



Animal Biotechnology: Where to from here?

**2nd Symposium for Agricultural Biotechnology Risk Analysis Research
Ethical, Legal, and Social Implications (ELSI)**

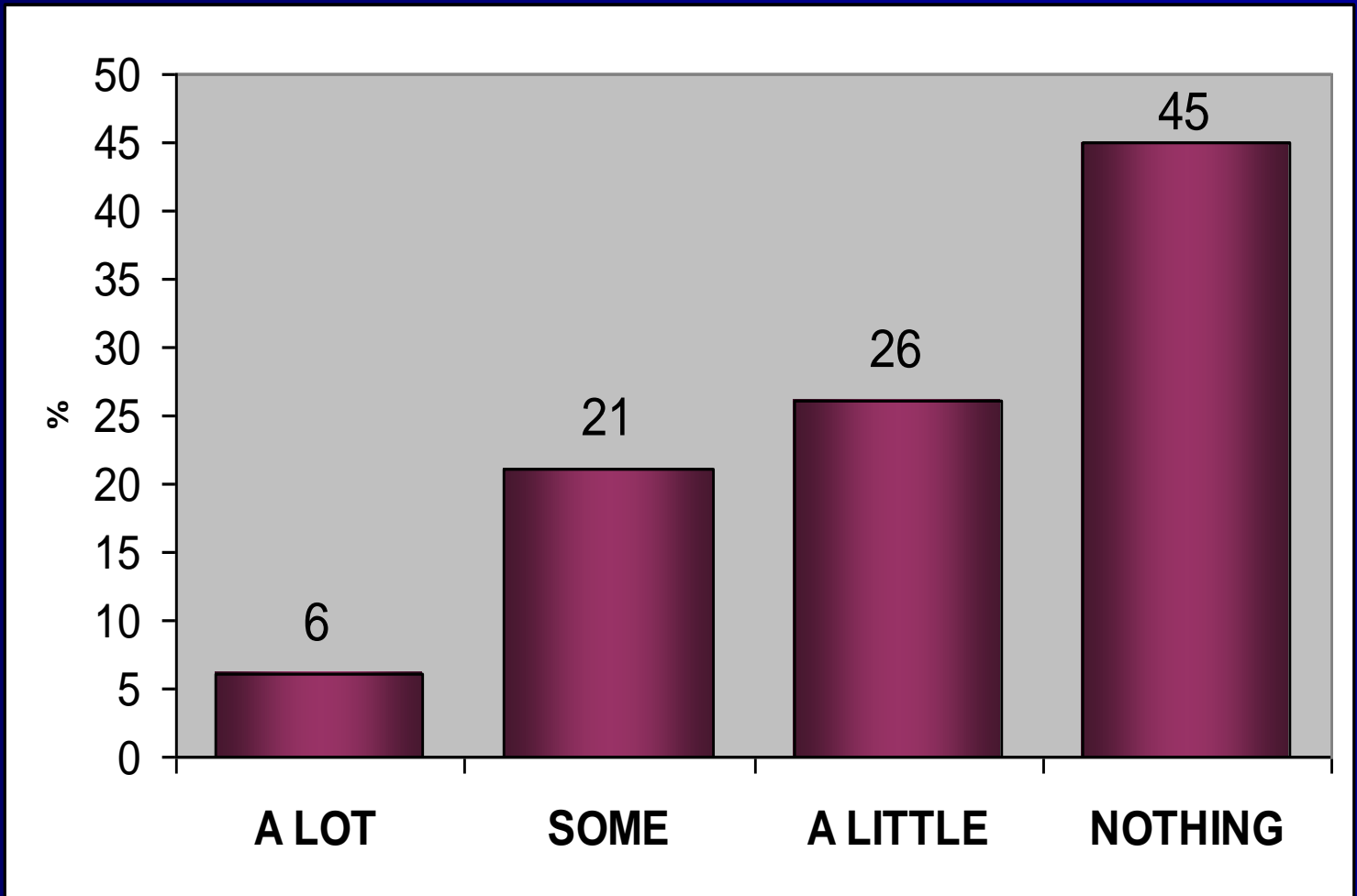
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12/6/2007



US Public Attitude Surveys

How much have you heard about animal biotechnology ? (IFIC, 2005)





"I know it when I see it"

Of the people who say they know nothing about biotechnology, genetic engineering or genetic modification; almost half (46%) disapprove of the use of genetic modification to create plant-based foods, and 66% disapprove of animal-based genetic modification.

