Clone, clone on the range

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Since many cloned farm animals are born with abnormalities, how safe is their meat and milk?

When the U.S. Food and Drug Administration announced in January that food from cloned farm animals was safe to eat, the agency said the science was clear. Officials said meat and milk from cloned cows, pigs, and goats are exactly the same as conventional food.

“The food in every respect is indistinguishable from food from any other animal so it is beyond our imagination to even find a theory that would cause the food to be unsafe,” Stephen Sundlof, director of the FDA’s Center for Food Safety and Applied Nutrition, told reporters at a news conference in Washington, D.C.

In her office outside Paris, one of the world’s leading cloning researchers, Pascale Chavatte-Palmer, didn’t think the research was clear at all. Working out of the French government’s National Institute for Agricultural Research, she helps supervise one of only two or three noncorporate research facilities worldwide studying the long-term health of—and food products from—large numbers of cloned animals.

Chavatte-Palmer, a group research leader at the INRA, has found milk and meat from cloned cows are, indeed, different. “The full maturation of muscle is delayed in clones,” she said over the phone from her office 25 kilometres southwest of Paris. “This probably will affect the quality [of the meat]. It will certainly be a bit different.”

And those aren’t the only differences she’s found between clones and normal animals. In a series of papers she has coauthored in leading scientific journals, Chavatte-Palmer has reported that clones of cows reached puberty 62 days later, on average, than normal animals and they were 56 kilograms heavier.
when they did so. And then there were the huge numbers of clones that didn’t make it that far.

At an INRA farm whose exact location Chavatte-Palmer can’t disclose for security reasons, she has helped produce some of the world’s most comprehensive research on what happens when we try to clone farm animals. Her studies are cited 54 times in the FDA’s mammoth 968-page risk assessment on food from clones.

The idea of cloning is to create a perfect genetic copy of an adult animal by taking the nucleus from one of its cells and transferring it into an egg that has no nucleus. In about 100 of 1,000 cases, the egg develops into an embryo that can then be implanted in a surrogate mother.

Of those 100 embryo transfers, the INRA research found more than 50 fetuses spontaneously abort in the first trimester of pregnancy because of genetic or physical anomalies or defects in the placenta—a rate two times higher than for conventionally bred cows.

Another 20 or so abort later in pregnancy, most often because of a grotesque ailment sometimes called large offspring syndrome, which results in a fetus 20 to 85 percent larger than average.

In the end, fewer than five of the fetuses, on average, are born alive, Chavatte-Palmer reported in a 2004 paper in the journal Cloning and Stem Cells. This finding is in line with a European Food Safety Authority draft scientific opinion on cloning released in December 2007 that said the success rate for clone fetuses reaching term is 0.5 percent to five percent.

The FDA risk assessment offers a similarly glum, if a tad less dismal, cloning success rate of five percent to 18 percent.

But making it into the world alive is just the beginning of the struggle for many clones. Many are born with limb and head deformities, contracted tendons, extreme diarrhea, diabetes, respiratory failure, heart disease, and kidney problems.

Contrary to the sunny views of FDA officials at the Washington news conference, the agency’s risk assessment makes for sombre reading about the unpredictable science of cloning. It cites one 2000 Japanese study that painted an especially unsettling picture: “Calves [numbered] 11, 13-15, 20 and 22
died at parturition [birth] or several days later and had significant morphological abnormalities of the kidney or cacomelia [limb deformity]; the neck was bent backwards, the hind legs were stretched tightly or the second joints were bent toward the opposite direction from the normal position…

“Calf number 12 was disemboweled at parturition and the face of calf 16 was warped and the second joints of both hind legs were bent in the opposite direction from the normal position.”

This study, published in the Journal of Reproduction and Fertility, also reported on the bizarre appearance of many clone calves at birth, which “had an ‘adult’ appearance” and displayed “many wrinkles in the skin, thick bone structure, and rough hairs resembling those of adult males”.

Some of these postnatal complications are, again, caused by large offspring syndrome, which occurs in 14 percent to 50 percent of successful clone births, compared to 9.5 percent of animals produced by in vitro fertilization.

As for older clones, virtually no research on their health and longevity has been done, even though it’s been 12 years since Dolly the sheep—the first mammal cloned from an adult cell—was born in 1996. Dolly herself had to be euthanized at the young age of six after developing arthritis and lung disease.

The FDA is quite frank about most of these problems in its risk assessment. “Many questions have been raised regarding the immune function of clones and their ability to resist or recover from disease, yet few studies have examined this issue directly in bovine clones,” it says.

So how can the FDA still okay food from clones? The reasoning goes like this: yes, almost all cloning attempts fail, and, yes, there is evidence the animals that do survive are genetically abnormal. But the FDA says it hasn’t been shown that such genetic abnormalities make food from clones unsafe. “The relevance of ‘epigenetic normality’ to food consumption risks is unclear,” its report notes.

So the FDA concludes that as long as clones are pronounced to be physically healthy by a food inspector, their meat and milk are safe to eat.

