these weakened strains are causing disease. All of them have found that the virus did not simply repair its damaged genetic material, but the weakened strains did undergo genetic changes during the course of the infections. It's unclear, however, whether these changes made the virus more virulent, or whether the animals' immune systems simply could no longer contain the weakened virus. It's also possible that the animals are infected with other pathogens that compromise their immunity. "Scientifically, it's extremely interesting," says Desrosiers.

Ruprecht makes sense of all these data with what she and her co-workers call the "threshold hypothesis," which they published last year in a supplemental issue of the journal *AIDS* (see graph). According to this theory, an attenuated virus must copy itself at a high enough rate to trigger an appropriate immune response, but not so high that it causes disease. (Obvious as this theory may sound, Ruprecht notes that the weakened poliovirus used in that vaccine replicates at the same rate as wild poliovirus.) Ruprecht theorizes that the immune systems in her sick animals at first kept the attenuated SIV below the disease threshold, but then, for an unknown reason, lost control of the virus. Lewis, who holds a similar view, notes that this creates a conundrum for the attenuated AIDS vaccine strategy. "The problem is, the safer you make the virus, the less it grows and the less effective it is," he says.

Desrosiers agrees, but thinks it may be possible to find the happy medium without putting humans at too high a risk. He points out that the attenuated vaccines he's been working with lately are much weaker. "I've not been advocating for years anything that was just delta-*nef* or even delta-3," he says. Currently, his lab is testing delta-4 SIVs that he says are "considerably more attenuated than delta-3." Ultimately, he says, "it really turns into a risk/benefit equation of what is acceptable." An attenuated HIV vaccine, he notes, should only be offered to people who are at a high risk of becoming infected by the virus: "This vaccine is not for babies."

For the first human trials, Desrosiers argues that researchers must err on the side of caution: "If we're going to make any mistake, let's be too far down on the scale of attenuation." Even then, he acknowledges that the vaccine may still cause adverse events. "Is it going to be absolutely, 100% safe? Forget it. It never will be. If you put it into enough people, there will be problems. That's true of every live, attenuated vaccine." But, he says, the question boils down to what the likelihood is of the person becoming naturally infected by HIV versus becoming injured by the vaccine: "We're never going to know until we put it into humans, and that's why people have different best guesses."

–Jon Cohen

SYNCHROTRON RESEARCH

Berkeley Facility Ranks Low On Advisory Panel's List

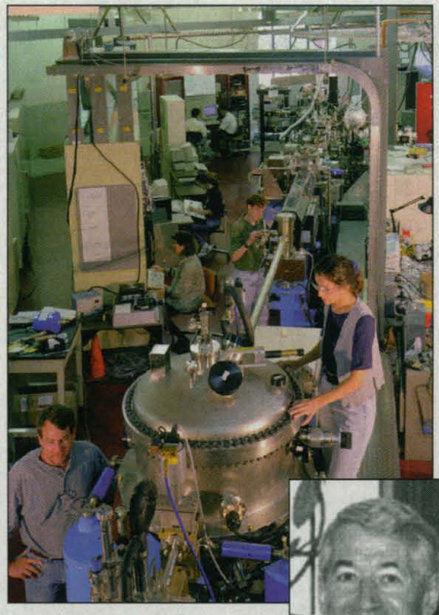
BOSTON—When a burgeoning field runs up against a stagnant budget, something has to give. Next week a Department of Energy (DOE) panel reviewing U.S. synchrotron research facilities is expected to suggest that the government put the squeeze on the Advanced Light Source (ALS) at Lawrence Berkeley National Lab in California rather than on Stanford's Synchrotron Radiation Laboratory (SSRL) and the National Synchrotron Light Source (NSLS) at Brookhaven National Laboratory in Upton, New York. The Advanced Photon Source (APS) at Argonne National Laboratory near Chicago, meanwhile, would continue operations, but without major upgrades in the near future. These and other recommendations promise to trigger a lively debate when they are aired on 8 October at a meeting in Washington, D.C.