Hallman, W. K., Hebden, W. C., Aquino, H.L., Cuite, C.L. and Lang, J.T. 2003. *Public Perceptions of Genetically Modified Foods: A National Study of American Knowledge and Opinion*. Rutgers - The State University of New Jersey.



Genetically-modified animals





Animal biotechnology is a broad term

- Artificial selection (breeding programs)
- Artificial Insemination
- Hormone use
- Using DNA information for the marker-assisted selection of superior animals
- Genomics
- Cloning
- Genetic engineering

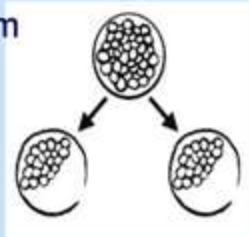




Mechanical embryo splitting

Cloning by Embryo Splitting

Embryo is split to form two half-embryos



Embryos are transferred to an unrelated surrogate mother



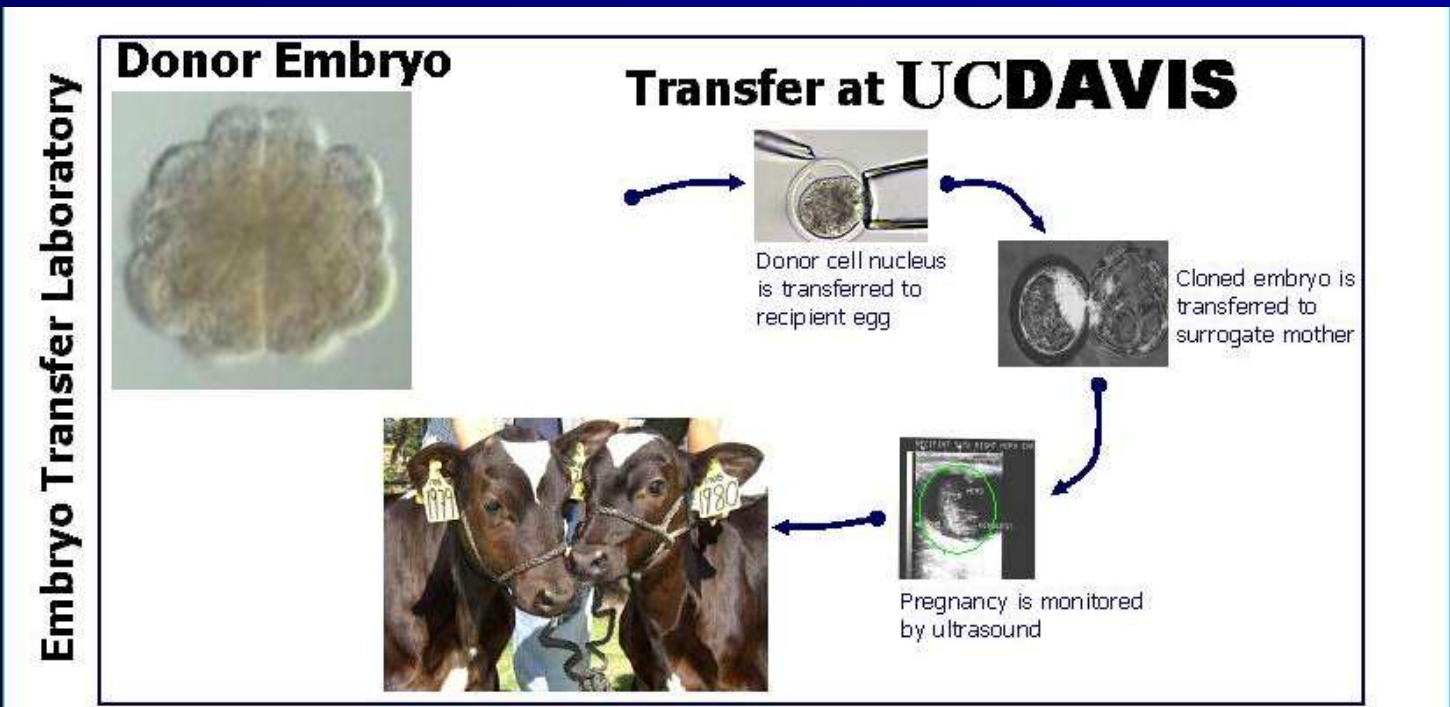
Pregnancy is monitored by ultrasound



Sheep gives birth to identical twins

The Holstein association of America has registered 2319 embryo split clones (ETS) through October 2002 – probably the most widely recognized were **DUPLICATE** and **DIVIDE**.

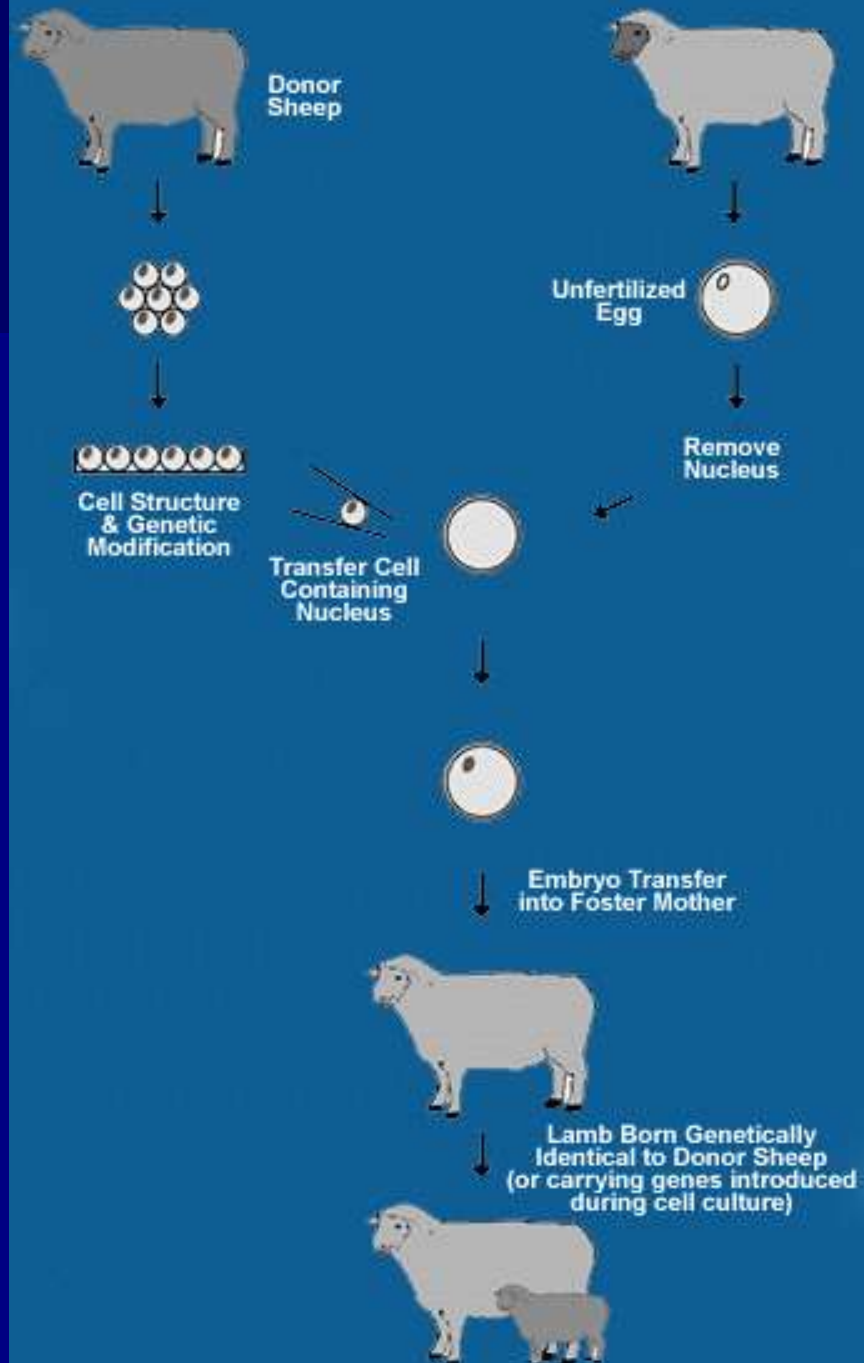
Nuclear transfer from an embryonic donor cell into an enucleated oocyte.



