no longer submit the agency’s standard 15-page application. Instead, they write a four-page preliminary proposal that is stripped of many details about methodology, budgets, references, and collaborators. It is reviewed by three scientists rather than the usual five. (The slimmer proposals don’t require so-called ad hoc reviewers with special expertise, NSF decided.) And program officers typically invite only about one-fourth of preliminary applications to proceed to the second round, where a review panel vets a full proposal. About one-quarter of the full proposals are ultimately funded (see table, p. 528).

Other federal agencies also use preliminary proposals, GAO notes. But they’ve been less effective at reducing workloads because the initial assessment isn’t binding or because the agencies filter out a far lower percentage of preliminary proposals. Other variations that GAO cites offer even less relief: The National Institutes of Health, for example, simply allows applicants to hold off submitting some details of their application until after a proposal has received a favorable score from reviewers and is assured of moving forward.

At NSF, the pilot has been a godsend to overworked program officers, says Alan Tessier, DEB’s deputy director in Arlington, Virginia. He admits that an overall success rate of less than 8% is not a happy situation. But the new procedures have helped ease the stress created by a decade of rising application numbers, which peaked in 2010 and created what Tessier calls an “unsustainable” situation. For instance, “instead of asking 12,000 people to be ad hoc reviewers, it’s now more like 2000,” he says. (Recruiting qualified reviewers is a chronic problem at NSF.) In addition, the second panel has far fewer proposals to vet, meaning the final reviewers can spend more time discussing higher quality proposals.

“We were prepared to pull the plug [on the pilot] after the first year if we were really causing damage,” Tessier says, “but that doesn’t seem to be the case.” An outside evaluation, including interviews with affected scientists, is due to be completed early next year. NSF will then decide whether to make the changes permanent and, perhaps, whether the system should be extended to other directorates.

Wainwright hopes that won’t happen. “Of course there’s a lot of frustration because success rates are so low,” he says. “And we understand that’s not something NSF can control. However, I predict that a community survey would find that most scientists would like NSF to take a third approach [to reducing workload], something that doesn’t require such short and binding preliminary proposals and annual deadlines. That’s a very tough world to live in.”

**Infectious Disease**

**Zika vaccine has a good shot**

By Jon Cohen

When it comes to making vaccines, not all viruses are created equal: Some, like HIV, notoriously find ways to outmuscle the immune responses raised by a vaccine. This week, new studies in monkeys put Zika virus squarely in the wimp corner, welcome news as the first human vaccine trial against it begins.

A vaccine is sorely needed. The virus has blasted through Latin America, leaving severe birth defects and other maladies in its wake. Just this week, Florida health officials confirmed the first cases of local transmission in the United States; until now, all cases here involved people who had traveled to affected countries. These Florida cases were mainly infected by mosquitoes within a 2.5-square-kilometer area of northern Miami.

Since Brazilian health officials first reported local transmission of Zika virus in May 2015, researchers have been scrambling to develop a vaccine. The monkey studies, published online this week in *Science*, suggest that outwitting Zika virus should present few obstacles. A research team from the Beth Israel Deaconess Medical Center in Boston and the Walter Reed Army Institute of Research in Silver Spring, Maryland, vaccinated 16 monkeys with three experimental vaccines and then “challenged” them with injections of Zika virus. As a control, they challenged 12 unvaccinated monkeys. None of the vaccinated monkeys became infected, whereas the Zika virus rose to high levels in the blood of all of the control animals. “The protection was striking, and it certainly raises optimism about development of a Zika virus vaccine for humans,” says Dan Barouch, an immunologist at Beth Israel who co-led the studies.

The group tested three different approaches. One is a traditional vaccine that uses a whole, killed Zika virus. The second contains DNA from Zika woven into a small, harmless circle of DNA called a plasmid; once in cells, this DNA produces Zika proteins that spark an immune response against them. The third strategy stitched Zika genes into adenoviruses, which act as Trojan horses and infect cells to trigger immune responses.

Barouch stresses that his group’s data do not predict which vaccine will work best in humans. “The goal of the study was not to have a cook-off of different vaccine modalities,” he says. Instead, a key aim was to identify which components of the immune response correlated with protection against the virus to help guide human trials. Specifically, the monkey studies showed that even low levels of antibodies directed toward the Zika virus completely protected the animals.

On 26 July, Inovio Pharmaceuticals, a small company based in Plymouth Meeting, Pennsylvania, began the first human trials of a Zika vaccine. The biotech’s DNA vaccine is
being tested in a phase I study on 40 healthy people for safety and its ability to trigger immune responses. Others are in the works. The National Institute of Allergy and Infectious Diseases (NIAID) in Rockville, Maryland, is collaborating with the Walter Reed group, the Butantan Institute in São Paulo, Brazil, and the pharmaceutical company Sanofi Pasteur in Swiftwater, Pennsylvania, to develop three other Zika vaccines, including one that also uses Zika DNA alone and will likely enter human studies within the next few weeks.

