pilot study had followed the diet for more than 3 years. He added that the Women's Health Trial is designed with some flexibility: Even if the difference in fat consumption narrowed by as much as 50%, it would still be enough to provide a valid answer.

■ **Credibility.** Even assuming the women are eager to follow instructions, some board members said, it won't be possible to monitor them objectively. Their behavior will be checked by "self-reporting." Greenwald conceded that NCI has not yet found a biomarker that can tell whether a person has adhered to a prescribed diet, but Maureen Henderson, principal investigator for a pilot version of the trial at the Fred Hutchinson Cancer Research Center in Seattle, says that average cholesterol data can be used to keep track of group behavior.

■ **Educating the poor.** It is difficult enough to get middle-class people to change habits. This trial would face an additional challenge: It would have to motivate poor black and Hispanic women as well. By law, public health studies must include a "representative number" of minority and poor participants, and NCI's plan calls for one clinical center to focus on blacks and another on Hispanics. But board members, including Erwin Bettinghaus of Michigan State University, predicted that if the success of the study depends on getting poor people to follow the protocol, it will fail. Others suggested it would be hard to get the oldest participants, some of them over 80, to keep good records. These issues prompted a call for additional research.

■ **Ethics.** Some board members pointed out that the NCI has already declared that everyone should reduce fat intake to 30% of total calories to lower the risk of cancer. Given that this is federal policy, would it be right to allow women in a clinical trial to adhere to a less rigorous diet? Korn said it would be "unfortunate if people in 2003 were to look back at this in terms of a 1990s Tuskegee trial"—a reference to the syphilis study in which researchers withheld medication to enhance the quality of data. Criticism of this kind is unfair, says Henderson. She argues that in preventive studies like this, the control group always gets the usual and customary treatment—which in this case would be a pamphlet describing good dietary habits. The fact that some women would get extra help does not mean that the controls would be getting substandard therapy.

All of these issues will be reexamined as NCI officials try to respond to the questions that arose in the advisory board. But if Congress takes an interest—as Schroeder expects—it may not be able to take 3 years to get the answers. ■ ELIOT MARSHALL

Deficits Trip U.K. Science Funding Agencies

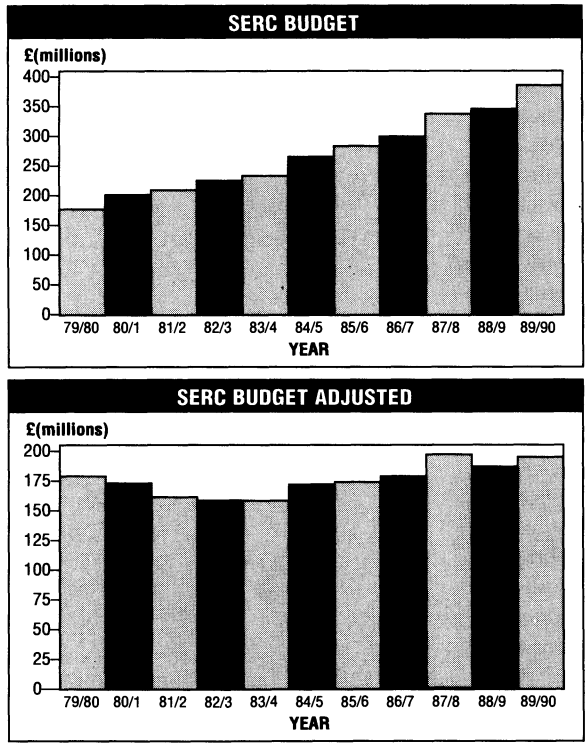
The Science and Engineering Research Council is the latest agency to be hobbled by a financial shortfall

A WAVE OF RED INK IS WASHING OVER BRITish science funding—with dire results for government-supported researchers. The Medical Research Council recently announced a freeze on recruitment and grants to make up for a deficit of £3.5 million. The Agricultural and Food Research Council is preparing to axe 300 jobs because of its deficit. And now the Science and Engineering Research Council (SERC), the largest source of government funds for nonmilitary research in Britain, facing a £40-million deficit, has frozen all new grants and fellowships for science students. In addition, SERC is embarking on a reconsideration of future priorities that may entail pulling out of "big science" projects that involve international collaborations. "There should be no stone unturned," said Sir Mark Richmond, SERC's chairman since October. "We have got to get our spending down by £40 million."

SERC's difficulties stem largely from "underindexation," government inflation forecasts that have consistently turned out to be low. Last year, the treasury figured 5% inflation into its grant to SERC of £407 million. Universities, however, agreed to a pay increase of 11% for researchers, and SERC is obliged to pay many researchers according to university pay-scales—but has no voice in salary negotiations. "Almost half the amount that we will be overspent is [the result of] underindexation," said Geoff Heaford, spokesman for SERC. Much of the other half is due to currency fluctuations that make Britain's contributions to international collaborations such as CERN more expensive than anticipated.

SERC's immediate cheese-paring consists of "natural wastage" of staff, along with halts on new research grants and training for doctoral candidates. Staff vacancies will not be filled, although there will be no layoffs—because SERC cannot afford severance pay. Research grants last year totaled £150 million, 37% of the budget. This year's first round of grants ended last month, and some lucky winners have already received letters notifying them of their awards. Those "will be honored," says Heaford. The rest will miss out: Their applications will go into the second round—next spring. Richmond acknowledges the unfairness of this expedient, adding that "the tragedy is that much excellent work will be jeopardized."