Holstein Association USA first registered clones from nuclear transfer in 1989. Approximately 1,200–1,500 cows and bulls produced by embryonic cell nuclear transfer in North America in the 1980s and 1990s.



Dolly (1996), the first adult SCNT clone





Regulation of SCNT cloned animals

<http://www.cyagra.com>

<http://www.viagen.com>

- In 2001, FDA imposed a voluntary moratorium on the sale of the products of cloned animals and their progeny into the human and animal food supplies and began assessing the risks expected from the cloning of food animals.



Regulation of SCNT cloned animals



- The FDA's 678-page draft risk assessment based on a four-year analysis of hundreds of peer-reviewed publications and other studies on the health and food composition of clones and their offspring was released in December 2006 found that "***food products derived from animal clones and their offspring are likely to be as safe to eat as food from their non-clone counterparts, based on all the evidence available***"
- Public comment period ended **5/3/2007**
- "*The agency will review comments and evaluate additional data that may be shared during the comment period. The FDA will then issue a final risk assessment, risk management plan, and guidance for industry. The FDA will continue to closely monitor any changes in cloning technology and the development of clones and their offspring as a source for food as further data become available.*" http://69.20.19.211/fdac/features/2007/207_clones.html



Ethics and the regulation of SCNT cloned animals

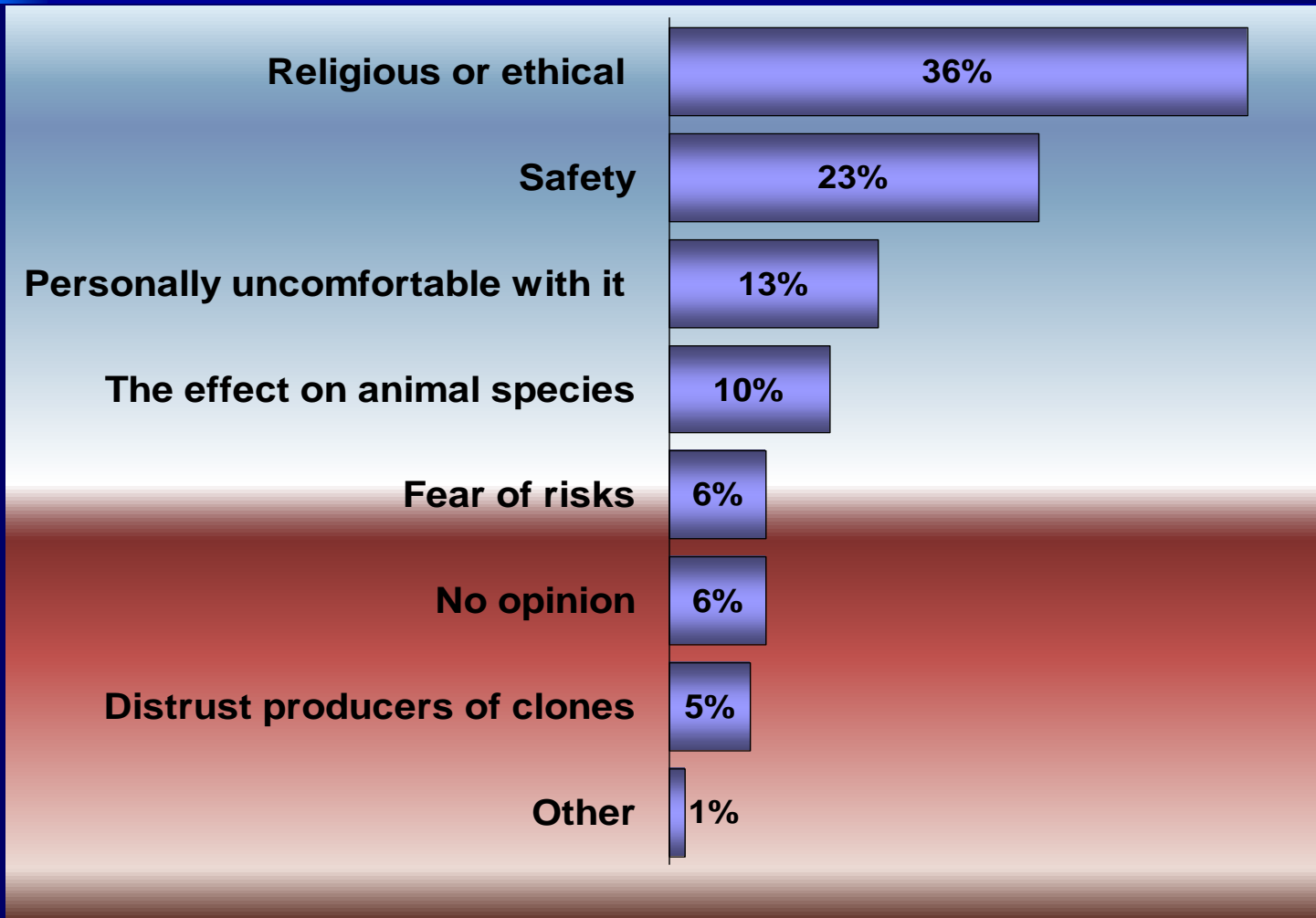


“The mandate of FDA is purely science-based. Moral and ethical issues cannot be considered in the context of making regulatory decisions about whether to allow the marketing of the products of animal biotechnology. In particular, FDA cannot address any ethical concerns about regarding whether a given technology should be commercialized or not; their decision is based solely on whether a product meets the FFDCA’s standards.”

Options for Future Discussions of Food Animal Biotechnology and Ethics
<http://pewagbiotech.org/events/1019/WorkshopReport.pdf>



Of the Americans who are uncomfortable or unsure about animal cloning; their primary concern is:



10/2005

Animal cloning regulations that included ethical considerations in Denmark and Norway resulted in the prohibition of cloning for food and ag purposes.



Ethical considerations were therefore given 100% weighting in these decisions





Let the market decide?

“While science may determine what is safe, society will decide what is acceptable”

Kochhar, H.P.S. and B.R. Evans. 2007. Current status of regulating biotechnology-derived animals in Canada – animal health and food safety considerations. 67:188.

