CANADA

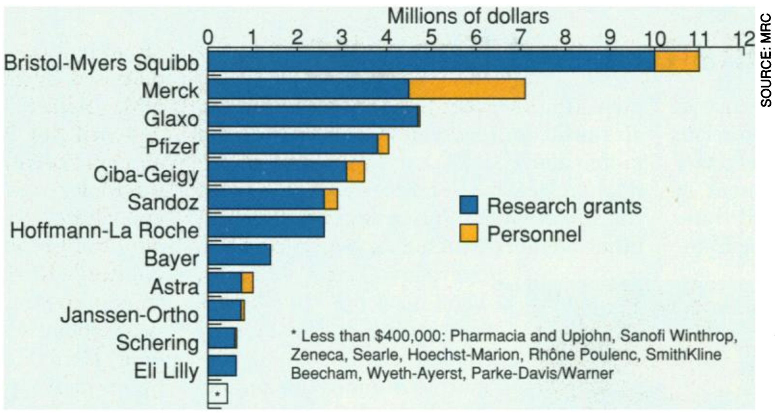
Drug Industry Misses Target For Funding Work on Campus

OTTAWA—The agreement was to have been a simple quid pro quo. In exchange for help from academics in persuading Canadian legislators to extend patent protection for brand-name drugs, the 62 members of the Pharmaceutical Manufacturers Association of Canada (PMAC) would spend $200 million over 5 years on university research, including a "significant" amount on personnel and training. The money would be doled out through a new partnership between the PMAC and the Medical Research Council (MRC), the government's chief agency for funding biomedical research. The MRC even agreed to sweeten the pot by spending $1 for every $4 that a drug company funneled into a peer-reviewed, approved project.

The drug companies got what they wanted—20 years of protection and an end to the practice of companies making cheap knock-offs for only a royalty payment. But three-and-a-half years later, they haven't delivered on their end of the bargain: They have spent just $65 million—barely half—of the promised amount to date, including many projects that were in the pipeline before the plan was created. In the ongoing debate over the reasons for that funding shortfall, the only consensus is that the arrangement, known as the PMAC/MRC Health Program, hasn't gone according to plan.

Academic researchers aren't just angry about the drug companies' failure to pay up. They also resent the fact that the MRC, by its partial matching of funding, is supporting industrial projects rather than academic research during a period of reduced government funding. In turn, the PMAC has complained that the MRC's "extremely cumbersome" peer-review process has inhibited their investment. And the MRC, while defending its review process, is unhappy about the tiny share of the money for these projects, about $6.4 million, that has been spent on personnel and training. Two task forces have failed to resolve the disagreements, which include spats over whether money spent on required clinical trials should count toward industry's contribution and whether the MRC's peer-review process can properly evaluate commercially oriented research.

Indeed, peer review lies at the heart of the dispute. Even academic researchers who are veterans of MRC reviews complain that the evaluation process, as McGill University professor of medicine Alan Tanenhouse puts it, has been "an enormous pain in the ass." Three years ago, Tanenhouse, director of the bone metabolism division at Montreal General Hospital, won glowing marks from a peer-review panel appointed by the government's National Health Research Development Program (NHRDP), the primary source of funding for his $9 million study of risk factors associated with skeletal fracture and osteoporosis. Those monies included a $1.76 million contribution he lined up from Merck Frosst Canada, Eli Lilly Canada, and Procter & Gamble Pharmaceutical Canada.



Uneven load. A few drug companies are putting up most of the money for Canada's new Health Program.

But before he could gain access to the industrial monies, the companies and the MRC "encouraged" him to roll the project under the new health program. "I had just had it reviewed by NHRDP," he says, "and [the MRC] simply repeated the process." While his protocol eventually passed the test and qualified for an additional $400,000 from the MRC, Tanenhouse says it is frustrating to line up industrial collaborators and then subject them to additional scientific scrutiny. The MRC's peer review "is enormously cumbersome," he says. "But then, so is everything MRC does."

