NEWS

Still strict on stem cells

Even some Bush-approved cell lines could be denied federal funding.

US stem-cell researchers are applauding draft guidelines released by the National Institutes of Health (NIH) last week to govern federally funded research on human embryonic stem-cell lines. Some, however, say the provisional rules are still too restrictive because they would exclude lines derived from embryos created for research purposes.

The provisional rules come 39 days after President Barack Obama signed an executive order freeing up federal money for such research. They would limit federal funding to work on stem-cell lines derived from embryos created by *in vitro* fertilization (IVF) solely for reproductive purposes, and no longer needed for that purpose. Researchers would have to document that parents had voluntarily donated the embryos, without inducements and without researcher influence.

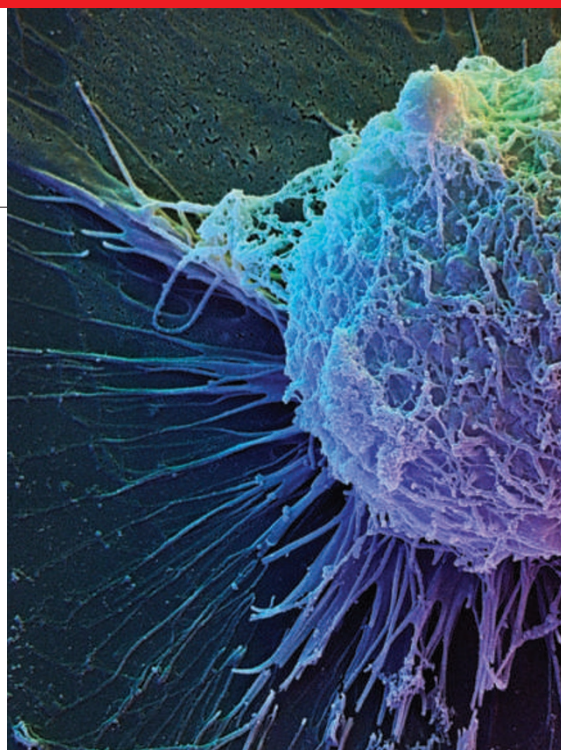
Disappointingly for some researchers, the guidelines explicitly disqualify from funding any stem-cell lines derived from embryos created for research purposes, whether by standard IVF methods or by somatic-cell nuclear transfer. The draft guidelines also forbid funding for lines derived through parthenogenesis, a form of asexual reproduction in which an unfertilized egg is developed into an embryo.

The guidelines, if adopted as issued last week, could create an immediate problem for researchers already working on the score of lines approved for federal funding in August 2001 by former president George W. Bush. Of those lines, "not all are likely to be eligible for continued federal funding" under the new draft guidelines, says Thomas Murray, president of the Hastings Center, a bioethics think tank in Garrison, New York. "I would counsel the NIH to consider creating an exception for these cell lines if they continue to have very significant scientific value," he says.

Others go further. The agency's informed consent requirements are "fine going forwards. But I think they are going to have to loosen those expectations a little bit for [all] pre-existing lines," says Sean Morrison, director of the University of Michigan Center for Stem Cell Biology in Ann Arbor.

The NIH is publishing its proposed guidelines this week in the Federal Register, kicking off a 30-day public comment period. It has until 7 July to finalize the guidelines.

"This represents a great expansion in opportunity for scientists doing research in this field," says Raynard Kington, acting director of the agency based in Bethesda, Maryland. Defending its decision to exclude lines derived from embryos created for research purposes, he says: "We don't believe that there is yet even consensus within the scientific community that would warrant going to the next step."



An embryonic stem cells — made to be born?

Once the guidelines are finalized, the agency will periodically revisit them to see if adjustments are needed to reflect evolving science.

The NIH estimates that more than 760 human embryonic-stem-cell lines exist, and Kington says he expects "many" will meet the final eligibility standards.

Review and funding of current applications for stem-cell research proposals will be deferred until the final guidelines are issued. At that point, researchers will have the opportunity to modify their applications to comply with the guidelines before funding decisions are made.