“FDA is not recommending any additional measures relating to food derived from adult clones and their offspring, including labeling. .. there is no science-based reason to use labels to distinguish between milk derived from clones and that from conventional animals.”

http://www.fda.gov/cvm/CloningRA_FAQConsumers.htm



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Pharma and industrial applications of animal biotechnology (cloning and genetic engineering)





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August 1, 2006

Production of Recombinant Therapeutic Proteins in the Milk of Transgenic Animals

By Yann Echelard, Carol A. Ziomek, Harry M. Meade

European panel now recommends GTC anti-clotting drug's surgical use

OCTOBER 15 2006 FRAMINGHAM — A European drug regulation committee reversed itself yesterday and recommended that a GTC Biotherapeutics Inc. anti-clotting drug (human antithrombin) drawn from the milk of genetically altered goats be approved for use in surgical patients

<http://www.gtc-bio.com>





Cloned transchromosomal calves producing human immunoglobulin

Yoshimi Kuroiwa¹, Poothappillai Kasinathan², Yoon J. Choi³, Rizwan Naeem⁴, Kazuma Tomizuka¹, Eddie J. Sullivan², Jason G. Knott², Anae Duteau³, Richard A. Goldsby³, Barbara A. Osborne⁵, Isao Ishida^{1*}, and James M. Robl^{2*}

Published online: 12 August 2002, doi:10.1038/nbt727

Human polyclonal antibodies (hPABs) are useful therapeutics, but because they are available only from human donors, their supply and application is limited. To address this need, we prepared a human artificial chromosome (HAC) vector containing the entire unrearranged sequences of the human immunoglobulin (hIg) heavy-chain (*H*) and lambda (λ) light-chain loci. The HAC vector was introduced into bovine primary fetal fibroblasts using a microcell-mediated chromosome transfer (MMCT) approach. Primary selection was carried out, and the cells were used to produce cloned bovine fetuses. Secondary selection was done on the regenerated fetal cell lines, which were then used to produce four healthy transchromosomal (Tc) calves. The HAC was retained at a high rate (78–100% of cells) in calves and the hIg loci underwent rearrangement and expressed diversified transcripts. Human immunoglobulin proteins were detected in the blood of newborn calves. The production of Tc calves is an important step in the development of a system for producing therapeutic hPABs.

p <http://www.nature.com/naturebiotechnology>



<http://www.hematech.com>



Agricultural applications of animal biotechnology



CONFERENCE PROGRAM

Transgenic Animals in Agriculture

AUGUST 24-27, 1997

GRANLIBAKKEN CONFERENCE CENTER
TAHIDE CITY, CALIFORNIA

UCDAVIS
BIOTECHNOLOGY PROGRAM
DEPARTMENT OF ANIMAL SCIENCE

Selected Participants

- ABS Global
- Columbus Farming Corp.
- Food and Agriculture Organization of the UN
- NZ Ministry of Agriculture
- DeKalb Poultry Research
- Hy-Line International
- AgResearch (NZ)
- MetaMorphix
- National Institute of Animal Industry, Japan
- PIC Group
- Victorian Institute of Animal Science, Australia



U.S. Regulation of GE animals

FDA Center for Veterinary Medicine

- The U.S. Food and Drug Administration (**FDA**) has asserted jurisdiction over genetically engineered animals on the grounds that the transgene and any expressed proteins, affect the “structure and function” of the receiving animal analogous to the modalities of alternative veterinary drug formulations.
- Aqua Bounty AquaAdvantage™ growth-enhanced salmon submitted to the FDA over 10 years ago
- Hopes to launch in 2009

Ag applications on hold



Transgenic Research (2005) 14:563–567
DOI 10.1007/s11248-005-0670-8

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Perspective

Engineering disease resistant cattle*

David M. Donovan¹, David E. Kerr² & Robert J. Wall^{1,*}

¹*Biotechnology and Germplasm Laboratory, Agricultural Research Service, United States Department of Agriculture, Beltsville, Maryland 20705, USA*

²*Department of Animal Sciences, University of Vermont, Burlington, Vermont 05405, USA*

Received 7 June 2005; accepted 21 June 2005

Key words: bovine, disease resistance, mastitis, transgene



- Genetically engineered cows resistant to intra-mammary *Staphylococcus aureus* infection (2005)
- Production of transgenic goats expressing human lysozyme in their mammary gland (2006)
- Production of cattle lacking prion protein that causes “mad cow disease” (2007)