The PMAC says it's concerned that the MRC has brought an overly academic attitude to the peer-review process. "There's a total lack of understanding … about how the industry functions," says PMAC president Judy Erola. "It's like someone asking GM to start making bicycles." For example, she notes that reviewers appear to pay little heed to corporate timetables or linking research to corporate objectives.

Alan Bernstein, a molecular geneticist at the University of Toronto and director of Mount Sinai Hospital's Samuel Lunenfeld Research Institute, says that tensions between companies and the MRC were heightened when MRC panels rejected 60 of the first 101 industrially sponsored applications as scientifically flawed. Bernstein, who won a $10.5 million renewal for a Bristol-Myers Squibb–funded project to create mutant mice with knockout genes relating to the cardiovascular system, cancer, early development, or blood formation, believes part of the reason is that a project which a firm finds compelling may be seen by academics as pedestrian. "What peer review can tell a company is whether this is good science or not, not whether it fits in with its own strategic objectives," says Bernstein. Matthew Spence, president of the Alberta Heritage Foundation for Medical Research, says the high rejection rate shows that drug companies are willing to support projects that aren't at the scientific "cutting edge" but that still deliver the desired goods.

There are also widespread reports that scientists with existing corporate support are reluctant to submit proposals to the Health Program for fear that knowledge of such support will reduce their chances of success in subsequent MRC grant competitions. No scientist has publicly confessed to such conduct, however, and MRC President Henry Friesen says he has little patience with scientists who won't submit to peer review because they've been "double-dipping," or with industrial managers who sign off on less than compelling protocols. "Cumbersome is sometimes also used as a rationalization for disappointment," he says.

But Friesen is upset that when the MRC asked for $40 million over 3 years to fund 10 to 12 scholars and 40 to 50 fellowships a year, PMAC came up with a one-time "donation" of $1 million. Erola says that industry is not responsible for maintaining core university competency: "We're not a substitute for government cutbacks."

Without that additional money, however, many academics view the MRC's financial contributions to the program as an unnecessary subsidy of industrial research costs. There is a perception that the program has "ended up creating a sweetheart arrangement to get [industrial] research done in the academic environment at virtually no cost," says Lewis Slotin, managing director of the

NeuroScience Network, a national center of excellence studying neural regeneration and recovery. The MRC has no business using limited resources on profit-driven research, adds Montreal Neurological Institute director Richard Murphy. "MRC cannot afford to take money out of its current coffers and try to lever this targeted money. ... MRC's role is to fund excellent science."

Friesen counters that the MRC can do more than that. Its funding provides incentives for industry to invest in research, he says, as well as promoting university-industry collaborations.

Despite the continuing controversy, PMAC and MRC officials may be headed toward at least a temporary reconciliation. The two groups are forming a president's panel to review megaprojects, starting a media campaign to tout the program, and creating an operations committee to tackle such ongoing disputes as accounting for corporate sponsorship of required clinical trials. As for funding, Friesen forecasts "explosive" growth in industrial outlays for the program over the next 2 years, while Erola says a bevy of new investments are "in the pipeline."

But the real impetus for the reconciliation and the apparent increase in funding may be political. In February, a parliamentary committee will review the patent legislation, including industrial spending under the Health Program. In addition, the generic drug industry, supported by complaints about rising drug prices, has launched a massive lobbying campaign to force Parliament to retreat from the 1992 law.

But opponents face an uphill battle: Overall PMAC spending on R&D (primarily clinical trials) rose last year by 11%, to $624 million, prompting Science Minister Jon Gerrard to say that the government is "satisfied" with PMAC outlays. And the big drug companies have a potent political issue in their favor: Quebec separatism. With separatist forces "rising in arms" at the hint of revisions, explains one member of the ruling Liberal Party, "there's no way in hell we'll take on the Montreal-based drug industry." That unwillingness may cool PMAC's newfound ardor for the Health Program and leave it little changed once the political spotlight has been turned off.

