A Brave New World?

With FDA approval of meat and milk from cloned animals and their offspring, industry officials promise an orderly transition of products into the marketplace.

by ***Linda Robbins***

Mark Walton, president of Austin, Texas-based ViaGen, is convinced more people would be supportive of food animal cloning if they had a better understanding of what it is, how it is done, and its current and potential usefulness to the food industry.

"We applaud the release of the U.S. Food and Drug Administration's (FDA's) rigorous scientific analysis of the safety of food from cloned animals and their offspring," he states. "FDA's determination that meat and milk from animal clones is safe to eat concludes the most extensive food safety review in FDA's history."

In addition to ViaGen, Trans Ova Genetics, a Sioux Center, Iowa-based company that supplies assisted reproductive technologies to livestock producers, and Bovance, a cattle cloning company formed in 2007 as a joint venture by the two companies, have expressed support for the FDA's final conclusions, along with other livestock industry organizations.

The Biotechnology Industry Organization (BIO), an organization representing 1,100 companies, academic institutions, state biotechnology centers and related organizations across the U.S. and in 31 other nations, and the Federation of Animal Science Societies (FASS), a professional association of approximately 10,000 scientists, among others, have all expressed confidence in FDA's science-based conclusions, which mirror the conclusions of other scientific organizations around the world.

New Zealand and Australia have released

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reports concluding that meat and milk from cloned animals are safe. Canada and Argentina are reported to be close to doing the same. And even in Europe, where consumers are relatively uncomfortable with agricultural biotechnology, the European Union's (EU's) European Food Safety Authority (EFSA) has expressed agreement in its recently released draft guidance that supports the scientific studies of the safety of food from cloned animals and their offspring. The only difference between the FDA conclusion and the EFSA draft document is that the European agency supports mandatory labeling.

ViaGen and Trans Ova, who account for about 75% of the commercial cloning market, working closely with other U.S. livestock industry stakeholders, unveiled in December 2007 a voluntary supply chain management plan under which cloned animals would be registered and separated from the conventional meat-processing channels. In accordance with the plan, some food distributors could be allowed to label their products "clone-free."

According to FDA spokeswoman Julie Zawisza, the agency received around 30,500 comments on its draft risk assessment released in December 2006. While FDA has not revealed how many of the comments were favorable or negative, the voluntary supply chain management plan may be seen as a way to placate a number of activists and legislators who have called for a way for consumers to avoid products from cloned animals.

Currently, there are only about 600 cloned animals in the U.S., which is, according to Walton, "a minuscule number," compared to the total livestock population of 200 million meat-producing animals from the major species. Because cloning is now an expensive and relatively rare procedure, cloned animals will be used as elite breeding stock to pass on desirable traits such as disease resistance or higher-quality meat to production herds.

"It is really very unlikely that consumers will eat products from cloned animals," Walton says.

The next step

"Cloning is the most recent advance in animal agriculture, with the most powerful thing about it, compared to other assisted reproductive techniques, is that breeders can produce an exact genetic copy of an animal," Walton says. Once a producer has identified an animal with a desirable trait or traits, Walton says, the animal can be cloned so that those desirable characteristics can be passed on with certainty to conventionally reproduced progeny.

"Every Angus breeder can use cloning to advance genetic progress, particularly on the bull side of the equation," Walton asserts. "For instance, a really good sire can produce (by natural breeding), say, 20-40 offspring per year. By the time he has produced sons, grandsons and great-grandsons, the genetic time lag is considerable. With cloning, a breeder who currently sells semen and provides semen for his own herd or for commercial herds can skip that genetic time lag and reduce genetic variability, while advancing genetic progress in his or her herd."

As for whether or not consumers will accept this new technology for food production, Walton explains that it will probably not be used on a large scale. He says he trusts people to look for the facts and make their choices based on an understanding of the technology and its safety.

Consumer acceptance

The International Food Information Council, a nonprofit organization that gathers consumer insights on food safety/nutrition issues and communicates science-based information to a variety of audiences, has conducted a consumer survey on biotechnology-related issues for the past 10 years. As an organization primarily supported by the broad-based food, beverage and agricultural industries, it doesn't represent individual companies,

Common cloning myths

The FDA web site notes that there are numerous myths associated with cloning. A few of the most common myths (in bold) and explanations for why they are myths follow:

- **Cloning is a new technology.** The history of cloning actually goes back more than 100 years. According to the FDA web site, we eat clones all the time in the form of bananas and grafted fruits. For plants, cloning is referred to as "vegetative propagation." Because it takes about 30 years to breed a banana from seed, most bananas, potatoes, apples, grapes, pears and peaches are clones. Some animals, such as starfish and other relatively simple sea creatures, can reproduce themselves by vegetative propagation. Identical twin mammals can be thought of as naturally occurring clones.
- **Clones are a specific animal's DNA grafted onto another body.** In spite of the stories in science fiction books and movies, clones are born just like any other animal. Clones simply don't require a sperm and egg to come together to make an embryo. Clone embryos are made using a cell from a donor animal and fusing it to an egg cell that has had its nucleus removed. The embryo is then implanted into the uterus of a surrogate to grow just as if it came from ET or in vitro fertilization.
- **The offspring of clones are clones, and each generation gets weaker and weaker and has more and more problems.** A clone produces offspring by sex just like any other animal. Whether or not one or both parents are clones has no effect on the offspring. The progeny of clones are not clones.
- **Clones are always identical in looks.** Actually, like identical twins, clones can have slight variations in appearance. They have the same genes, but these genes are "expressed" differently. Twin Holstein cows with the same genes can have a different pattern to their spots or shape to their ears, and their nose prints will be unique to each animal. Human identical twins, though they have the same genes, can also have different freckles or features and will have unique fingerprint patterns.
- **Clones are "genetically modified."** Clones don't have any new genes added to them. They are just clones. Many people confuse cloning with genetically engineered animals, which have had genes added to them. Although some genetically engineered animals have been reproduced by cloning, animals that are just clones will do the same things as their conventional counterparts. (See *www.fda.gov/cvm/CloningRA_Myths.htm* for the full list of myths.)