The logic baffles Jaydee Hanson, a policy analyst at the Washington, D.C.–based Center for Food Safety. “They have no data. The standard way to assess something like this is to do long-term studies of feeding it
[cloned-animal products] to animals,” he said, speaking on the phone from his office.

“The [FDA’s] basic assumption is if an animal can walk in the door of a slaughterhouse, it’s safe to eat. I don’t know what slaughterhouses they visited. There are tremendous problems in slaughterhouses about whether we’re packaging meat we shouldn’t.”

But beyond that, it’s still an open question whether or not any clones are really healthy. The FDA acknowledges as much. Its report cites a 2004 paper in the New England Journal of Medicine by cloning pioneer Rudolf Jaenisch, the MIT biologist who created the first genetically engineered animals in the 1970s.

He wrote: “Gene-expression analyses indicate that four to five percent of the overall genome and 30 to 50 percent of imprinted genes are not correctly expressed in tissues of newborn cloned mice. These data represent strong molecular evidence that cloned animals, even if they survive to birth, have serious gene-expression abnormalities.”

In France, Chavatte-Palmer concluded in a paper last year in the journal Animal: “Cloned animals, although apparently normal, are however significantly different from contemporary controls maintained in the same conditions.”

It also turns out there’s no solid evidence for saying the meat and milk of clones really are the same as those from conventionally bred animals. No large-scale studies have been done. “Information on the composition of meat or milk from animal clones has been limited,” the FDA’s report says.

The agency explored the idea of sending some clone food for lab tests but dropped the plan because, apparently, it didn’t have access to enough sample material for a statistically valid result.

Instead, the FDA relied on several small-scale studies of meat and milk composition involving an average of five clones each. Five of the 10 studies found differences between food from clones and conventionally bred animals.

One study coauthored by Chavatte-Palmer last year in the journal Theriogenology reported statistically significant differences in vital fatty acids and enzymes in milk from clones compared to conventional animals.
Of five studies of cow meat, two—including Chavatte-Palmer’s Theriogenology paper—found significant differences in fat content, proteins, fatty acids, and enzymes between beef from clones and that from conventionally bred cows. For pork, only two studies were cited involving five clones in total, both from biotech company ViaGen. They found the clones had less back-fat thickness and meat yield than control animals, plus their meat was darker and redder.

No studies have been done at all on food from goats, the third clone species that the FDA okayed for food production.

Apart from these 10 studies, the FDA cited three others that also showed differences in clone meat or milk, but the reason may have been the varying diet of the animals.

These less-than-stellar results went unmentioned when U.S. officials spoke to reporters in January about the decision to okay clone food. “These products are not different than food from traditionally bred animals,” said Bruce Knight, the agriculture department’s undersecretary for marketing and regulatory programs, at the news conference. He described cloning as just “another breeding technique” that “has now been demonstrated to be safe”.

Chavatte-Palmer thinks more study is still needed. She’s no anti-biotech advocate, and she personally believes that meat and milk from clones are probably safe to eat. But she added: “I think we should know more. Our study is one of the biggest published, but it’s still limited. There is not enough data to indicate there will be no problem. We feel there is a rush to accept those clones.”

Food from cloned animals could officially enter the U.S. food supply starting as soon as a few months. The short delay is because of a temporary voluntary moratorium suggested to the industry by the U.S. Department of Agriculture—time to work out a plan to assuage the concerns of consumers in the U.S. and abroad.

The moratorium would be extended at least another year by a farm bill that the U.S. Senate passed in December requiring an outside study by the National Academy of Sciences of the safety of food from clones and impacts on human health. That bill is now the subject of negotiations with the House to reconcile different versions.
If the moratorium is lifted, clone food seems likely to slip largely unnoticed into American grocery stores without much possibility of being tracked. That’s thanks in part to the FDA’s decision not to require labels on the food or any tracking mechanism for cloned animals and their offspring.

There’s also a practical reason the food will be virtually impossible to track: there’s no way to test whether an animal is cloned or had a clone ancestor. “The answer is no,” said the FDA’s Sundlof when a reporter at the January news conference asked if such a test is possible. “These animals are indistinguishable; both the animal and any food produced from those animals is absolutely indistinguishable from any other food source.”

And despite the voluntary moratorium, food from clones has already been entering the U.S. marketplace for about 20 years, according to Donald Coover, a Galesburg, Kansas, veterinarian and owner of SEK Genetics, which retails cow semen to farmers. Coover said he himself has sold U.S. ranchers several dozen clone offspring as well as “thousands of units of semen” from clones. He put the number of other U.S. cloning businesses flouting the ban at “dozens at least, hundreds probably”.

“It’s not illegal and it’s not unethical,” said Coover, reached on his cellphone at the Iowa Beef Expo. “Instead of having just another damn horse, you have Secretariat every time. That is why it’s enormously useful.”

Coover said food from clones first entered American diets in the 1980s and early 1990s from an initial generation of clones made with split embryos. This was long before Dolly, who was cloned from an adult cell. The earlier clones didn’t catch on with ranchers because it was a crapshoot trying to predict if an embryo would turn into a superior animal as an adult.