**H. Niemann
(1998)**

Transgenic farm animals get off the ground

Transgenic Animals in Agriculture, Conference Tahoe City,
California, USA

August 24–27, 1997, sponsored by the University of California at
Davis

“An important factor that should not be underestimated is the considerable resistance of public opinion in several countries, particularly Europe, against this technology. This could affect private and public funding in these countries and thereby slow down further progress. Given the broad range of serious problems that mankind is facing in the years ahead, one can hope that rational approaches will be taken to ensure that the huge benefits of transgenic farm animals will not be an unexploited resource.”





European project to map research and commercial activities worldwide for animal cloning and genetic modification

Animal cloning and genetic modification. A prospective study Joint Research Center Institute for Prospective Technological Studies. European Commission, Seville. *In preparation*

- Number of published papers on animal GM/GE increased over the period 1985 – 1998 and then leveled off, with most coming from the EU, followed by the USA.
- Number published papers on cloning increased from 1990 – 2000 but this has since leveled off. Most of the work was done in the USA with Europe coming third (after the Far East). The work concentrated on technical aspects and was mostly publicly funded.



USDA National Research Initiative (major funding source for academic agricultural research in the U.S.)



43.0 Animal Genome (A): Translational Animal Genomics

FY 2008 Priorities for Research Projects – Applicants must address at least one of the following priorities.

1. Identification and mapping of genomic markers, including quantitative-trait loci (QTL), economic trait loci (ETL), causative mutations, and candidate genes for traits of importance to animals in agriculture, including aquaculture species.
 2. SNP-based cost-effective genotyping as it relates to whole genome enabled animal selection, genomic capabilities that enable parentage, and identity verification (traceability) and genetic diversity.
 3. Development and application of methods to modify the animal genome to aid in the understanding of gene function or expression (e.g. RNAi, nuclear transfer, embryonic stem cells, and transgenics).
- Applications whose primary aim is to improve the efficiency in the production of clones or transgenic animals through manipulation of the nucleus will no longer be accepted by the Animal Genome program.

