

Controversial HSC clinical trials report made public

Another episode in the Canadian drama involving the Hospital for Sick Children (HSC), a senior clinical researcher (Nancy Olivieri) and the pharmaceutical company, Apotex, unfolded last month. On December 9th, the hospital Board of Trustees held a press conference to release a review of the events that have plagued HSC for over two years. The 153-page report reveals the depth of the questionable legal, professional and ethical actions of each party in gritty detail, and as expected, has itself become the subject of controversy. On December 10th, Olivieri called a press conference to decry its contents.

The review was conducted by Arnold Naimark, professor of Medicine and Physiology at the University of Manitoba, in association with Bartha Knoppers, professor of the Law Faculty at Montreal University, and Frederick Lowy, former dean of Toronto University's Faculty of Medicine and founder of its Centre for Bioethics.

The controversy centers on clinical trials of an Apotex treatment (deferiprone) for thalassemia conducted by Olivieri (*Nature Med.* 4, 1095; 1998). According to Olivieri, she discovered that the drug undergoes loss of efficacy in reducing body iron levels with prolonged use, and that it has the potential to cause liver fibrosis. In brief, she says that HSC did not support her in trying to make these discoveries public in the face of legal action threatened by Apotex for breach of contract (see *Letters*, page 2).

Although none of the parties involved comes out of the report well, it focuses particularly heavily on the role played by Olivieri. Perhaps the most serious charge against her is that she "observed exacerbation of liver fibrosis" by the drug before December 1996, but did not immediately inform the hospital Research Ethics Board of her findings, with the result that patients continued to receive deferiprone until at least the following February. HSC is referring this charge to the Canadian Medical Advisory Committee. Olivieri denies the accusation.

Sections of the report focus on Olivieri's professional relationships within HSC, and suggest that she was generally unhappy with her employment conditions before the Apotex affair began. It also points out that Olivieri—and colleagues that support her—did not cooperate fully with the Naimark investigation and withheld documents that they claim contain important facts. Prior to the investigation, Olivieri warned that she

would not cooperate and explained at her press conference that she is waiting for a "truly independent, unbiased inquiry" through which to release her information.

Brenda Gallie, HSC Cancer and Blood program head, was by Olivieri's side at the press conference along with 11 international researchers. Gallie described the report as a "shallowly constructed, inexpert, and inaccurate attack on Olivieri's integrity." Olivieri has also received the backing of the Canadian Association of University Teachers, which accuses HSC of unilaterally appointing Naimark to carry out the investigation and refutes its validity.

The report concluded that HSC was remiss in its support for investigators—it

failed to oversee properly two contracts that Olivieri entered into with Apotex, despite the fact that they involved HSC patients. The Board of Trustees will now carry out a second phase of the review aimed at "overhauling policies and procedures relating to third party funding of medical research." The report suggested that HSC establish a "Clinical Trials Secretariat" to provide coordinated and effective policy support. In addition, president of the Canadian Medical Research Council, Henry Friesen, is to lead a national study to develop new guidelines for clinical research. A copy of the report—which is unlikely to be the last word on the matter—is available at <http://www.sickkids.on.ca/HSCWeb/Review/Reviewhome.html>.

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Japan celebrates ten years of the HFSP

The Human Frontier Science Program (HFSP), which supports international research on molecular biology and neuroscience, celebrated its tenth anniversary in Tokyo last month, at the first of three ceremonies planned to mark the occasion. Although, when it was initiated in 1989 some Western governments thought HFSP was merely a political gesture that would be of little scientific benefit, ten years later this skepticism has been replaced with admiration as hundreds of international research groups have received grants and thousands of fellowships have been awarded.

"When I look back at the planning stage of the HFSP when the world science community was so dubious about its significance, the fact that it is so warmly received is almost like a dream for me", says Masao Ito, head of the RIKEN Brain Science Institute. The concept that basic science can be supported by a common funding mechanism among major industrialized countries was very new, he adds.

When the initiative was proposed in 1989 by the then-Prime Minister, Yasuhiro Nakasone, Japan was viewed as a "research parasite" by much of the Western research community due to its economically successful exploitation of research conducted in western nations. "We were being criticized and wanted to contribute to international basic research," says Nakasone.

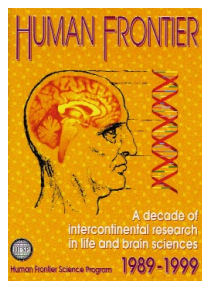
The ambitious plan called for billions of dollars of investment, and Japan has

contributed generously: HSFP, headquartered in Strasbourg, receives more than 75 percent of its annual US\$47 million budget from Japan, with the remaining funding coming from five European countries, the European Union, the United States and Canada. Japan has financed 82 percent (\$298 million) of the program since it was started.