Pharmaceutical companies join forces on HIV

GlaxoSmithKline (GSK) and Pfizer plan to merge their HIV drug divisions in an unusual move designed to shore up their poor market positions. The marriage will create a new company, yet to be named, which will use the existing research and market portfolios of the parent companies to develop new combination drugs, the mainstay of HIV treatment.

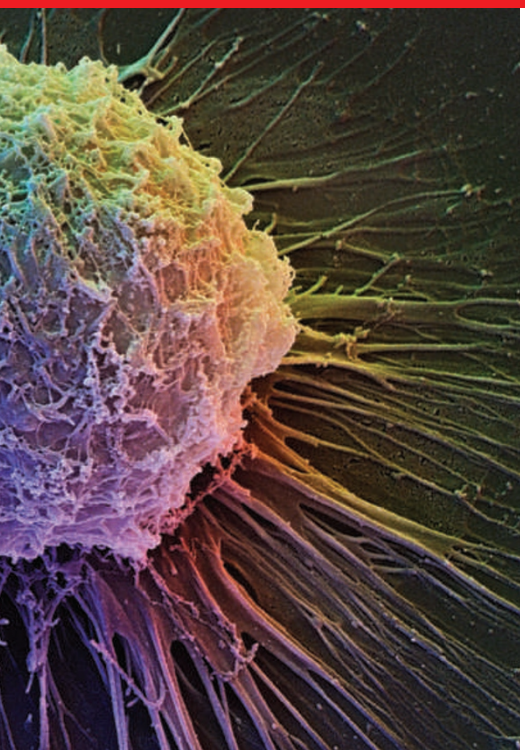
"The fact that GSK needs a partner reflects its weakness in this market," says Holger Rovini, an analyst at consultancy Datamonitor Healthcare in London. Although London-based GSK has a much greater share of the anti-HIV drug market than Pfizer, its drugs are nearing patent expiration and sales are slowing. Pfizer, based in New York, has a smaller market presence, but owns a healthier pipeline of candidate HIV drugs.

The venture will start with a 19% share of the US$12.3-billion global HIV treatment market and a pool of 17 drug entities — including six new molecules — to trawl for new combinations. It will carry out HIV drug discovery by contracting out from GSK and Pfizer's in-house research and development arms, and will be able to negotiate exclusive rights to any new HIV-related compounds developed by either company. The venture will also be free to seek out its own research and licensing deals from other companies.

A key benefit for the parent companies is that they will share the risk of pipeline drugs failing and get ready access to new compounds. GSK will own 85% of the shares in the new company, with Pfizer taking the remaining 15%. Profits from fruitful combinations would be shared as company stock, with a weighting applied depending on which parent company provided the active compounds.

The new company will be hoping to create a drug combination to rival the blockbuster anti-HIV combination Atripla, created by teaming two drugs made by Gilead Sciences of Foster City, California, with efavirenz, a compound owned by New York-based Bristol-Myers Squibb. Approved by the US Food and Drug Administration in 2006, Atripla marked the first time that anti-HIV drugs owned by different companies had been united into a single product. The combination helped to push Gilead's worldwide sales of HIV drugs to US$4.3 billion last year, almost double GSK's HIV drug sales of $2.4 billion.

The GSK–Pfizer venture reinforces the importance of sharing intellectual property to tackle HIV, says Ellen 't Hoen, a senior adviser on intellectual property at UNITAID, an international drug-purchase facility hosted by the World Health Organization in Geneva, Switzerland. 't Hoen is leading



Mark Kay, a geneticist and stem-cell researcher at Stanford University School of Medicine in California, says he would have liked to see the guidelines embrace stem cells derived outside the reproductive context. Still, he says, the draft effort "is a step in the right direction".

Meri Firpo, who uses stem cells in diabetes research at the University of Minnesota in Minneapolis, says that "there are issues that probably need clarifying". Among them, she says, is whether lines derived from embryos created from donated sperm or ova would qualify. They do not under guidelines adopted in the past by the US National Academies. ■

Meredith Wadman

UNITAID's plan to launch a 'patent pool' by the end of this year that would allow multiple companies to license their anti-HIV drugs in return for royalties. This initiative would speed up the development of new antiretroviral combinations, she says, by providing access to a broader range of drugs than the GSK–Pfizer alliance affords.