Earlier this year, DOE asked the panel, led by Robert Birgeneau, science dean at the Massachusetts Institute of Technology, to recommend priorities for synchrotron radiation research in the coming decade. A wide array of materials, biological, and environmental researchers are clamoring to use machines that generate beams of x-rays to probe matter (*Science*, 8 August, p. 756). But given projections of a flat budget, the department faces some hard choices in deciding the proper level of support for two aging facilities—SSRL and NSLS—two expensive ones recently brought online, and initial planning for a next-generation facility.

The panel's solution is to look favorably on proposed upgrades to the older facilities, to reject immediate expansion plans by ALS and the new $812 million APS at Argonne, and to raise questions about the payoff from ALS, according to panel members who requested anonymity. They also urge DOE to spend modest sums planning next-generation machines so that it can make a decision in the middle of the next decade.

The biggest hue and cry over these conclusions is likely to be raised by managers and users of the $100 million ALS. The panel questioned the type and quantity of work there, as well as the lab's $100 million request for upgrades and a boost to operating funds. Unlike the other synchrotron sources that produce hard x-rays, ALS produces soft x-rays that are used for specialized areas such as surface science. It was built with novel applications in mind, such as industrial uses for computers and advanced optics, some of which are just getting under way. That uncharted territory, says one DOE lab official, makes it "a rich area to explore, but difficult to exploit."

It's also expensive. ALS's annual budget of $33 million is 50% higher than Stanford's, for example, while its user community of 300 is less than half the size. ALS supporters argue that it is a unique source that hasn't had a chance to demonstrate its worth. But as one panel member points out, "just because you are unique doesn't mean that you are necessarily [being put] to good use."



S. ADAMS/LBNL

Dim prospects? Birgeneau panel questions value of soft x-rays delivered by Lawrence Berkeley's Advanced Light Source for work in surface and materials science.

Panelists say they are not recommending closing the 4-year-old machine. "It's not our proposal to drop ALS out of the picture, but to reexamine that area of science and what can be done," says one panel member, who adds that other facilities like Brookhaven's NSLS are capable of producing soft x-rays. "Somehow we got the cart before the horse," the scientist adds, by building a facility without understanding the kinds and numbers of users it would draw. "I don't want to see it go away," he adds. "But we were struck by the comparison of ALS against the others, and it falls to the bottom."

Birgeneau panel members looked more favorably on the science at Stanford Linear Accelerator Center's SSRL in Menlo Park, California. The Stanford lab "has put effort into making itself a true user facility" by increasing the reliability of its beamlines and encouraging a new generation of users from many fields, says one panel member, "so I'm not surprised they came out well." Stanford officials told the panel they want to spend $150 million above their current costs to increase brightness and beamlines.

The panel findings also will be a relief to managers and researchers at Brookhaven's NSLS, which has an annual budget of $29 million. In contrast to Stanford, the Brookhaven source is still struggling to make itself more attractive to nontraditional users, such as biologists and environmental researchers. But panel members say it stands out because of the sheer number of researchers who flock to the site—56% of all DOE synchrotron users—and the high number of citations in the literature for research carried out there. "Brookhaven needs to upgrade and become a real user facility," one panel member says. "With APS opening, it has to change the way it does things." Facility managers propose a $65 million boost for a host of upgrades, plus some additional operating money.

The Birgeneau panel also endorses continued operation of the APS, which opened last year, but rejects its pleas for pricey upgrades. "Those fell on deaf ears," a panel member says. Argonne officials argued for $216 million in new lab offices, beamlines, and other additions, along with $5 million a year extra for operating the facility. But because APS is still in its infancy and already has the largest annual budget of all the sources—$81 million in 1997—panel members argued against major immediate upgrades.

The panel was also asked to determine the importance of a next-generation facility, one that could use free-electron lasers, for example, to generate x-rays. "We tried to make sure we carved some money out for [the next] generation so a decade from now we'll have a good idea what should be built," one panel member says. The committee discussed ways to help researchers conduct their work at the facilities, such as by offering more lab-provided equipment, and other sources of funding, both within DOE and at other federal agencies.