Among the largest awards to be frozen are three for Interdisciplinary Research Centers, large units designed to tackle academic problems that yield technologically exploitable results. One is for work on biomedical materials, one for work on biomechanical engineering, and the other for studies of nervous systems of simple animals. William Bonfield, head of the department of materials at Queen Mary and Westfield College at the University of London, and director designate of the IRC on biomedical materials, says he is "very hopeful" a rescue can be mounted. "It's obviously im-



Not so sterling. *The SERC budget (above) has grown steadily, but adjusted for inflation (below), it has been essentially flat.*

portant to reduce health care costs with new materials," Bonfield says.

Richmond is believed to be concerned about the long-term commitment to IRCs, which receive funds for 6 years, with a review after four. A molecular biologist, he is less wedded to the idea of big science than some of his predecessors at SERC have been. Some research groups have become IRCs when they might have been better supported by smaller grants, Richmond says. He is enthusiastic about shifting money from big projects to small grants and studentships. "I think that's the way in which really bright young scientists emerge," he told reporters.

The budget crunch and the emphasis on small grants may endanger some collaborative projects that the U.K. has a current or planned role in. Participation in the efforts to build a new 8-meter telescope, for example, may go down the tubes. Two schemes are under consideration, one involving the U.S. and Canada, the other Spain. But while Britain's tab for either project is likely to be around £20 million, the immediate savings if it is scrapped are minimal—around £1 million. Likewise a planned Anglo-German gravity wave detector, pencilled in at £5 million, offers no savings now, because the money was not due to be spent for a couple of years.

Other ventures that might wind up being axed are collaboration in Lyman-FUSE, the U.S.-Canadian far-ultraviolet telescope, and Spectrum-X, a joint Soviet-European x-ray astronomy mission; Britain's part in the European Space Agency program; and the neutron source at the Institut Laue-Langevin (ILL) in Grenoble, France. ILL costs SERC £8.5 million a year, and the collaborative agreement with France and Germany is due for review next year. SERC already has a neutron source, Isis, at its Rutherford Laboratory, and Richmond wants SERC to take a hard look at its participation in ILL.

None of these dire scenarios, however, will come to pass immediately. SERC has set up "mini-policy groups" in each of its five subject boards to find savings now and examine future options. The policy groups will then put their suggestions to the full council. A meeting is scheduled for 19 December, but sources say it looks "increasingly unlikely" that any review will be available then. SERC's council is not due to meet again until February. ■ JEREMY CHERFAS

Parallel Track: Where Should It Intersect Science?

Boston—By now, most scientists are aware of the heartrending conflicts involved in AIDS drug testing—the tension between the need for solid clinical information and the desire to provide hope for dying patients. Many biomedical researchers hoped mechanisms such as "parallel tracking" would resolve the tension—scientific data would be collected as usual in clinical trials while promising therapies were made available through simultaneous release in exchange for an agreement by physicians that some data would be collected on that track as well. But, as a novel conference called "Expedited Access to Unproven Pharmaceuticals: Risk, Regulation, and Personal Autonomy" revealed last month, parallel tracking raises as many questions as it answers.

In particular, there was sharp debate at the meeting between AIDS activists and researchers over how much data should be collected on the parallel track. Activists, it turns out, fear innovative programs may grind to a halt as physicians struggle to cope with the paperwork required by data collection. Furthermore, clinicians at the conference were told that parallel tracking represents a fundamental shift in the accepted model of drug testing—a shift in which patients assume far more of the risk of unproved drugs.

Developments like these could turn traditional drug trials into anachronisms in the case of life-threatening diseases. The standard model for drug testing includes small phase I studies to evaluate safety and dosage; randomized phase II clinical studies of effectiveness; and large phase III trials to compare the drug to others. Rigid adherence to that system is a "sacred cow needing to be knocked down," says Thomas Chalmers, associate director of the Technology Assessment Group at the Harvard School of Public Health.

In fact, the sacred cow is already on its knees, as has been apparent since AZT was given free of charge to thousands of AIDS patients, largely through the efforts of AIDS activists, while clinical trials of the drug continued. The first such release was carried out under an existing FDA mechanism for expanded release called a treatment IND. Parallel tracking will expand the FDA exception and institutionalize it by making new drugs available to people with HIV-related disease who can't participate in a clinical study because they don't meet eligibility requirements or don't live near a trial center.

> ***"If I had malignant melanoma. . .I would want access to [an experimental] drug, even though it might kill me."***
>
> —LOUIS LASAGNA

But despite all the publicity it has received, the parallel tracking system has not yet been formally instituted. Instead, the surgeon general's office published a draft report on it last May. That report, Assistant Surgeon General James Allen said at the conference, has elicited more than 1200 comments, the majority amounting to "Sounds good. Go ahead." For the moment, however, Allen said, "The closest thing around to parallel track" is the program of expanded access to the anti-AIDS drug dideoxyinosine (ddI). And that program is seen differently by activists and researchers.

Since expanded access is aimed at treatment—not research—little data should be collected, Mark Harrington, an activist with ACT-UP, argued at the Boston meeting. Harrington claimed that physicians administering ddI under the current expanded access program had been overwhelmed by efforts to collect the data they had been asked to gather.

Researchers had a different concern. "It would be a shame," says Susan Ellenberg, "to waste the opportunity to collect some simple data on adverse drug reactions, safety and simple efficacy." Ellenberg, who heads the National Institute of Allergy and Infectious Disease's AIDS biostatistics research board, notes that before ddI went into expanded access, fewer than 100 patients had been taking it in clinical trials—a sample so small that fatal toxicities might have been missed. In expanded access almost 14,000 people have received the drug.

One solution to some of these problems might be to come up with a third track—a parallel track version of clinical trials that is compatible with expanded access. Such an effort was recently made by Ellenberg and 21 of her colleagues, led by David Byar, director of clinical trials at the National Cancer Institute (NCI). In a recent paper in *The New England Journal of Medicine*, that group called for large, simple trials of