–Wayne Kondro

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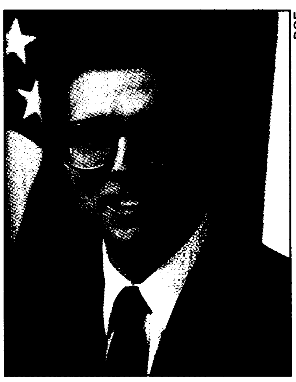
CABINET APPOINTMENTS

Clinton Picks Peña to Lead Energy

Ethnic politics won out over experience in the energy field as President Bill Clinton late last month picked Transportation Secretary Federico Peña to lead the Department of Energy (DOE). The choice surprised those who were expecting Clinton to name Elizabeth Moler, currently the chief of a federal energy regulatory body. And it disappointed supporters of mechanical engineer Chang-Lin Tien, chancellor of the University of California, Berkeley, who was touted by congressional Democrats from California. With the earlier selection of Chicago lawyer William Daley as Commerce Secretary-designee, Clinton has filled his second-term roster of major science and technology officials.



DOE

Loyal aide. Peña kept a low profile at transportation.

DOE officials and congressional sources say they are not sure what to expect from Peña. "He's a blank slate," says one DOE manager. Peña's involvement with energy issues is limited to his dealings with DOE's Rocky Flats facility and with the oil and gas industry during his time as a Colorado legislator and mayor of Denver in the 1980s. One Transportation official who has worked closely with Peña characterizes him as a micromanager who takes his cues from the White House. "And he is not a political animal or a dealmaker," the official adds. That loyalty, combined with the fact that he's a known quantity and a Hispanic, apparently pushed him to the top of the president's list. "It was obviously a political choice," says one congressional staffer.

Peña spent the first term leading a department that oversees the nation's highways, air traffic, railroads, and Coast Guard with more than 100,000 employees and an annual budget of $36 billion—roughly twice the size of DOE. Unlike several other Cabinet members, including departing DOE Secretary Hazel O'Leary, Peña is said to have kept a low profile and made only modest changes to the department during his tenure. He chopped the number of employees by about 10%, pressed for greater use of advanced technology in U.S. road and highway construction, and emphasized transportation safety. "He did a pretty effective job," according to one Senate staffer. He drew flak, however, for his handling of airline disasters and for making slow progress in revamping the Federal Aviation Administration, congressional aides say. He had already announced his intention to step down from the post.

Peña's status should ease his second encounter with the Senate. Even so, Senator Frank Murkowski (R–AK), who chairs the Energy and Natural Resources Committee responsible for the confirmation, warned the day before Peña's nomination that the job demands someone "with the proper professional background and a stiff backbone."

Clinton said at a White House briefing that he expects Peña to continue the efforts begun by O'Leary to streamline DOE, which he characterized as a "diverse and sprawling operation." The nominee declined to discuss any changes in the department, but one issue on his plate is a major restructuring of DOE proposed by Senator Pete Domenici (R–NM) (*Science*, 13 December, p. 1831).

Until just hours before the president's announcement, the front-runner for the job was Moler, who chairs the independent Federal Energy Regulatory Commission. Administration officials say that one factor in Clinton's final decision was unhappiness among Hispanic groups who feared losing two Cabinet seats—Peña and Housing Secretary Henry Cisneros, who is being replaced by one of his deputies, Andrew Cuomo. Another leading candidate for the DOE job was thought to be Tien. Last month, 14 California lawmakers urged the president to choose him for the post, citing his achievements as a mechanical engineer and an experienced administrator.

Clinton also recently named William Daley to take over from Mickey Kantor as Commerce secretary. Daley will inherit the controversy over a variety of Commerce programs that involve partnerships with industry, particularly the Advanced Technology Program (ATP). These have drawn heavy fire from Congress in the past 2 years, and Republican lawmakers are expected to be gunning for them again next year.

Daley is a Chicago lawyer with limited experience in the research and technology fields, although he did represent a group lobbying for the R&D tax credit extension in the early 1990s. "And he did a very good job," says Ken Kay, an attorney with the Washington law firm Podesta Associates, who was part of that effort. Kay says that Daley is pro-business and can work in a bipartisan manner despite his background as a partisan Democrat. Both of those traits may prove important for the future of controversial R&D programs like ATP.

–Andrew Lawler