FDA finds meat from animal

The famous Dolly

The U.S. Food and Drug Administration (FDA) recently issued Draft Documents on the Safety of Animal Clones. MI reviews the FDA's findings, the response from the EU, and takes an in-depth look at the issues surrounding animal cloning.

By Robert Vink, with text from the FDA

After four years, the most comprehensive examination of the health of livestock clones that has ever been conducted is complete. The purpose of the examination was to determine whether cloning posed a risk to animal health or to humans eating food from clones or their offspring (http://www.fda.gov/cvm/cloning.htm). The results of the study formed the basis of a draft risk assessment, proposed risk management plan, and draft guidance for the American meat industry.

Draft risk assessment

It's important to remember that the purpose of clones is for breeding, not eating. Beef, or pork clones will make up a tiny fraction of the total number of food producing animals in the United States. Instead, their offspring will be the animals actually producing meat for the food supply.

The draft risk assessment finds that meat from clones of adult cattle, pigs and goats, and their offspring, are as safe to eat as food from conventionally bred animals. The assessment was peer-reviewed by a group of independent scientific experts in cloning and animal health. They agreed with the methods FDA used to evaluate the data and the conclusions set out in the document.

The draft risk assessment presents an overview of assisted reproductive methods widely used in animal agriculture, the extensive scientific information available on animal health and food consumption risks, and draws science-based conclusions. These conclusions agree with those of the National Academies of Sciences, released in a 2002 report.

Strangely enough, while sheep cloning maybe the most well known, made famous by "Dolly the sheep," due to limited data on sheep clones, FDA recommends that sheep clones not be used for human food.

"Based on FDA's analysis of hundreds of peer-reviewed publications and other studies on the health and food composition of clones and their offspring, the draft risk assessment has determined that meat and milk from clones and their offspring are as safe as food we eat every day," said Stephen F. Sundlof, D.V.M., Ph.D., director of FDA's Center for Veterinary Medicine (CVM). "Cloning poses no unique risks to animal health when compared to other assisted reproductive technologies currently in use in U.S. agriculture."

clones is safe

Proposed risk management plan

The proposed risk management plan addresses risks to animal health and potential remaining uncertainties associated with feed and food from animal clones and their offspring.

The proposed plan outlines measures that FDA might take to address the risks that cloning poses to animals involved in the cloning process. These risks all have been observed in other assisted reproductive technologies currently in use in common agricultural practices.

One such measure could be that the agency would work with scientific and professional societies with expertise in animal health and reproduction to develop a set of care standards for animals involved in the cloning process. Although the agency does not have authority to address the ethics of animal cloning, the proposed risk management plan does state that FDA plans to continue to provide scientific expertise to interested parties working on these issues.

Draft guidance for industry

The draft guidance for industry addresses the use of food and feed products derived from clones and their offspring. The guidance is directed at clone producers, livestock breeders, and farmers and ranchers purchasing clones. It provides the agency's current thinking on use of clones and their offspring in human food or animal feed.

In the draft guidance, FDA does not recommend any special measures relating to human food use of offspring of clones of any species. Because of their cost and rarity, clones will be used as are any other elite breeding stock; to pass on naturally-occurring, desirable traits such as disease resistance and higher quality meat to production herds. As clones will be used primarily for breeding, almost all of the food that comes from the cloning process is expected to be from sexually-reproduced offspring and descendents of clones, and not the clones themselves.

The EU responds

In response to the FDA announcement, the European Commission (EC) has requested the European Food Safety Authority (EFSA) for an opinion on the possible implications of cloning for food safety, animal health, animal welfare and environment in the European Union (EU).

At present in Europe cloning is not a commercial practice and there is no specific regulation on the authorisation of food products from cloned animals for human consumption in the EU. EFSA's opinion will therefore help inform any future EU measures for cloned animals and their products.

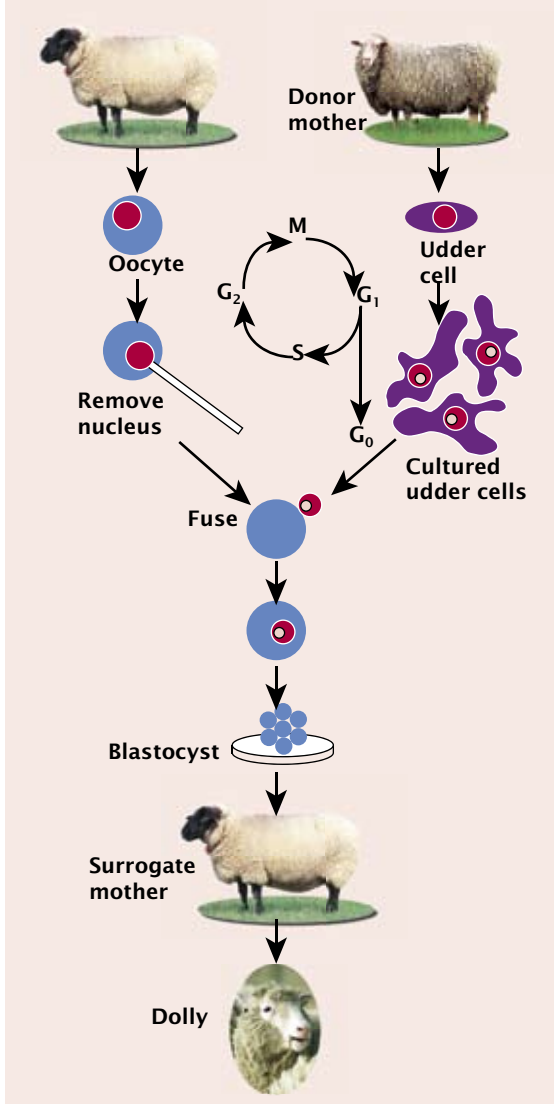
EFSA had already begun considering how best to address this issue in anticipation of the possibility of such a request, and will now discuss with the Commission the request received. A final mandate will be agreed upon with the Commission, taking into account issues such as the proposed timetable for working on such a complex opinion.