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products or brands or take formal positions on policy.

In its 2007 survey, "Food Biotechnology: A Study of U.S. Consumer Trends," a quantitative survey of 1,000 consumers, it noted that U.S. consumers are growing less wary of animal cloning. Approval of cloning in the 2007 survey was at its highest since questions concerning cloning were first asked in 2004.

Additionally, questions concerning the offspring of cloned animals were not asked until 2006. In the 2007 report, 22% were favorable to animal cloning as opposed to 16% in 2006. In both years about 28% of participants were neutral.

When asked if FDA approval of animal cloning would increase acceptability, participants in the 2007 survey answered yes. In the event of FDA approval, 46% of participants in 2007 were somewhat or very likely to purchase products from cloned animals. For the offspring of cloned animals, FDA approval raised consumer favorability in the 2007 survey to 49%.

A similar increase in favorability in the 2007 survey occurred when consumers were asked about animals cloned for breeding purposes, with 25% somewhat or very likely to purchase those products compared to 18% in 2006. In both years about one-third were neutral on that issue.

Overall, the survey found that for both plant and animal biotechnology, the more consumers know about a technology, the more they are likely to accept it.

Cloning process review for nonscientists

Most cloning today uses somatic cell nuclear transfer (SCNT), a process in use since 1996. In the SCNT cloning process, scientists use unfertilized oocytes (eggs) from ovaries obtained from packing plants that are incubated until they are mature enough to receive the donor embryo cell. With the gene-containing nucleus, or hereditary instructions, removed, the egg's development is then directed by the nucleus of the cell from the donor embryo. After the removal of the nucleus, what remains is a cell that contains nutrients essential for embryo development and other cellular machinery waiting for a new set of instructions.

A somatic cell from an animal with known desirable traits (a "donor"), or in some cases just the cell's nucleus, is cultured in an incubator and then injected under the coating of the unfertilized oocyte. Somatic cells are any cells of the body except sperm and eggs. The donor nucleus frequently comes from a skin cell taken from a live or recently deceased animal. Stimulated by a mild electrical pulse, the oocyte cytoplasm (everything in the cell but the nucleus) and the genetic material from the donated somatic cell combine.

If everything is successful, the resulting fused cell divides just as if it were a fertilized egg and produces an embryo. The embryo is then implanted in the uterus of a surrogate dam, which carries it to term and delivers it like her own offspring.

Low success rates and scientific challenges

When the process isn't successful, scientists believe the cause is the differentiation, or specialization, of the mature cells used in the SCNT process. Scientists currently believe that early in a plant or an animal's development there are unorganized cell masses that, through a series of processes in the egg or spore, differentiate into organs and organ systems. This is called epigenesis. The unlocking and resetting of these inherent instructions without making changes to the genetic code is called epigenetic reprogramming. Epigenetic effects involve changes in gene function that do not involve changes in DNA sequence. (See "Evaluating Epigenetics" on page 119 for more regarding epigenetics.)

There are epigenetic effects in every reproductive process, from in vitro fertilization (IVF) to artificial insemination (AI). One example of an epigenetic effect in typical human birth is the different fingerprint patterns in identical twins.

There are also epigenetic effects at work in cloning, according to Steven Stice, professor in the College of Agricultural and Environmental Sciences and director of the Regenerative Bioscience Center at the University of Georgia. That is one way livestock clones with matching DNA can look different from the donor animal. In addition, according to Mark Allan, beef cattle geneticist at the Roman L. Hruska U.S. Meat Animal Research Center (USMARC), there are also scientific questions about the role mitochondrial DNA from the host oocyte (or the host egg) can play in the development of the resulting animal clone. Allan says not enough research has been done to know whether maternally-inherited mitochondrial DNA will have measurable effects on cloned females. There are some scientists who suggest that because of mitochondrial DNA from the host oocyte, animals resulting from the SCNT process are not true clones.

Sally Northcutt, director of genetic research with the American Angus Association, says "Not with respect to cloned animals, but early work conducted at Iowa State and North Carolina using an animal model evaluation reported nonsignificant effects for cytoplasmic lines in beef cattle," she explains. "This work was done tracing cytoplasmic lineages, essentially tracking the whole cytoplasm in the egg, and then within that is the mitochondrial DNA."

Northcutt says there were reports of significant effects noted in dairy cattle, but for beef it was negligible. While she says it's a consideration, she thinks it would depend on the mitochondrial influence on particular traits.

Northcutt says the industry impact of cloning is still in its infancy and that she's not sure anyone knows the exact amount of the effect.

A tool for genetic improvement?

Bill Bowman, Association director of performance programs, says the application of cloning for genetic improvement will ultimately be the decision of individual breeders and the goals they have for their operations.

"If I'm able to identify 10 animals to be used as parents that are all superior for a trait or suite of traits that I want to improve, then I stand to make more of a change in that population's genetics using cloning," Bowman explains. "In that case it would be a viable tool for genetic change."

Both say they support the current cloning technology and FDA's conclusions; they simply don't see any immediate effect since the technology is still so new.

"Individual breeders will have to [determine] the best genetics to clone, and then weigh that against the cost and how it will fit into their program," Northcutt says. "And then they will have to decide if it could rapidly advance the population in terms of genetic improvement for traits of economic importance."