acknowledges that the field trials for *DSM-IV* were far from perfect. For example, his trials failed to identify the dramatic surge in diagnoses of attention-deficit/hyperactivity disorder that followed changes made in *DSM-IV*. The trials suggested that there would be an increase of about 15% in the disorder. Instead, says Frances, the diagnosis rose threefold. "We missed the boat," he says. "But at least we had some sense that there would be an increase."

Results from the *DSM-5* academic field trials have yet to be presented, but early calculations suggest that, in general, there will be no big differences in the frequency of diagnoses, says Darrel Regier, vice-chair of the *DSM-5* task force and APA director of research. That claim has done little to alleviate concerns, however, because the trials enrolled patients who were initially diagnosed under *DSM-IV* standards. This leaves untested the possibility that the *DSM-5* criteria will capture many more patients who were previously deemed healthy, notes Widiger.

Observers are also alarmed by the statistical thresholds that the trials used to assess reliability, or the likelihood that two or more clinicians would arrive at the same diagnosis using the proposed criteria. This likelihood is often expressed as a statistical term called 'Cohen's kappa'. A kappa of 0 means that there is no agreement between the clinicians; a value of 1 means that the clinicians agree totally.

Researchers in the field often strive to reach a kappa of 0.6–0.8, indicating that the independent diagnoses agree more often than not. But in the Commentary, lead author Helena Kraemer, an emeritus statistician at Stanford School of Medicine in California, argued that a kappa of 0.2–0.4 could sometimes be acceptable. Kraemer later elaborated to *Nature* that the task force was largely aiming for a kappa of 0.4–0.6, but that it wanted to prepare the field for seeing values as low as 0.2 in particularly rare diagnoses or in those without biological markers.

Unlike tests on the previous edition, the reliability tests on *DSM-5* were performed on separate occasions, so that the clinicians involved were unaware of each other's diagnoses. Widiger says that he supports the more rigorous approach, but that accepting a value as low as 0.2 gives him pause. "I've never seen anybody argue that a kappa of 0.2 is acceptable," he says. "You just can't get much lower than that."

Not everyone is worried about a surge in diagnoses. Thomas Frazier, a paediatric psychologist at the Cleveland Clinic in Ohio, has carried out his own study of *DSM-5* criteria for autism spectrum disorder. His results, published online last year (T. W. Frazier *et al. J. Am. Acad. Child Adolesc. Psychiatry* **51,** 28–40; 2012), suggested that the new definition would omit some patients with autism, but that this could be easily corrected by requiring one less symptom to meet the threshold for a positive diagnosis. "Unfortunately, the *DSM* committees are not systematically doing these kinds of studies," he says. ■

FUNDING

Stem-cell agency faces budget dilemma

The California Institute for Regenerative Medicine plans for a future without state support.

BY ERIKA CHECK HAYDEN

Halfway through its initial ten-year mandate, the California Institute for Regenerative Medicine (CIRM) in San Francisco is confronting a topic familiar to anyone at middle age: its own mortality.

The publicly funded institute, one of the world's largest supporters of stem-cell research, was born from a state referendum in 2004. Endorsements from celebrities such as then-state governor Arnold Schwarzenegger and the late actor Christopher Reeve, who had been paralysed by a spinal injury, helped to garner voter support for a public bond to underwrite the institute. But with half of the US$3 billion that it received from the state now spent and the rest expected to run out by 2021, CIRM is now actively planning for a future that may not include any further state support.

"It would be premature to even consider another bond measure at this time," wrote Jonathan Thomas, CIRM's chairman, in a draft of a transition plan requested by the state legislature. Thomas outlined the plan on 24 January at a public hearing held in San Francisco by the US Institute of Medicine, which CIRM has asked to review its operations.

Given that California is facing severe budget shortfalls, several billion dollars more for stem-cell science may strike residents as a luxury that they can ill afford. It may also prove difficult for CIRM's supporters to point to any treatments that have emerged from the state's investment. So far, the agency has funded only one clinical trial using embryonic stem cells, and that was halted by its sponsor, Geron of Menlo Park, California, last November.

Yet the institute has spent just over $1 billion on new buildings and labs, basic research, training and translational research, often for projects that scientists say are crucial and would be difficult to get funded any other way. So the prospect of a future without CIRM is provoking unease. "It would be a very different landscape if CIRM were not around," says Howard Chang, a dermatologist and genome scientist at Stanford University in California.

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Chang has a CIRM grant to examine epigenetics in human embryonic stem cells, and is part of another CIRM-funded team that is preparing a developmental regulatory protein for use as a regenerative therapy. Both projects would be difficult to continue without the agency, he says. Federal funding for research using human embryonic stem cells remains controversial, and could dry up altogether after the next presidential election (see *Nature* **481,** 421–423; 2012). And neither of Chang's other funders — the US National Institutes of Health (NIH) and the Howard Hughes Medical Institute in Chevy Chase, Maryland — supports his interdisciplinary translational work. Irina Conboy, a stem-cell engineer at the University of California, Berkeley, who draws half of her lab's funding from CIRM, agrees that in supporting work that has specific clinical goals, the agency occupies a niche that will not easily be filled by basic-research funders. "The NIH might say that the work does not have a strong theoretical component, so you're not learning anything new," she says.

"It would be a very different landscape if CIRM were not around."

CIRM is developing plans to help its grantees to continue their work if the agency closes. One option is a non-profit 'venture philanthropy' fund that would raise money from private sources to support stem-cell research. The agency is also writing a strategic plan for the rest of its ten-year mandate that focuses on translating research into the clinic, acknowledging that CIRM's best shot at survival — and at sustaining future funding for stem-cell researchers — could come from a clinical success.

As CIRM board member Claire Pomeroy, chief executive of the University of California, Davis, Health System in Sacramento, noted at the agency's board meeting on 17 January: "If you asked the public what they would define as success, they would say a patient benefited." ■