Nonetheless, Coover said hundreds of split-embryo clones were produced, and their meat and milk quietly entered the U.S. food supply without any formal assessment of the products’ safety. “I’m not aware of any large-scale studies,” said Coover. “It just was not considered as a health or nutrition issue by the FDA.”

FDA spokesperson Brad Swezey refused comment, saying in an e-mail: “We aren’t doing interviews on cloning.”

Coover said it’s very possible some offspring of split-embryo clones also entered Canada’s food supply. “I would be stunned [if that wasn’t the case]. I
can tell you for certain there was nobody up there looking at this.”

In Canada, food from both adult and split-embryo clones is banned by order of Health Canada. The Canadian Food Inspection Agency, which enforces the ban and monitors food imports, didn’t respond to a request for comment on Coover’s claim or how it plans to stop clones from entering the country.

Health Canada is now studying the FDA risk assessment as part of a reevaluation of the Canadian policy on food from clones.

Analyst Jaydee Hanson says there’s no proof that clones are safe to eat.

For all the attention on food from clones, the fact is you’ll never see a clone T-bone at your butcher. That’s because clones are up to 10 times more expensive to produce than conventional animals—$10,000 to $16,000 for a cow and $6,000 for a pig. Instead, most clone food in our diets would not come directly from clones themselves.

Remember all those abnormal clones that are euthanized or die prematurely? You didn’t think they’d go to waste, did you? The FDA says their meat is unsafe to eat. However, its risk assessment says an acceptable disposal method would be to send the carcasses to rendering plants, where they would
get chopped up and cooked with spoiled meat from grocery stores, dead animals from zoos and shelters and butcher-shop trimmings, then turned into pet food and human food products like lard.

The FDA cites no research on whether or not rendered food from abnormal clones is safe. “There is not a single study of that,” says Jaydee Hanson, of the Center for Food Safety. “They don’t let animals with mad-cow disease enter the food supply through rendering.”

The other big source of clone-derived food would be the naturally bred offspring of clones. “Everything in those tissues is the same as what you’re seeing with our natural conceived animals,” Bernadette Dunham, director of the FDA Center for Veterinary Medicine, told reporters in January.

But again, the FDA acknowledges in its assessment that the science is limited on the health of clone offspring or the composition of their meat and milk. The FDA risk assessment cites only two studies on pork from the offspring of pig clones—one of them from biotech company ViaGen. They found the clone offspring had less fatty acids, shorter back and loin lengths, and less bacon yield. No studies at all were cited on beef or milk from the offspring of clones. A few studies have found clone progeny tend to be born with fewer abnormalities than their parents, but there is little longer-term research on offspring as they age.

Nonetheless, the FDA concludes that any genetic errors in clones are likely “reset” in their offspring. Because of the lack of research on offspring of livestock clones, the agency cites evidence from the so-called mouse model: research on mice that suggests offspring of clones benefit from some kind of genetic reset button.

“We don’t have enough data to say that is 100-percent true,” Chavatte-Palmer said. “The mouse model has been shown not to be a good model for humans. I don’t see why it would be a good model for cows. The best model for cows would be cows.”

One of the few scientists who has looked into the health of clone offspring is Dean Betts, an associate professor of biomedical sciences at the University of Guelph in Ontario. Betts coauthored a pair of studies in the journal Molecular Reproduction and Development in 2005 and 2007 that found sheep and goat clones and their offspring have significantly shorter telomeres, the
chromosome endings believed to control aging and susceptibility to cancer.

“It [the telomere] provides chromosomal stability. Without it, you have a greater chance of genomic instability, which leads to cancer,” Betts said in an interview from his office at the university.

Shorter telomere lengths could explain why many clones seem to age faster than normal animals. Dolly the sheep, for one, was found to have shorter telomeres. “Do they [the offspring of clones] have a possibility of shorter life spans and age-related diseases?” Betts asked. “We don’t know what it means or if it has health impacts. I would say not enough study has been done…There could be some impacts on the species itself over generations.”

Asked if he agrees with the FDA’s assertion that genetic errors are probably reset in the offspring of clones, Betts said: “Based on my study, I wouldn’t support that statement. My study would say the opposite, that they are not reset.”

Back in France, Chavatte-Palmer had high hopes she could get some answers about the health, longevity, and food of clones and their offspring. But her cloning work has ground virtually to a halt. She said grant-funding agencies have turned down most of INRA’s proposals to study the facility’s 70 clones and offspring—one of only two or three such large groups of animals at a noncorporate facility anywhere in the world.

Now money has run out to maintain a group of normal animals in similar conditions as the clones—necessary in order to have a good comparison sample, Chavatte-Palmer said.

“We have piles of data that we haven’t had time and money to get help to analyze…It’s very difficult to get funding in this area of research. Europe doesn’t want to hear about it, even though we are told it [clone food] is safe. It’s frustrating, very frustrating. I’m thinking at some point it’s best to move on to something else.”

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