Details of FDA examination

An animal clone is a genetic copy of a donor animal, similar to identical twins but born at different times. Cloning is not the same as genetic engineering, which involves altering, adding or deleting DNA; cloning does not change the gene sequence.

FDA conducted a thorough search of the scientific literature on clones, and identified hundreds of peer-reviewed scientific journal articles, which it then reviewed. They were also able to obtain health records and blood samples from almost all of the cattle clones that have been produced in the

Figure 1 - Diagram of the laboratory procedures used to create Dolly.



Donor udder cells were removed from an adult sheep (top right), grown in laboratory culture dishes, and arrested in the G0 phase of the cell cycle. A single udder cell (arrested in G0) was fused with an oocyte from a different sheep after the nucleus of the egg cell had been removed (left). The fused cell developed in a culture dish to form a blastocyst and was then transferred to a surrogate mother sheep, which gave birth. Of 277 fused cells that were prepared in this way, only one survived to become the cloned sheep named Dolly.

United States and data from clones produced in other countries. FDA compared these health records, and the independently analyzed blood results with similar samples from conventional animals of the same age and breed that were raised on the same farms.

After reviewing all this information, FDA found that it could not tell a healthy clone from a healthy conventionally bred animal. All of the blood values, overall health records, and behaviours were in the same range for clones and conventional animals of the same breed raised on the same farms. FDA also saw that milk from dairy clones does not differ significantly in composition from milk from conventionally bred animals.

For another study similar to the one conducted on cow clones, the agency also evaluated the health of offspring sexually derived from swine clones, as well as the composition of their meat. After reviewing this very large data set, the agency concluded that all of the blood values, overall health records, and meat composition profiles of the progeny of clones were in the same range as for very closely genetically related conventionally bred swine. Based on these results, other studies from scientific journals, and FDA's understanding of the biological processes involved in cloning, the agency agreed with NAS that food from the sexually reproduced offspring of clones is as safe as food that consumers eat every day. These offspring animals will produce almost all of the food from the overall cloning/breeding process.

How to make clones

Most cloning today uses a process called somatic cell nuclear transfer (SCNT). Just as with in vitro fertilization, scientists take an immature egg from a female animal (often from ovaries obtained at the slaughterhouse). However, instead of combining it with sperm, they remove the nucleus (which contains the egg's genes). This leaves behind the other components necessary for an embryo to develop. Scientists then add the nucleus containing the desirable traits from the animal the producer wishes to copy. After a few other steps, the donor nucleus and egg fuse, start dividing, and an embryo begins to form. The embryo is then implanted in the uterus of a surrogate dam (again the same as with in vitro fertilization), which carries it to term. The clone is delivered just like any other baby animal. *(See Figure 1)*

Higher health risks at birth

There are no complications that are unique to cloning. These problems are also seen in animals born from natural mating or ARTs. They seem to happen more often in clones for a number of reasons that probably have to do with parts of the procedure that occur outside the body. The embryo may fail to develop properly during the in vitro stage or early on after transfer to the surrogate and may be flushed out of the uterus. If it does develop, the embryo may not implant properly into the uterus of the surrogate dam. Alternatively, the placenta may not form properly, and the developing animal won't get the nourishment it needs.

Large Offspring Syndrome (LOS) is seen in pregnancies of cattle and sheep that come from both assisted reproductive technologies and cloning. With LOS, the fetus grows too large in the uterus, making problems for the animal and its surrogate dam. LOS has not been observed in goats and swine.

As a group, livestock clones tend to have more health problems at birth, and may die more often right after birth than conventionally bred animals. If clones survive the first few days after birth, they seem to become just as healthy and strong as other animals of the same age. By the time clones are young adults, it's not possible to tell them apart from other animals of the same age, even if you conduct a detailed examination. Scientists at FDA and research institutions have looked at blood work for clones that's similar to what people get when they have physicals. These results show that the clones are perfectly healthy, and walk, wean, grow, mature, and behave just like conventional animals.

