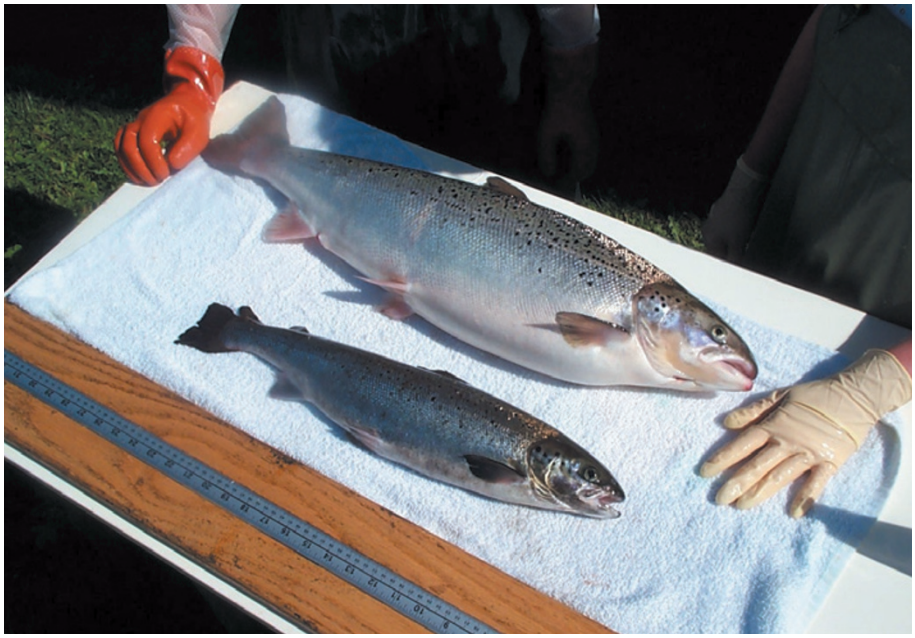
AQUABOUNTY



A genetically engineered salmon (top) grows twice as fast as its wild counterpart (bottom).

BIOTECHNOLOGY

# Transgenic salmon nears approval

*Slow US regulatory process highlights hurdles of getting engineered food animals to dinner tables.*

BY HEIDI LEDFORD

In the remote highlands of Panama, in tanks protected by netting, barbed wire and guard dogs, swim the world's most expensive and scrutinized fish. These swift-growing salmon have been at the centre of a 18-year, US$60-million battle to bring the first genetically modified (GM) animal to US dinner tables — a struggle that may be nearing its end.

Last week marked the end of the public's opportunity to weigh in on a US Food and Drug Administration (FDA) draft assessment of the salmon. Genetically engineered to grow twice as fast as their unaltered brethren, the fish pose no significant environmental threat to the United States when grown in landlocked tanks, says the FDA. The agency needs only to finalize that assessment before deciding whether to approve the fish for human consumption. The number of opportunities for a surprise delay — a recurring theme in the history of these salmon — is dwindling (see 'Against the current').

Environmental groups are preparing to take the battle to consumers by fighting the sale of the fish in grocery stores across the country. Others point out that it will be years before the salmon are anything more than a curiosity. At full capacity, the Panama facility can produce only about 100 tonnes of salmon a year, says Gregory Jaffe, director of biotechnology at the Center for Science in the Public Interest, a consumer group in Washington DC that monitors the regulation of GM foods. That amount is a trifle compared to the roughly 230,000 tonnes of farmed Atlantic salmon that the United States imported in 2012. "You'd have to try hard to eat it," says Jaffe. "It won't be as hard as winning the lottery, but it will be close."

For the firm that developed the fish, AquaBounty Technologies of Maynard, Massachusetts, those 100 tonnes are a hard-won prize. In 1989, the salmon were engineered to overexpress a growth-hormone gene. The result: 'AquAdvantage' fish that grew to full size in around 18 months rather than the usual 3 years. The company applied for FDA approval in 1995 and has been stuck in regulatory limbo ever since. AquaBounty has had to demonstrate the food's safety, and gauge the environmental risk of the sterile fish escaping its tanks and successfully mating with wild salmon. By contrast, the FDA approved the first GM crop for human consumption — the Flavr Savr tomato — after just three years of regulatory consideration.



## CASH CRISIS

The uncertainty has taken its toll. To save money, AquaBounty has reduced its staff by more than half. Last year, the company sold off its research and development arm and lost one of its biggest investors. In March, AquaBounty came within a week of running out of cash, says chief executive Ronald Stotish. The firm was saved by last-minute refinancing and fresh investment from Intrexon, a synthetic-biology company based in Blacksburg, Virginia.

At first glance, the Panama facility hardly seems to be the key to financial prosperity. With salmon selling for around $6.50 per kilogram, AquaBounty would make less than $1 million each year from the salmon. It would take decades for the company to make back its $60-million investment if it relied solely on the Panama farm.

Stotish says that the company must expand. Following FDA approval, AquaBounty hopes to sell its salmon eggs to farmers and expand to markets in Argentina, Canada, Chile and China.

To sell AquAdvantage fish in the United States, each farm would require separate FDA approval, but because the food safety of the fish has already been vetted, the approval process would require only an environmental evaluation, says Jaffe.

Yet even with regulatory approval, the battle over AquaBounty's salmon will be far from over. In March, several speciality grocery stores, including Whole Foods, an international chain based in Austin, Texas, said that they would not sell AquAdvantage fish. Lawmakers in Alaska and Oregon, which both export wild salmon, have repeatedly tried to block the GM fish because they fear contamination of the wild stock and worry that it could drive down the price of farmed salmon.

