Science and Social Responsibility

Biomedical research produces many important benefits for society but announcements and uses of those results need to be handled appropriately. Last year we focused on dual use research and this year we want to continue the theme by talking about three important issues: the potential consequences of publishing results from studies of specific human populations; how announcements of new discoveries are made to the public through the press; and how materials can/should be shared with collaborators.

Case 1 – Potential Consequences of Epidemiological Studies

In 1988, investigators from the NIH and A & T University launched a longitudinal study of a population living in an Appalachian county in the U.S. People enrolled in the study were healthy adults, aged 18-65. The population was 90% white, 4% Native American, 4% black, and 2% Asian. The goals of the study were to (1) estimate incidence of different types of cancer and (2) identify genetic and environmental factors related to cancer in this population. To promote the study and enhance recruitment efforts, the investigators collaborated with influential organizations in the community, including the public health department, a local medical clinic, the county commissioners, the local newspaper, and several churches. They formed a community advisory board that included representatives from these different organizations and was very supportive of the research project. The investigators promised to share their results with the board prior to publication.

The investigators recruited 7,500 subjects from this population of approximately 100,000 people to participate in the study. At enrollment, information about diet, smoking, work, exercise, behaviors, and various environmental exposures was recorded, and samples were taken for genetic analysis. Over the years, changes in health behaviors and outcomes (such as disease and mortality) were also recorded. Now that the study has been going for 20 years, there have been sufficient numbers of cancers for the investigators to obtain some interesting results. The population has a lower incidence of colorectal, breast, and ovarian cancer (compared to the U.S. population), but a higher incidence of prostate and testicular cancer, alcoholism, substance abuse, dementia, promiscuity, and HIV/AIDS. The researchers have also identified genetic and environmental factors associated with increased or decreased risk of some types of cancer in the population. When the investigators discuss these results with the board, the board members are pleased to learn about the cancer results, but they are disturbed to learn of the higher risk of the other outcomes, including those that are considered to reflect health behaviors that might reflect poorly on their community. The investigators assure the board that they will not mention the name or precise geographic location of the community in any publications, but the board is concerned that people will still be able to use some of the demographic and genetic information that is published to identify the community and that this will bring shame to the population and potentially affect access to health care. They ask the investigators to publish only the “less controversial” results.

How should the investigators handle this situation? Should they publish only the "less controversial" results? Does the form of the investigators' "promise" make a difference, e.g., oral vs. in writing?

Does the wording of the original consent obtained for the study affect how the investigators might handle this situation? If the purpose of the study broadened beyond the focus on cancer, what should the investigators have done at that time?

Should they publish the study after removing data that could be used to identify the population? Does it make a difference if the data might identify only the county being studied, rather than specific population groups or individual subjects? What if these data are crucial to the study?

How could this situation have been prevented? How specific should the investigators' "promise" to the community have been?

The ***Nature*** editorial (Nature 461:1174, 2009) **Mind the Spin** addresses comparable issues related to a press release on a clinical trial and is directly relevant to both this case and the next one.

Mind the spin

Scientists — and their institutions — should resist the ever-present temptation to hype their results.

The circumstances surrounding the recent announcement of results from an HIV vaccine trial in Thailand are troubling. The sponsors of the US$119-million phase III clinical trial, a consortium led by the US Army, the National Institutes of Health and the Thai government, announced on 24 September that the trial had been a success: an analysis of the data showed that the vaccine had a statistically significant effect on preventing infection.

Other scientists could not immediately assess that claim, however: the full data from the trial were not made available until 20 October, when they were presented at an AIDS vaccine conference in Paris and in an article published online the same day (S. Rerks-Ngarm *et al. N. Engl. J. Med.* doi:10.1056/nejmoa0908492; 2009). The article contained two other data analyses, not mentioned in the initial announcement, showing smaller effects that were not statistically significant (see page 1187).

The trial's sponsors defend the premature announcement on the grounds that they had promised to inform the Thai people of the results first ; 24 September is also Mahidol Day, the anniversary of the death of the king's father and a day of national observance in Thailand. The sponsors also argue that announcing the less-upbeat analyses along with the positive result would have been too complicated for the public to understand ; they wanted to quickly deliver a clear-cut message on the trial's findings. Making the full data immediately available to scientists on 24 September would also have been impossible, they add, because of the conference and journal embargoes.

To their credit, the scientists involved did emphasize in their public statements that any vaccine effect was “modest”, and that the vaccine itself was of no immediate public-health utility. At the same time, however, they hammered home the message that this was “the first time an HIV vaccine has successfully prevented HIV infection in humans” , and implied that the event was somehow historic. Such statements, together with the selective initial presentation of the data, are well outside the scientific norms for presenting the results of clinical trials. They inevitably create suspicion that the trial sponsors may have put an excessively positive spin on results that are far from clear-cut, in a trial that has long been controversial (T. V. Padma *Nature Med.* **10,** 1267; 2004) . The trial has also been six years in the works, and so there seems no particular public-health urgency to justify publication by press conference.

