, members simply print pages from the PDF files on their laser printer. Is this an ethical application of the fair use doctrine?

J1G says: This is fair use gone berserk. Without approval from the copyright holder, copyright restrictions are as stated in the publication, and distribution rights are as limited in the user agreement. Okay, people don't take these things seriously enough. On the other hand, I believe that scientific journals have a moral obligation to make their online contents open to the world. Nonetheless, copyright is copyright. What other laws does this outfit break, one wonders?

K5F says: It is the goal of many institutions to have a paperless, on-line library for their investigators. The intent of this research consortium is therefore not unlike many others. If they had an institutional (library) subscription for the journals, there might not be a problem here. However, it sounds like they have a few individual subscription names and passwords that they are circulating among many individuals. Hence, this is contrary to the intent of international copyright law for scientific journals. Even with an institutional library subscription, there still has to be some controls in place for dissemination of copyrighted material. In many cases, company or university libraries have negotiated specific rights with publishers of on-line

Research Misconduct

journals involving set rules such as: limitations of only saving a single copy or printing a single copy to personal computer or printer, allowance to email a copy to those within the same institution but not to those outside of the company or university, limits on use for non-commercial (research or educational) purposes only, and appropriate prior approval for any other intended uses. Lack of such controls or agreements with publishers indicates a wanton disregard for intellectual property rights and copyright law.

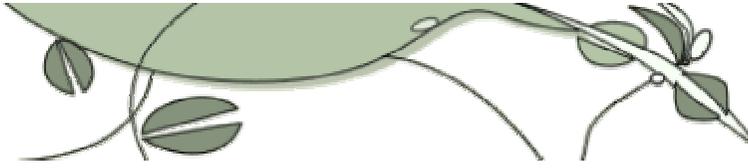
Research Impact of Changes to Guidelines

An ongoing research project is studying antibodies obtained by sacrificing mice. Following a review of its policies regarding animal subjects, the sponsoring institution determines that only in vitro methods may be used for this in the future. Any such change in procedure will invalidate all prior results, of course. Would it be appropriate for the project staff to contract with another institution, where guidelines still allow the original procedure, and send mice there from time to time for antibody harvesting? If not, would it be appropriate to contract with another institution to perform the entire procedure, using their own mice and only returning the antibodies for final analysis?

Padding a Budget

After reviewing your annual budget, the department head asks you to include certain additional items of equipment, which the department badly needs, assuring you that this will not affect the funding for items that you requested. You see the value of this additional equipment to the department but have no particular use for it in your own work. How do you respond to your supervisor's request?

JIG says: It's pointless to try to pad a budget, because reviewers and program staff review budgets quite closely. If equipment isn't justified for a project, it probably won't be approved in the funded budget.



Financial Conflicts of Interest

Divulging Information about Funding

A graduate student meeting with her potential doctoral program advisor for the first time asks about project funding, wishing to know its source, duration, and plans for soliciting alternative financial support. How should the faculty member respond?

J1G says: There's a question about this? Of course anyone involved in a project has a right to know who's funding it. Participants also have a right to know.

K5F says: Since there are huge implications for the future success of graduate students and post-docs based on the nature of funding sources, past success in grant receipt, and the duration of current funding sources in a laboratory, I think it is fair game for a student to ask these questions and expect a response. Answers to such questions may impact on the decision of which laboratory the student will join (and rightly so).

Accepting Funding with Strings Attached

A large corporation offers a grant to fund basic research, with only the proviso that any journal articles must be approved by their corporate publicity office before being submitted for publication. The facility needs this grant to buy necessary equipment and fund attendance at conferences; moreover, the director expects that corporate oversight will have no impact on the normal publication process. Should he accept the grant?

J1G says: No. It's a Faustian deal. Better to do no science than to sell your soul to do it.

K5F says: Of course he should accept the grant. As long as there are arbitration clauses written into the grant contract beforehand (which is standard for a university-corporate research contract), any disputes about what can or should be published can be peacefully resolved. Any investigator who refuses a grant with strings attached is greatly limiting their opportunity to fund better research.

Evaluating Research Results for Commercial Applications

A managed care health plan has the policy that it will not pay for any treatment if a less costly intervention would achieve identical results. Noting that clinical trials generally compare new and often expensive drugs and treatments only to a placebo, may the health plan decline to pay for any such new intervention until additional research has shown it to be more effective than less expensive or generic alternatives? Or, must the health plan accept self-servings opinion of industry researchers, even when their clinical trials do not address the relative effectiveness of alternative treatments?

5S replies: The practice of comparing a new intervention with a placebo, while ethically correct from a research perspective, rarely produces negative results. It tells little about the relative benefits versus available alternatives and nothing about the cost-benefit tradeoff. Nonetheless, before declining to pay for a new drug or treatment, the health plan must show that the innovation is less effective than existing alternatives, perhaps by comparing the results of different clinical trials that measured the effectiveness of each against a placebo.

Working for a Competitor Company

A graduate student is preparing a dissertation on a government funded project to develop a new type of stent. He is offered a part-time job, working only weekends, in the shipping room of a company that manufactures various surgical appliances, including the kind of stent that his dissertation work will make obsolete. Is this a conflict of interest? Suppose the work were during the normal, 9-to-5 weekday? Suppose the student is aware that this company has its own research program, without knowing any details? Suppose, instead of the shipping room, the student is offered a job in the laboratory where this research is performed?

C4R says: An apparent conflict exists and therefore he should not work there in any capacity.

Working for the Competitor of a Sponsor

A graduate student completes a dissertation based on research that was partly funded by a corporate sponsor. After graduation, the student is offered a job working for another corporation that competes with the first. There can be no doubt that the dissertation and experience with a competitor's research played a role in this offer. Is there a conflict? Does it matter whether the student personally received any funding from the corporate sponsor?

Use of Proprietary Educational Material

A college professor offers his undergraduate students a choice of several optional term projects for extra credit. One of these requires the purchase of a workbook, authored by the professor, who makes it available for purchase through the campus bookstore as a Xeroxed, loose-leaf volume. Is this a conflict of interest? Does it matter whether the book is sold at cost or at a profit? Would it matter if someone else wrote the workbook that the professor is selling?

J1G says: Well, if this is deemed a conflict of interest, then we're condemning thousands of academics to a mire of conflict. This practice is so common -- including asking students to purchase an expensive textbook written by the professor -- that no one questions it anymore. Is it sleazy? Often. Is it a source of great income for most professors? Hardly. It's difficult for an author to make much on the sale of 30, 60, or even 600 books.

K5F says: There is no conflict of interest here. The professor has offered multiple options including the use of his own textbook. Many professors/authors have used their own textbook in teaching their own classes and offered the book for sale at the local university bookstore--not because they will make any profit out of it (the royalty payments from textbooks are appallingly small) but because they probably honestly believe that it is the best treatise on that particular subject and/or is more germane to the topics that professor and their classes are focused on. Certainly, the professor could make a donation in some form to the class as a re-imbusement for their expense if his conscience required it, but I don't see any real ethical dilemma in this case, even if the book was required for a regular grade rather than being an option for extra credit.