Holly and friends - Australia's first cloned calves (Source: The Institute of Reproduction and Development)

Reasons to Clone

The main use of clones is to produce breeding stock, not food. Clones allow producers to upgrade the overall quality of their herds by providing more copies of the best animals in the herd. These animals are then used for conventional breeding, and the sexually reproduced offspring become the food producing animals. Just as producers wouldn't use their best conventionally bred breeding animals as sources of food, they are equally unlikely to do so for clones.

Some examples of desirable characteristics in livestock that producers might want in their herds include disease resistance, suitability to climate, quality body type, fertility, and market preference.

Disease resistance

Sick animals are expensive for producers. Veterinary bills add up, and unhealthy animals don't produce as much meat. A herd that is resistant to disease is extremely valuable because it doesn't lose any production time to illness, and doesn't cost the producers extra money for veterinary treatment.

Suitability to Climate

Different types of livestock grow well in different climates. Pork production has traditionally been centred in the eastern United States, but is moving to different regions (e.g., Utah). Cloning could allow producers to select those pigs that naturally do well in the new climate, and use

them to breed more pigs to be used for food production.

Quality body type

Farmers naturally want an animal whose body is well suited to its production function. For animals that produce meat, producers breed for strong, heavily-muscled, quick-maturing animals that will yield high quality meat in the shortest time possible. The most desirable bulls produce offspring that are relatively small at birth (so that they are easier for the female to carry and deliver), but that grow rapidly and are healthy after birth.

Fertility

Beef cattle or pigs need to have high fertility rates in order to replace animals that are sent to slaughter. Cloning allows producers to clone those animals with high fertility rates so that they could bear offspring that would also tend to be very fertile.

Market preference

Producers may also want to breed livestock to meet the changing tastes of consumers. These include traits like leanness, tenderness, colour, size of various cuts, etc. Preferences also vary by culture, and cloning may help tailor products to the preferences of various international markets and ethnic groups.

FDA considering the ethics

FDA recognizes that animal cloning raises ethical issues that are important to some members of the public. The agency's jurisdiction, however, is limited to health and safety issues, and does not extend to ethical issues related to animal cloning. FDA is also aware that ethical concerns can become intertwined with, and amplifies concerns about food safety. They plan to participate in discussions on the ethical issues posed by animal cloning to provide their scientific expertise.

Clone labelling

The FDA is not recommending any additional measures relating to food derived from adult clones and their offspring, including labelling. For instance, FDA scientists found that the milk components from dairy clones were of the same type and present in the same amounts as milk sold every day. Therefore there is no science-based reason to use labels to distinguish between milk derived from clones and that from conventional animals.

Cloning in other countries

Scientists in many other countries are using cloning technology. Dolly the sheep was from Scotland. There are a number of livestock clones in Australia, Canada, France, Italy, Japan, New Zealand, and South Korea, and other animals have been cloned in other countries (e.g., horses in Italy). The FDA understands, however, that no country has yet allowed food from animal clones in their food supplies. *(See photo 2)*

Cloning and Organic

According to USDA's National Organic Program regulations (7 CFR 205) clones and animals derived from this process would fall under the definition of excluded methods, which are prohibited by organic operations. Excluded methods include, among other things, processes that are not considered compatible with organic production. This should be regarded as an informal opinion issued before AMS has had an opportunity to fully consider this issue, including the information provided by FDA in the Draft Risk Assessment, and other materials being released for comment at this time.

Newborns need special care

Commercially available clones will be born at facilities operated by clone producers with considerable expertise in assisted reproductive technologies and animal husbandry. In order to assure that all clone producers have access to the best sources of information on the care of these animals, CVM will work with clone producers and scientific and professional organizations dedicated to animal health and the care of food-producing animals in order to develop care standards for newborn clones and their surrogate dams.

Males more prone to cloning

Cloning researchers recently announced that potential clone producers who want to boost their success rates should try using male cells. The advice is based on a new study in the Proceedings of the National Academy of Sciences (DOI: 10.1073/pnas.0611358104). The study showed that mouse embryos created from male adult cells were more than three times as likely to develop to term as those created from female adult cells.

Cloning an adult animal usually involves putting the nucleus from an adult cell into an egg that has been stripped of its chromosomes. However, progress has been hindered by the fact that "reprogramming" adult nuclei in this way has very low success rates.

To get around this problem, a team led by Peter Mombaerts and Elaine Fuchs at Rockefeller University in New York, US, tried using adult skin stem cells, which are less differentiated and so, should be easier to reprogram. The success rate was still very low, but they did find that 5.4% of embryos created from male cells developed to term, compared with 1.6% for comparable cells from females.

What's next

Since the release of the FDA examination of cloning safety, a 90-day period began for public comment on the risk assessment. Said FDA's Sundlof, "Because the release of the draft risk assessment and proposed risk management plan marks the beginning of our interaction with the public on these issues, we are continuing to ask producers of clones and livestock breeders to voluntarily refrain from introducing food products from these animals into commerce so that we will have the opportunity to consider the public's comments and to issue any final documents as warranted." **MI**