Other countries seem to have benefited from the program disproportionately. Between 1990 and 1998, 32 percent of research grants awardees were from the United States, whereas Japanese researchers only received 16 percent. However, in May 1997, an intergovernmental conference in Washington extended the program for a further five years and issued 'guidelines' for increasing

contributions by countries other than Japan by 2002. Although Japan was seeking funding parity, with an increase in total program funding to \$70 million, it had to settle for a funding 'target' of \$60 million and smaller raises in donations from other countries. Subsequently, the US increased its funding for the Program by \$500,000 bringing its contribution to 9 percent. The EU is set to increase its funding of the program from \$1 million to \$3 million over the next two years. Japan has held its contributions steady over the last few years despite growing economic problems at home and pressure from the Ministry of Finance to cut government spending.

"I think the request of Japan for a 50





Distribution of 1571 awardees that received research grants between 1990 and 1998.

in its peer review than the EU," Milstein told *Nature Medicine*.

Nobel Prize winner John Walker, a senior scientist at the MRC Laboratory of Molecular Biology in Cambridge, agrees with Milstein. "We have a lot of confidence in the HFSP selection procedure whereas we certainly do not in the EU equivalent, which is subject to all kinds of political whims." Walker, an HFSP grant recipient, points out that while members of the trustee and scientific board are known for HFSP,

there is no public knowledge of who evaluates EU grant applications. Moreover, EU grant preparation and participation requires extensive paperwork for the investigator, whereas HFSP documentation is simple and straightforward. "HFSP selects the best young scientists and they're supporting many of tomorrow's leaders in neuroscience and molecular

biology," says Walker.

Grants are worth on average \$240,000 per year, are awarded for three years and are non-renewable. The principle applicant must come from one of the countries backing the program but other participants can come from anywhere in the world. HFSP fellowships provide US\$40,000 per annum for two years to visit abroad to enable post-doctoral scientists to do research at leading international laboratories. Fellows must come from or go to a participating country.

Nobel Laureate Stanley Prusiner says that the fellowships have opened up opportunities for young European researchers to work in his California laboratory: "Without HFSP support most would not have a chance to come to the US." Prusiner is now using a grant from the HFSP to collaborate with scientists in Switzerland, Sweden and the USA, combining genetic and neurological approaches to analyze how prions cause infection.

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percent contribution was a very reasonable one," says Nobel Prize winner Cesar Milstein, a former member of the HFSP scientific committee. Milstein believes that the European Union (EU) money would be better spent on HFSP than many of the research grants it currently gives out. "In my view, HFSP is better administered, less bureaucratic and more rigorous

US public may gain access to research data

A measure quietly inserted into the 1999 US Federal budget bill has some researchers 'crying foul.' By extending the Freedom of Information Act (FOIA) to include raw data from government-funded extramural research, the law would force many scientists to provide their data to anyone who pays a fee and requests them.

Senator Richard Shelby (R-AL), who drafted the measure, explains that "the taxpayers have a right to much of this information, and I believe the results of these changes will be very positive." Not everyone is as enthusiastic. Some fear that the provision—apparently inserted at the insistence of special interest groups—will have far-reaching and possibly disastrous implications for scientists.

The FOIA, implemented in 1966 to improve accountability, was not designed to cover scientific data and as a result the White House Office of Management and Budget (OMB), which must formulate regulations to enforce the new measure, will be working in uncharted territory. On December 7th, Congressman George Brown (D-CA), who opposes the provision, sent a letter signed by 23 members of Congress to OMB to urge caution in crafting the new rules.

The letter, a copy of which was obtained by *Nature Medicine*, identifies several areas

of concern. Although the FOIA includes protections for certain types of information, it is unclear whether these would be sufficient to guarantee patient confidentiality in medical studies. "Even if they were," the letter states, "we believe individuals will be reluctant to divulge sensitive personal information knowing that this information effectively becomes the property of the U.S. Government as an official record."

Brown also argues that the measure could facilitate the theft of intellectual property. The timing of data release could have a dramatic impact on publication and peer review, possibly placing US government-funded researchers at a disadvantage compared with their counterparts in other countries. And because many scientists receive funding from a combination of government and non-government sources, determining which data fall under the FOIA may pose a considerable challenge.

Wendy Baldwin, Deputy Director of Extramural Research at the National Institutes of Health, agrees that the measure raises a host of questions. "Issues that will need to be clarified are the definition of 'data,' the timing of the release of data, protection of confidentiality and privacy issues, concerns regarding intellectual property and the costs of compliance...

and those are just the first to come to mind," says Baldwin.

The measure could also lead to harassment of researchers. George Thurston, a professor in the Department of Environmental Science at New York University, argues that industry groups, activists and lobbyists could abuse the measure by reinterpreting raw data out of context to discredit studies. "Thus, policies as democratic as [the FOIA] can be subverted and employed as mechanisms for vested interests to 'attack the messenger' when the research is financially or politically unwelcome," Thurston told *Nature Medicine*.

Michael Gough, Director of Science and Risk Studies at the Cato Institute, a conservative think-tank in Washington, DC, counters that good scientists need not worry: "Either your data are good and your interpretations are justifiable, or you're going to hide behind these things." He concedes that the possibility of harassment is real, but asserts that additional legislation could fix problems that might arise.

The OMB is expected to release its proposed regulations for comment soon, and sources close to the issue estimate that rules could be finalized within six months. No matter what form the details of the regulations take, Baldwin states that "there will be considerable burden both on the agencies and on the researchers."

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