GloFish™ is the only product of animal biotechnology thus far on the U.S. market

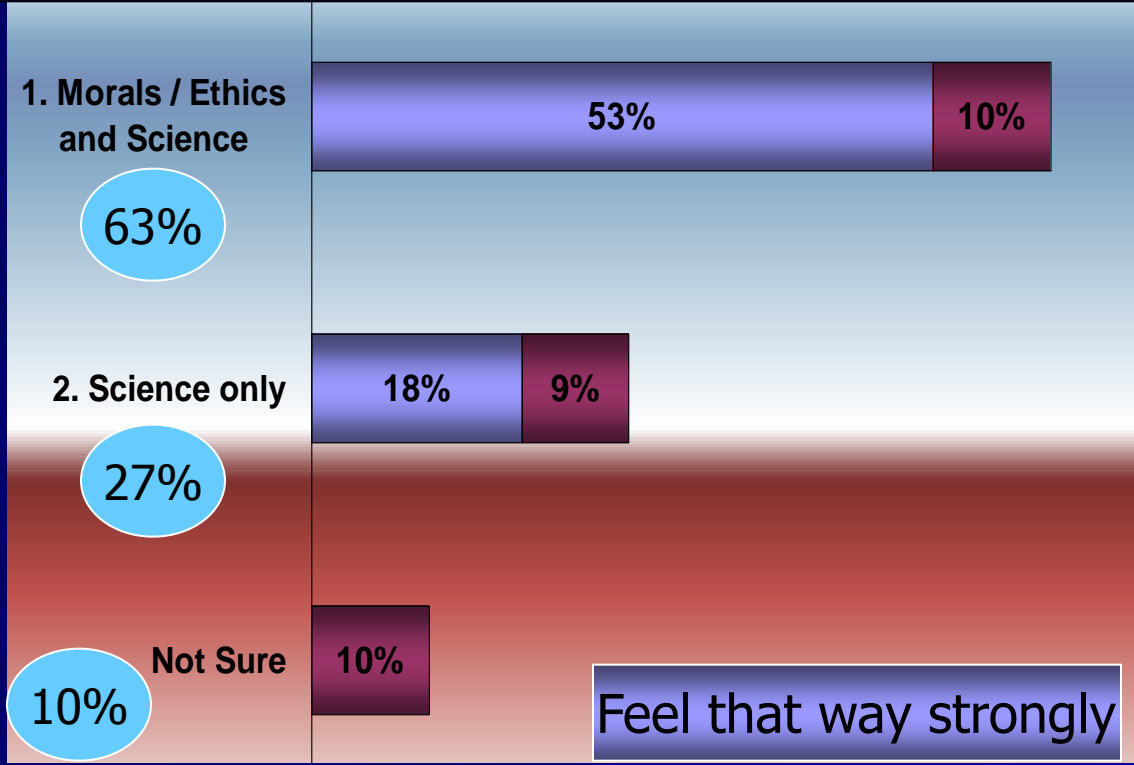


<http://www.glofish.com>



1. Government regulators should include ethical and moral considerations, in addition to scientific evaluation of risks and benefits, when making regulatory decisions about cloning or genetically modifying animals.

2. Though ethical and moral considerations are important, government regulators should consider only scientific evaluation of risks and benefits when making regulatory decisions about cloning and genetically modifying animals.





How to incorporate social and ethical issues into regulatory decisions ?

- American consumers (75%) and scientists (70%) agree that cloning and genetic engineering of animals raise some moral and ethical issues
- However public is much less likely to approve (21-25%) of these technologies than scientists (60-68%)
- How to reach a societal consensus on ***which set of values*** will ultimately be applied to decide the acceptable uses of animal biotechnology ?

The President's Council on Bioethics



Advising the President on ethical issues related to advances in biomedical science and technology

"To advance human good and avoid harm, biotechnology must be used within ethical constraints. It is the task of bioethics to help society develop those constraints and bioethics, therefore, must be of concern to all of us."
Chairman's Bio



Edmund D.
Pellegrino
Chairman

Topics of Council Concern

Age-Retardation
(Life Extension)

Aging and End-of-Life

Beyond Therapy (Enhancement)

Biotechnology and Public Policy

Bioethics in Literature

Cloning

What's New...

Stem Cell Research Check for updates on adult, embryonic, and alternative sources of human pluripotent stem cells.

<http://www.bioethics.gov/>



Options for Future Discussions of Food Animal Biotechnology and Ethics

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Deliberative Institutions and Ethical Frames

(United States, UK, Canada)

Ethical Frame Type of Institution	Animal Welfare		Risk		Moral Order	
	Pain and Suffering	Costs/ Benefits	Risks to Health	Risks to Environment	Mechanization	Unnatural Creation
Legislative advisory body		X	X	X		
National ethics commission	X	?	X	X	X	X
Executive agency/ advisory committee	X	X	X	X		
Court			X	X	X	?
Independent science organization: NAS	X	X	X	X		
Independent ethics organization: Nuffield Council	X	?	X	X	X	X
University committee, IRB	X	X (in science)	X	X		
Industry non-governmental organization	X	X (mainly benefits)	X	X		
Non-industry non-governmental organization	X	X	X	X	X	X



SUMMARY



- Animal biotechnology faces unique ethical questions that were not part of plant biotechnology debate
- FDA regulates GE/cloned food animals in U.S.
- The mandate of FDA is purely science-based
- Even in the absence of an ethical discussion – or some may say because of that absence – long regulatory process for products of animal biotech
- No GE or SCNT cloned food animals are currently on the U.S. market
- Yet to see if the expense of the technology and the regulatory process results in commercial viability