Last year, Swiss company Roche abandoned its HIV research altogether, but GSK has denied speculation that the new venture is a prelude to its HIV division being sold off. "Both GSK and Pfizer are focused on building a business that has a profitable and sustainable long-term future," says Janet Morgan, director of UK science communications at GSK. "This transaction is about creating a stronger combined business, not about an 'exit strategy'." ■

Declan Butler

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Fees delay pharmed drug

Human tests of a potent antibody against HIV have been delayed by up to a year because of wrangling over the application to run a clinical trial in Europe, *Nature* has learned.

The consortium behind the project, which uses genetically modified (GM) tobacco plants to make the monoclonal antibody 2G12, now hopes to make its application in June. If approved, it will be the first academic-led clinical trial in Europe of a drug produced in a GM plant.

The Pharma-Planta consortium of 28 academic institutions and 4 small companies was awarded €12 million (US$15.6 million) in 2004 by the European Commission to carry out a five-year project to develop plant-derived pharmaceuticals for HIV, rabies and tuberculosis. One of the project's goals is to help improve the regulations that govern the production of drugs in plants, a potentially cheaper and more efficient technique than conventional manufacturing methods.

Internationally, only a handful of clinical trials of such drugs are under way, and there are currently no plant-pharmed drugs on the market. Scientists hope that improving the regulations will help to stimulate 'pharming' research in Europe. "Establishing regulation at an early stage is critical for new technologies," says Julian Ma, a molecular immunologist at St George's Hospital Medical School, University of London, UK, and leader of the consortium.

"The EMEA is blocking developments in this area."

In 2006, the team approached the European Medicines Agency (EMEA), which grants permission for marketing medicinal products in Europe, to discuss their project. "No one in Europe had made any decisions about molecular pharming, and the EMEA needed to develop overarching guidelines so that there is uniformity across Europe," Ma says.

But the group soon hit a roadblock. The EMEA insisted that any further meetings and discussions would be classed as formal scientific advice sessions, which at the time they provided for a fee of €35,000. "For an academic consortium that is publicly funded, this fee is astronomical and unaffordable," says Ma. The EMEA's scientific advice is sold to prospective applicants seeking marketing approval for a product, to help them ensure they meet the agency's safety and quality requirements. That advice does not guarantee that applications will be successful.

In contrast, the Medicines and Healthcare products Regulatory Agency (MHRA), the UK body responsible for ensuring the quality and safety of medicines and devices, charges up to about £4,600 (US$6,700) for similar advice, whereas the US Food and Drug Administration levies no charge.

Although the EMEA provides a 90% discount for small companies, it has no such policy for universities. After negotiating with the consortium, the EMEA agreed in 2008 to grant a 50% discount — on an increased advice fee of €75,500, which came into effect on 1 April this year.

The researchers chose not to pay the fee, and focused on developing guidelines with the European Food Safety Authority on risk assessment of drugs produced by GM plants, which the authority expects to publish in the next few months. The consortium also sought scientific advice from the MHRA, to which they now intend to submit their clinical-trial application.

The EMEA did not answer *Nature*'s specific questions about their interactions with Pharma-Planta, but confirmed in a statement that although "there are no specific fee reductions for universities", universities could submit a request for a fee reduction which will be considered and granted "in exceptional circumstances".

Since Pharma-Planta approached the EMEA, the agency has developed new pharming guidelines, which came into effect in February 2009. Unlike previous regulations, these account for the fact that the conditions for growing drugs in plants are intrinsically variable, and so the same standards of drug manufacture expected of cell-culture and fermentation systems cannot apply. But university researchers still face the EMEA's fees if they want advice on pharming projects, which Ma believes is a significant barrier to translating future academic research in the area.

Marc van Montagu, the president of the European Federation of Biotechnology, says it is "essential" that the EMEA reduces its fee for universities. "The EMEA is blocking developments in this area with their exorbitant bill," he says. ■

Natasha Gilbert

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