Fortunately, such stories are still rare in science. Witness the way scientists have behaved since the beginning of the current H1N1 flu pandemic, in which the urgent threat to health creates legitimate tensions between getting results out fast and respecting peer review. Most researchers have negotiated this tension well, through a combination of fast-track publication by journals and online pre-publication sharing of preliminary data —but not through hyping their results.

Yet the temptation for scientists and their institutions to spin their research to the media, or to go publicity-mongering, is always there. And — as illustrated by the excessive public-relations campaign surrounding Ida, a fossil presented as a missing link in human evolution (see *Nature* **459,** 484; 2009 and **461,** 1040; 2009) — too many in the media will buy into the initial hype.

Such behaviour is corrosive to the process of scholarly scientific communication. Research institutions must not allow it to become the norm.

Case 2 - Scientific Research and the Press

Ms. Newby, a graduate student, is interested in factors that control prion replication, and joins the lab of Dr. Bigshot, an expert in prions. Ms. Newby decides to artificially express the gene coding for prion protein in various mouse tissues, and investigate which ones are conducive to replicating prions upon infection. After three years of work, she finds that in this overexpression model system, some tissues (including muscle) permit prion replication, while other preclude the replication process. She and Dr. Bigshot write up these findings into a paper that is accepted by FancyJournal. A week before the paper is due to appear, Dr. Bigshot provides Ms. Newby with a draft Press Release titled “Scientists find Prions Replicating in Meat” that FancyJournal has prepared.

Ms. Newby is very excited that her first paper has generated so much interest. However, when she reads the press release, she finds that it is almost exclusively focused on one small aspect of the paper: that muscle is capable of replicating prions. Ms. Newby further discovers that the press release fails to mention that this work was done in artificially engineered mice. Moreover, the press release, and various quotes attributed to Dr. Bigshot, exaggerate the dangers of eating meat even though the new work does not provide any reason to believe muscles are a normal source of prions. Recent publicity about the Bovine Spongiform Encephalopathy (BSE) epidemic in British cattle and a resultant rise in Creutzfeld-Jakob Disease in humans, thought to be due to eating the BSE

infectious agent, a misfolded prion protein, which is present in meat, has made people around the world worried about eating beef. Ms. Newby is concerned that readers of this press release will get an inaccurate view of the paper's findings, and she brings up her concerns with Dr. Bigshot.

Dr. Bigshot dismisses her concerns; he says that the press always exaggerates findings, and that the excitement generated will be good for her career. Plus, he says he doesn't have any control over what the press chooses to write, and the actual press release does not contain any false statements.

What are your responsibilites in conveying research to the non-scientific community accurately and fairly?

What are the NIH guidelines regarding communications with the scientific and non-scientific press? Are they different if the communication is oral versus written?

Is there a difference between inaccuracies versus selective reporting and what does this example represent?

What control do authors have regarding press releases prepared by journals?

What recourse do authors have if journals or the popular press mis-represent their research? What if you were contacted by a journal to comment on someone else's new research?

You may find it useful to try a mock interview, using the suggested interview questions below:

Mock Interview between Dr. Bigshot and a writer for the Vegan Society Newsletter, an online publication:

A PI should volunteer to be Dr. Bigshot
A fellow should volunteer to be the interviewer

Two ***Nature*** editorials directly relevant to the topic of the press and scientists:

Caught on Camera, Nature 461:848, 2009

Cheerleader or Watchdog, Nature 459:1033, 2009

CASE 3: Intellectual Property – Why Use an MTA

A Material Transfer Agreement (MTA) is utilized when any proprietary material is exchanged, and when the receiving party intends to use it for his/her own research purposes. Neither rights in intellectual property nor rights for commercial purposes may be granted under this type of agreement. MTAs define the terms and conditions under which the recipients of materials, provided by either the NIH scientist or the other party, may use the materials. Included in the MTA are the requirements that the materials be used for research purposes only and that the materials cannot be used in human subjects. The purpose of a Cooperative Research and Development Agreement (CRADA) is to make Government facilities, intellectual property, and expertise available for collaborative interactions to further the development of scientific and technological knowledge into useful, marketable products.
Contact the Technology Development Coordinator
<http://ott.od.nih.gov/nih_staff/tdc.aspx> for your institute for further information.