AquaBounty's long struggle has discouraged other US companies from producing GM animals for food. Mark Walton, chief marketing officer at Recombinetics, an animal-biotechnology company in St Paul, Minnesota, says that his company will focus initially on medical applications — using modified farm animals as disease models, for example — rather than on livestock for food. Medical applications of GM technology do not stir consumer passions in the same way as GM foods, and there is a regulatory precedent: in 2009, the FDA approved a goat that makes an anti-clotting drug in its milk. If Recombinetics invests in agricultural products, Walton adds, the items will ▶

## AGAINST THE CURRENT

The US Food and Drug Administration (FDA) has been slow to approve a genetically modified (GM) salmon made by AquaBounty of Maynard, Massachusetts. The fish would be the first GM animal authorized for human consumption.

AQUABOUNTY

**1989** Canadian researchers engineer wild Atlantic salmon to overexpress growth hormone.

**1995** AquaBounty files an Investigational New Animal Drug application with the FDA.

**2001** AquaBounty submits its first regulatory study to the FDA.

**2009** The FDA releases guidance for its evaluation of genetically engineered animals as veterinary drugs; AquaBounty completes its FDA submission.

**2010** The FDA says that GM salmon is safe to eat.

**2012** The FDA completes its draft environmental assessment in May, but does not release it to the public until December.

**2013** The public-comment period for the draft environmental assessment is extended by two months and concludes on 26 April.

▶ probably be marketed outside the United States first. "The AquaBounty example has [made] the company very sceptical about how much investment to pour into the US regulatory process," he says.

Yet Stotish says that GM animal products will inevitably find their way to grocery stores. He points to heavy investment in the technology in China, where dozens of GM farm animals are in development. "I think we will end up eating genetically modified animals of a variety of species," says Stotish. "But they'll come from other countries." ■

MEDICINE

# Targeted drugs to tackle hepatitis C

*But experts debate US screening recommendations.*

**BY BETH MOLE**

John strains to recall the gap between learning that he had hepatitis C and deciding to get treated: it was either four years or five. His thinking is clouded by the combination of three drugs that he is taking to clear the infection. After the treatments' other side effects set in — severe flu-like symptoms, depression and exhaustion — he took leave from his job as a chef in New York. John, whose name has been changed to protect his privacy, was at high risk of catching the virus, having once been addicted to crystal methamphetamine. But as a 51-year-old, he is also a baby boomer — a member of the generation born between 1945 and 1965 — millions of whom will face the disease and its sometimes harrowing treatment.

Better drugs are on the way. But the possibility of improved treatment is intensifying a debate about whether to screen a broad swathe of the US population for hepatitis C.

Last month, the pharmaceutical company Gilead, based in Foster City, California, submitted its hepatitis-C drug sofosbuvir to the US Food and Drug Administration for approval, after phase II trials showed a 100% success rate in a few patient groups when it was used in combination with existing drugs. Last week, the first phase III results showed similarly promising results (E. Lawitz *et al. N. Engl. J. Med.* http://doi.org/mcc; 2013).

The drug is one of at least ten in phase III trials in the United States that promise to improve results or reduce side effects. The first of these drugs could reach the market as early as 2014, and a recommendation from the US Centers for Disease Control and Prevention (CDC) in Atlanta, Georgia, to screen an entire generation for the disease could create vast demand for them.

John is a part of a demographic time bomb. Up to 4 million Americans are infected with hepatitis C, which can irreparably damage the liver and lead to liver cancer, but because it inflicts injury slowly over decades, as many as 85% of carriers do not know that they have it. Baby boomers account for about 27% of the US population, but up to 75% of those infected with hepatitis C, possibly because injecting drugs — one infection route — was more common during their youth than in other eras. Last August, the CDC recommended screening the entire generation of people born between 1945 and 1965, as well as people in high-risk populations such as intravenous-drug users. The CDC predicts that generational screening would find an extra 800,000 cases and prevent at least 120,000 deaths. "We have an opportunity to make a real dent in the impact of the disease," says Kimberly Page, an epidemiologist at the University of California, San Francisco.

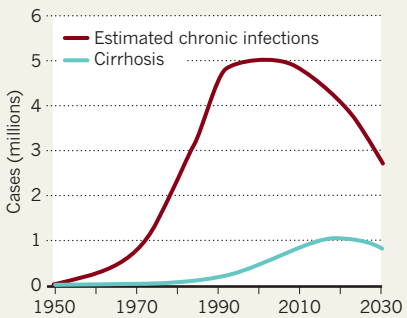
John's doctor, infectious-disease specialist Kristen Marks of Weill Cornell Medical College in New York, says that screening is especially important for baby boomers because early symptoms of hepatitis C, such as fatigue and malaise, are difficult to distinguish from signs of ageing. People dismiss symptoms, says Marks, and some might not remember trying intravenous drugs in their youth. Even if they do, she adds, "they might not tell their doctor". A peak in cases of liver scarring from untreated hepatitis C is expected in the next few years (see 'An approaching burden'). But with the new drugs on the horizon, now is an optimistic time for treatment, says Marks. "Historically, not having good treatments was a disincentive for screening," she says. "Now, I think there's a renewed interest."

But last November, the US Preventive Services Task Force (USPSTF), a panel of experts assembled by the US Department of Health and Human Services, released a draft statement giving the screening recommendation a 'grade C'.

**NATURE.COM**
For more on Hepatitis C, visit:
go.nature.com/yxxtwh

### AN APPROACHING BURDEN

The high number of hepatitis-C infections in the United States is expected to lead to a peak in cases of cirrhosis, or liver scarring, by around 2020.




SOURCE: G. L. DAVIS *ET AL. GASTROENTEROLOGY* **138**, 513–521 (2010)