Scientists Say Genome Canada's Cofunding Rules Stymie Good Ideas

OTTAWA, CANADA—Does it make sense to reject a study of whether poplar trees can help mitigate global warming simply because the trees were going to be planted anyway? That Zen-like question has become a rallying cry for scientists protesting rules about cofunding of research proposals in Canada.

Last month, Genome Canada rejected a proposal from University of Toronto botanist Malcolm Campbell to team up with the Canadian Forest Service (CFS) on an $18.4 million poplar genomics initiative that would have examined the role of the trees as carbon sinks or feedstock for biofuels. It was one of 27 ideas shot down in the first of a two-stage process that focused on the financial, rather than scientific, merits of each application. Some 66 proposals remain in the running for $132 million in this, the third round of funding from Genome Canada.

The rejected scientists fell victim to a flawed process, say 39 prominent researchers who last month released a public letter suggesting that cofunding may be undermining the country’s ability to support cutting-edge research (Science, 24 June, p. 1867). “It does sound like sour grapes,” admits Campbell, who says he was lured home last fall from Oxford University in the U.K. because of the “promising” environment created by a raft of new Canadian programs such as Genome Canada. “But it’s sour because one does not expect when formulating a scientific proposal to have it evaluated first on the grounds of management criteria.”

But Martin Godbout, president of Genome Canada, says the complaints have no merit. Cofunding is essential for stretching scarce resources, he says, and is an integral part of Genome Canada’s mission to collaborate with provincial and local governments, industry, and private foundations.

PESTICIDE TESTING

EPA Draft Rules for Human Subjects Draw Fire

Efforts by the Environmental Protection Agency (EPA) to adopt ethical guidelines for controversial testing of pesticides on humans have run into trouble.

Last week, the Senate, as part of a measure setting the agency’s 2006 budget, voted to bar EPA from using any such studies in its regulatory decisions. The House had passed an identical amendment in May, although differences in the two bills must still be reconciled. And a leaked version of draft regulations has already drawn criticism from scientists who say the rules don’t go far enough. “This document is not about protecting human subjects,” says toxicologist and environmental activist Ellen Silbergeld of Johns Hopkins University in Baltimore, Maryland.

The issue of human testing flared up in 1998, when the Environmental Working Group, an advocacy organization in Washington, D.C., released a report questioning whether it was ethical for EPA to use studies based on volunteers being fed pesticides to help determine how to regulate the compounds. In 2001, EPA turned to the National Academies for advice. The academies’ study, published last year, concluded that some research was acceptable under certain conditions (Science, 27 February 2004, p. 1272).

Meanwhile, EPA had begun to work on rules that would extend a federal ethics code for human research to studies not conducted or funded by EPA. Last week, Representative Hilda Solis (D–CA) and Senator Barbara Boxer (D–CA), who introduced the EPA amendments in their respective bodies, made public a copy that was scheduled for release in August.

Critics are unhappy with the scope of the rules to protect pregnant women and children. The ethical requirements would only apply to studies conducted to identify or quantify a toxic effect, with the results intended for EPA’s use. The agency could still ignore an academies’ recommendation to create an outside expert panel to review proposals for pesticide tests and determine if they would be ethically acceptable. EPA believes that approach would “unnecessarily confine EPA’s discretion to adopt more effective or efficient approaches in the future,” according to the leaked draft.

The agency’s stance does have its backers in Congress. In addition to Boxer’s measure, the Senate passed an amendment offered by Senator Conrad Burns (R–MT) for EPA to stay the course and issue final rules within 6 months.

Growing unhappiness. Malcolm Campbell and other Canadian scientists don’t like how Genome Canada weeds out grant proposals.

—ERIK STOKSTAD
A new National Research Council (NRC) report* finds that although the risks of low-level radiation are small, there is no safe level. That conclusion has grown stronger over the past 15 years, says the NRC committee, dismissing the hypothesis that tiny amounts of radiation are harmless or even beneficial.

The risk of low-level radiation has huge economic implications because it affects standards for protecting nuclear workers and for cleaning up radioactive waste. The Biological Effects of Ionizing Radiation VII (BEIR VII) panel examined radiation doses at or below 0.1 sieverts (Sv), which is about twice the yearly limit for workers and 40 times the natural background amount the average person is exposed to each year. For typical Americans, 82% of exposure stems from natural sources such as radon gas seeping from Earth; the rest is humanmade, coming mostly from medical procedures such as x-rays.