There was a real case in the early 2000s in which use of an MTA might have reduced the problems faced by a scientist (Science, 299: 489, 2003). As reported in Science 303:1743, 2004, Dr. Thomas Butler, a professor of microbiology at Texas Tech University, captured national headlines in January 2003 after he reported that 30 vials of plague bacteria that he had originally collected in Tanzania were missing from his Texas Tech laboratory, sparking a bioterror scare and a massive investigation. The government ultimately charged Butler with 69 counts of lying to investigators, which included moving the bacteria without proper permits. He was found guilty of just three plague-related offenses, all linked to a mismarked Federal Express package containing plague samples that Butler sent back to Tanzania. In his defense, Dr. Butler said the "export of bacteria to Tanzania was done for humanitarian reasons ... so that the Tanzanians could continue their research in this area that we started together. The specimens arrived safely. No one was harmed." Judge Cummings noted that "very few cases brought before this court have the potential to impact not only science, medicine, and research, but society as a whole." Butler was sentenced to 2 years in prison for mishandling plague samples that he mailed to Africa, as well as defrauding Texas Tech University, and was required to pay back the university more than $300,000.

Case 3

Part A. Claudia is a postdoctoral fellow in Dr. Smith's lab. She has been using a vaccinia virus expressing PanCa, a novel pancarcinoma antigen, to treat tumor-bearing mice. After publishing her initial results, she received an email from Dr. Barnes, a researcher in California, who requested the virus for some experiments he was doing. She talked with Dr. Smith who agreed that this would be a good collaborative project for them.

She shipped samples of the virus to Dr. Barnes. Six months later, Claudia is shocked to learn about a press release proclaiming that Dr. Barnes is the PI of a new phase I clinical trial using vaccinia expressing PanCa.

What could Claudia or Dr. Smith have done to ensure proper use of the virus?

Should they have used an MTA to provide the samples to Dr. Barnes?

How does one balance between making reagents available, preserving NIH intellectual property rights, and protecting patients from experimental agents?

Part B. Jeffrey is a clinical fellow working with Dr. Jane. They have a clinical trial utilizing a novel vaccine. One of the endpoints of the trial was a serologic analysis for the formation of new antibodies to tumor antigens. The laboratory they had been working with had recently undergone some personnel changes and could no longer do the analysis. Dr. Jane remembered her colleague, Dr. Mann at the University of Wisconsin, who frequently did this analysis. A quick email to Dr. Mann confirmed that he would be willing to collaborate on this analysis.

Since the protocol already is IRB-approved and contains language about doing the analysis, does it need to be amended to state what laboratory is doing the analysis?

Does an MTA need to be executed?

Points to Consider

- Clinical or epidemiological studies are often carried out on very specific populations, who might be identifiable because of their uniqueness – great care is required at the start of the study to ensure that none of the results could negatively impact the study population.

- Care needs to be taken in announcing one's results through the press since there is an inherent conflict between the press's desire for an exciting announcement and the ability of patients and their families, who are generally not scientists, to evaluate whether a new scientific result is directly and immediately applicable to their disease.

- Presenting one's results in any public forum, including a seminar or a meeting or conference, can impact the ability to obtain a patent on a discovery.

- NIH intramural scientists have an obligation to make reagents or other research materials developed in the course of their work widely available for research

purposes. At the same time, they need to be cognizant of the regulations that govern such sharing, and utilize mechanisms such as a Material Transfer Agreement (MTA) or even establishment of a Cooperative Research and Development Agreement (CRADA) to protect the government's ownership of these materials.

Useful resources

Press Releases

NIH Manuscript Clearance Form – which asks if the science is newsworthy
http://www1.od.nih.gov/oir/sourcebook/oversight/pub-clear-form.htm

NIH Manual Chapter 1184 on Scientific, Technical, and Other Professional Information Presented by NIH Employees: Review, Approval, and Distribution
http://www1.od.nih.gov/oma/manualchapters/management/1184/

Woloshin S, Schwartz LM. Press releases: translating research into news. JAMA 287:2856-8, 2002.

Woloshin S, Schwartz LM, Casella SL, Kennedy AT, Larson RJ. Press releases by academic medical centers: not so academic? Ann Intern Med 150:613-8, 2009

Stamm K, Williams JW, Hitchcock NoëlP, Rubin R. Helping journalists get it right: a physician's guide to improving health care reporting. J Gen Intern Med 18:138–145, 2003.

Wilson A, Bonevski B, Jones A, Henry D. Media reporting of health interventions: signs of improvement, but major problems persist. PLoS One. 4:e4831, 2009.

Rensberger B. Science journalism: Too close for comfort. Nature 459:1055-6, 2009.

Sharing of Research Materials

NIH Guide for Sharing Resources
http://www1.od.nih.gov/oir/sourcebook/ethic-conduct/resources.htm

Material Transfer Agreements & CRADAs
http://ott.od.nih.gov/cradas/model_agree.aspx

Model MTA
http://ott.od.nih.gov/forms_model_agreements/forms_model_agreements.aspx#MTACTA

Uniform Biological Material Transfer Agreement (“UBMTA”)
http://ott.od.nih.gov/pdfs/UBMTA_Master.pdf