NIAID Director Anthony Fauci says the monkey results are “encouraging” and add to other evidence that “strongly suggest we’ll get an effective vaccine.” But determining whether any Zika vaccine works in humans may present tricky challenges. Researchers hope to fast track vaccines that pass muster in phase I studies and go straight into efficacy trials in a few thousand people in regions of Latin America where the virus has spread rapidly. If all goes well, those prevention trials could start as early as the beginning of 2017 and determine within a year whether the vaccines protect people.

But Neil Ferguson, a mathematical modeler at Imperial College London, thinks the epidemic is racing so fast through Latin America that many people may have been exposed and become immune by the time efficacy trials begin, leading to a drop in transmission rates that, in turn, make it far more difficult to see the benefit of a vaccine. A similar drop hampered some vaccine trials during the Ebola epidemic in West Africa. Ferguson, who led a team that recently modeled the spread of Zika in Latin America (Science, 22 July, p. 353), says the virus has already peaked in Brazil and Colombia and that infected people will likely develop lifelong immunity. “My gut instinct is the way the epidemic is moving, by the end of next year there’ll be very little Zika left there.”

Ferguson suggests that instead of setting up vaccine trials in one place, researchers could run sequential trials in different populations. “We need to be ready to restart trials when new outbreaks are seen,” he says.

Fauci, however, expects to see large numbers of new Zika infections in South America for several years. It’s now winter in much of the continent, which explains why cases have precipitously dropped, he says, and he doubts that the level of so-called “herd immunity” in the population will significantly lower the spread of the virus there next summer when mosquito populations swell. “The second wave I’d assume is going to be less robust, but there’s still going to be enough infections to get an answer from vaccine trials,” Fauci says. “Unlike Ebola, Zika is not going to disappear.”

SCIENCE DIPLOMACY

Synchrotron aims to bridge divides in the Middle East

Light source in Jordan is just about ready to start shining

By Erik Stokstad, in Manchester, U.K.

A beleaguered experiment in science diplomacy is on the threshold of success. Last week, an $80 million synchrotron lab in Allan, Jordan, announced its first call for research that will be conducted on two beamlines of high-energy particles that are expected to switch on this autumn. Full-fledged studies should start early next year at the Synchrotron-light for Experimental Science and Applications in the Middle East (SESAME).

“The news is that it’s working, against the odds,” says Chris Llewellyn Smith, a physicist at the University of Oxford in the United Kingdom and president of the SESAME Council. The project was behind schedule because of political complications—visa problems for scientists (Science, 15 December 2006, p. 1668), for example, and sanctions against Iran, a partner—and a freak snowstorm that collapsed the main building’s roof in 2013. Now, “we are in the final stage,” Eliezer Rabinovici, a theoretical physicist at the Hebrew University of Jerusalem, said at a 27 July press conference here at the EuroScience Open Forum. “To see dreams become reality, this is a very special moment.”

A synchrotron is an important tool for many fields, as it creates intense beams of light that are used to probe biological samples or materials. There are about 60 synchrotrons in the world; SESAME is the first to come online in the Middle East. Projects envisioned for the synchrotron include analyzing breast cancer tissue samples, studying Red Sea corals and soil pollution, and probing the Dead Sea Scrolls and other archaeological remains. A focus on applied sciences relevant to the region helped SESAME scientists secure funding from their governments, says Alessandro Treves, a neuroscientist at the International School for Advanced Studies in Trieste, Italy, who has followed the initiative. “It was the key to make it successful.”

SESAME was founded in 1999 as a partnership of many Middle Eastern countries. Germany donated a big-ticket component: the injector that sends particles into the main storage ring. The initiative has attracted about $30 million in donations from outside the region, including $11 million from the European Union, supplementing the construction costs financed primarily by Israel, Jordan, and Turkey. Iran has pledged $5 million, but sanctions have delayed its contributions. SESAME’s operating costs are expected to be paid for by its members: Bahrain, Cyprus, Egypt, Iran, Israel, Jordan, Pakistan, the Palestinian National Authority, and Turkey.

Smith says the facility is on track for commissioning in December. Two beamlines will be ready this year—for x-ray and absorption and fluorescence, and infrared spectromicroscopy—and two more will be built by 2018 for materials science and macromolecular crystallography. Gihan Kamel, SESAME’s infrared beamline scientist, says researchers have already begun working at the facility, by hooking up detectors and microscopes to lower power sources at the facility. Once the synchrotron fires up, the resolution and brightness will increase dramatically.

In the conflict-riven Middle East, security is a worry. “There are severe concerns,” Rabinovici says. SESAME is building a guest house for visiting researchers inside its perimeter fence. Still, Rabinovici hopes the scientific oasis will help ease regional tensions. “We are offering light at the end of one tunnel.”
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