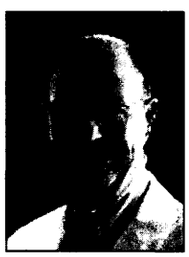
DOE's Basic Energy Sciences Advisory Committee meets next week to consider the panel's findings. If approved, the recommendations will then go to DOE officials. Birgeneau acknowledges that the report "doesn't make everyone happy," but he and other panel members believe their views eventually will prevail. "The priorities are not a defense of the status quo, but what serves the field best," another panelist says. "My suspicion is the community will look at this and say 'Hallelujah.' "

–Andrew Lawler

PROFESSIONAL SOCIETIES

Furor Over Company Deal Roils AMA

The days may be turning cooler across most of the country, but at the American Medical Association's (AMA's) offices in Chicago, it must feel like the summer heat wave never ended. Since mid-August, the 150-year-old organization of physicians has been fending off a barrage of criticism from the public and its own members after announcing, then canceling, a multimillion dollar contract to allow the Sunbeam Corp. to put the AMA logo on its health care products. Two weeks ago, the AMA purged three top-level executives involved with the deal. And last week, as the criticism continued, the AMA vowed to set new ethics guidelines for business ventures in an attempt to correct what AMA board of trustees chair Thomas Reardon calls "a breakdown of policies and procedures."



Course correction. Trustees chair Reardon.

The controversy was touched off on 12 August, when the AMA announced it would lend its name to heating pads, blood pressure monitors, and other products made by Sunbeam—products whose effectiveness the AMA would not have tested. The AMA was to receive royalties estimated at several million dollars for the deal, the AMA's first product endorsement since 1955. The move sparked a national outcry—including a blistering *New York Times* editorial—at a time when health care is increasingly viewed as a bottom line–oriented business. The AMA responded by announcing on 21 August that it would cancel the deal. Then came another blow: a $20 million breach-of-contract lawsuit by Sunbeam.

Relentless scrutiny has continued, including articles by the *Chicago Tribune* and the *Chicago Sun-Times*, which has reported on earlier, questionable proposed AMA deals—such as a canceled plan to take $800,000 from Procter & Gamble for co-sponsoring a fitness program linked to the Olympics—and pressure from affiliated medical societies for an investigation. On 19 September, the AMA trustees announced the immediate "departure" of chief operating officer Kenneth E. Monroe, business and management group vice president James F. Rappel, and vice president for marketing Larry Jellen. "There was a systemic breakdown of the AMA's internal systems, designed to ensure that arrangements with other entities are in accord with AMA policy and that significant initiatives are brought before" the trustees, the AMA explained in a statement. "The board never saw the contract [for the Sunbeam deal], discussed the contract, or asked about the contract," claims Reardon. "The board heard only that there was a preliminary discussion."

Last week, the AMA said it is forming a panel of staff, board, and House of Delegates members, and outside experts to draw up ethics guidelines for its business arrangements. An internal group is also examining the AMA's existing agreements. "We will look at everything we're doing," says Reardon, who notes that the AMA already has many "sponsorships." These range from Web sites on AIDS paid for by drug companies, to educational brochures on child-restraint seats paid for by General Motors, to media conferences in Washington, D.C., supported by drug companies to inform journalists about topics such as assisted suicide. Such deals help supplement the AMA's income from member dues, which account for about one-third of its operating funds. And, says Reardon, while "we certainly agree to" a policy of no product endorsements, "if we don't use these sponsorships, we're going to cut out a huge number of services for the public."

Not everyone thinks the AMA has clearly forsworn endorsements. "Every day it's a different story," says Michael Grodin, a medical ethics professor at Boston University. Last month, Grodin and a BU colleague began collecting e-mail signatures on a statement calling for AMA to "avoid involvement in the marketing or advertising of particular products or services through endorsements or other arrangements." And some think only the 485-member House of Delegates can be trusted to set new policies. "Whether a blue-ribbon panel of board and staff can credibly do the job is of concern," says Chicago physician Ann Dunlap.

Arthur Caplan, a bioethicist at the University of Pennsylvania, Philadelphia, notes that the AMA's business dabblings are "not an isolated thing." For example, the American Heart Association allows its name to be stamped on orange juice containers, and the Arthritis Foundation's name appears on Tylenol, for which the foundation takes a cut of sales. But the proposed Sunbeam deal is "kind of a supernova in the galaxy" of such business deals, Caplan says, adding "there are a lot of hard questions that need to be asked here."

–Jocelyn Kaiser