In its last report on the topic in 1990, a BEIR panel calculated risks by plotting cancer cases and doses for survivors of the two atomic bombs dropped on Japan in World War II. Risks appeared to increase linearly with the dose. Based on evidence that even a single “track” of radiation can damage a cell’s DNA, the panel extrapolated this relationship to very low doses to produce what is known as the linear no-threshold model (LNT).

Some scientists have challenged this LNT model, however, noting that some epidemiological and lab studies suggest that a little radiation is harmless and could even stimulate DNA repair enzymes and other processes that protect against later insults, an idea known as hormesis (Science, 17 October 2003, p. 378).

But the 712-page BEIR VII report finds that the LNT model still holds. The panel had the latest cancer incidence data on the bomb survivors, as well as new dose information. Committee members also reviewed fresh studies on nuclear workers and people exposed to medical radiation, all of which supported the LNT relationship. The model predicts that a single 0.1-Sv dose would cause cancer in 1 of 100 people over a lifetime. Such risks should be taken into account, the report cautions, when people consider full-body computed tomography scans, a recent fad that delivers a radiation dose of 0.012 Sv.

At the same time, notes panelist Ethel Gilbert, an epidemiologist at the National Cancer Institute in Bethesda, Maryland, “we can’t really pinpoint” the risk at the lowest doses. The BEIR VII panel examined the latest evidence for a threshold. But it found that “ecologic” studies suggesting that people in areas with naturally high background radiation levels do not have elevated rates of disease are of limited use because they don’t include direct measures of radiation exposures. The panel also concluded that animal and cell studies suggesting benefits or a threshold for harm are not “compelling,” although mechanisms for possible “hormetic effects” should be studied further.

Toxicologist Ed Calabrese of the University of Massachusetts, Amherst, a vocal proponent of the hormesis hypothesis, says the panel didn’t examine enough studies. “It would be better if more of the details were laid out instead of [hormesis] just being summarily dismissed,” he says. The panel’s chair, Harvard epidemiologist Richard Monson, acknowledges that the long-running debate over the LNT model won’t end with this report, noting that “some minds will be changed; others will not.” —JOCELYN KAISER

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* Health Risks from Exposure to Low Levels of Ionizing Radiation: BEIR VII Phase 2
books.nap.edu/catalog/11340.html

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Cofunding works,” he asserts. He also defends the initial screening, saying that it was needed to cope with the heavy workload and that it won’t affect which proposals ultimately receive funding.

The letter writers, including some whose proposals were rejected, argue that a “committee of accountants” scoured applications for any flaw that might be used as an excuse to whittle the field. In Campbell’s case, the agency decided that the CFS contribution amounted to trees that would be planted regardless of whether the project proceeded. “We all sat there, with our mouths agape, literally, for a minute,” says Campbell, describing his team’s reaction in a meeting with the due-diligence review committee. “We were at a complete loss as to how this did not qualify,” he added, noting that the project had passed muster with two of Genome Canada’s five regional genomics centers.

John Bergeron, chair of the department of anatomy and cell biology at McGill University in Montreal, couldn’t understand why a KPMG accountant who chaired the review committee viewed as an apparent conflict of interest the housing of mice for Bergeron’s proteomic studies of liver diseases at a company associated with his team. “It was so weird,” says Bergeron. “You’re sitting there, and you’re saying: What’s going on? This is wacko.”

Godbout doesn’t think so. Most of the projects rejected demonstrated a poor understanding of the goal of cofunding, he says, which is to generate novel funding sources. Another problem, he suggests, is that the results were delivered differently this year: Applicants who failed the financial review were informed immediately that they were out of the running. In previous years they were not notified until the winners had been chosen, leaving some with the impression that they’d failed the scientific review. “Next time, we will again run these two processes in parallel, within the same week,” Godbout announced. But he predicted that “the outcome will be the same.”

Regardless of which projects are chosen, Lou Siminovitch, an eminence grise within Canadian genetics and professor emeritus at the University of Toronto, fears that cofunding programs put too great an emphasis on grantsmanship and wooing potential investors to the detriment of science. “They’re making people spend so much time at their desks that they have no time to innovate,” he frets. —WAYNE KONDRO

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