



Animals and Transgenesis

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Overview

- **Introduction**
 - **Definitions**
- **Types of Transgenic Animals**
 - **How they are made**
- **Examination of Transgenic Claims**
 - **Statutes**
 - **Sample Claims**



Introduction: Definitions

■ Transgene

- A foreign gene that has been incorporated into the genome of an organism.
 - Random Integration
 - Homologous Recombination
 - Gain or Loss of Function

■ Transgenic Animal

- An organism that contains a transgene that is passed down to its descendents.



Introduction: Definitions

■ Phenotype

- **Any *observable characteristic* or trait of an organism: such as its morphology, development, biochemical or physiological properties, or behavior.**
 - **Results from expression (or lack thereof) of an organism's genes as well as the influence of environmental factors and possible interactions between the two.**
- **Correlates to uses of transgenic animals**



Types of Animals

Transgene and Method of Introduction=Type of transgenic Animal Made

- **Overexpressers**
 - **Random Integration**
 - **Gain of Function**
 - **Expression**
 - **Promoter**
 - **Phenotype**



Types of Animals (cont.)

- **Overexpressers (cont.)**
 - **Limitations**
 - **Transgene Expression Level**
 - **High/Low Expressers**
 - **Site of Integration**
 - **Copy Number**
 - **Unpredictability of Phenotypes**
 - **Different Species**
 - **Disease**
 - **Gene Function**



Types of Animals (cont.)

- **Knockouts/Knockins**
 - **Homologous Recombination**
 - **Targeted Insertion**
 - **Loss of Function**
 - **Targeted Gene is Disrupted**
 - **Lacks Expression**
 - **Gain of Function**
 - **Phenotype Correlates to Loss or Gain of Function**
 - **Homozygous**
 - **Embryonic Stem (ES) Cells**



Types of Animals (cont.)

- **Knockouts/Knockins (cont.)**
 - **Limitations**
 - **Availability of ES cells**
 - **Germline Transmission**
 - **Unpredictable Phenotype**
 - **Gene Function**
 - **Unknown**
 - **Phenotype May not Correlate with Function**
 - **Hybrid Genetic Background**



Types of Animals (cont.)

- **Nuclear Transfer Animals**
 - **Genetic Material from Donor Nucleus**
 - **Somatic Cell**
 - **Embryonic Stem Cell**
 - **Recipient Enucleated Oocyte**
 - **Genetically Modified Offspring**
 - **Fibroblast**
 - **Clones**



Types of Animals (cont.)

- **Nuclear Transfer Animals (cont.)**
 - **Limitations**
 - **Methodology Limited to Non-Primate Mammals**
 - **Cell Type of Transfected Donor Cells**
 - **Fibroblasts**



Common Examination Issues in Animal Patents

35 USC 101

- Utility
- Statutory Invention

35 USC 112, 1st paragraph

- Enablement
- Written Description

35 USC 103-Obviousness

35 USC 102-Noveltly



Examination Issues in Animal Patents-Utility

- **Specific, Substantial, and Credible**
 - Use must be based upon specific (particular) combination of elements
 - Transgene + Animal + phenotype
 - General use such as snake food would not be considered substantial, unless invention is directed to enhanced animal feed
 - Credibility assessed from perspective of skill and knowledge in the art



Examination Issues in Animal Patents-Utility (cont.)

Sample Claim:

A transgenic mouse whose genome comprises a homozygous disruption in gene X, wherein gene X is not expressed and the mouse has a phenotype of running in circles.



Examination Issues in Animal Patents-Utility (cont.)

■ Considerations:

- What is known about Gene X?
 - Art and Specification
 - Function?

- Is there a correlation between the disclosed phenotype (running in circles) and a disease or Gene X function?
 - Art and Specification

- What are the disclosed utilities of the transgenic mouse?
 - General or Specific?



Examination Issues in Animal Patents-Utility (cont.)

■ Considerations (cont.)

— Utility Guidelines

- Example 4-uncharacterized proteins
 - Gene X encodes an uncharacterized protein
- Example 11-animals with uncharacterized human genes
 - Correlation to Disease
 - Gene X has no apparent correlation to disease

<http://www.uspto.gov/web/patents/guides.htm>



Examination Issues in Animal Patents-Statutory Invention

Section 101 of title 35, United States Code, provides:

- Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.



Examination Issues in Animal Patents-Statutory Invention (cont.)

- As the Supreme Court has recognized, Congress chose the expansive language of 35 U.S.C. 101 so as to include “anything under the sun that is made by man” as statutory subject matter. *Diamond v. Chakrabarty*, 447 U.S. 303, 308-09, 206 USPQ 193, 197 (1980).
- **MPEP 2106**



Examination Issues in Animal Patents-Statutory Invention (cont.)

- **Is The Claimed Invention Statutory?**
 - **Product of Nature?**
 - **Hand of Man?**
 - **Humans?**
 - **1077 O.G. 24, April 21, 1987.**



Examination Issues in Animal Patents-Statutory Invention (cont.)

Sample Claim

- An animal comprising a mutation in gene Z.



Examination Issues in Animal Patents-Statutory Invention (cont.)

■ Considerations

- Product of Nature?
 - Hand of Man
 - Naturally Occurring Mutation in Gene Z
- Prior Art
 - Invention known
- Does the Claim Embrace Humans?



Examination Issues in Animal Patents-Enablement

- **How to “make” the animals**
 - **Random Integration-“Standard” zygote transduction**
 - **Now considered relatively routine**
 - **BUT, phenotype is often based upon a unique integration event and expression**
 - **Consider reproducibility and scope of claims**
 - **Homologous recombination**
 - **Embryonic stem cell availability often questionable**



Examination Issues in Animal Patents-Enablement (cont.)

- What is the “use” of the animal?
 - Is it based upon the phenotype?
 - Consider claiming a scope of animal/phenotype that would be expected to have a “useful” property
 - Is Transgene Expression Enough?
 - Reporter Molecules



Examination Issues in Animal Patents-Enablement (cont.)

- **Consider *Wands* factors-MPEP 2164.01(a)**
 - Breadth of the Claims
 - Nature of the Invention
 - The state of the Prior Art
 - The Level of One of Ordinary Skill
 - The Level of Predictability in the Art
 - The Amount of Direction Provided by the Inventor
 - The Existence of Working Examples
 - The Quantity of Experimentation Needed to Make or Use the Invention Based on the Content of the Disclosure



Examination Issues in Animal Patents-Enablement (cont.)

■ Sample Claim

A transgenic non-human animal whose genome comprises a transgene operably linked to a promoter, wherein the animal exhibits brain cancer resulting from expression of the transgene.



Examination Issues in Animal Patents-Enablement (cont.)

■ Considerations

- Is the phenotype (brain cancer) predictable across animal species?
 - Breadth of claims
 - Working Examples
 - State of Art Regarding Transgene Expression/Phenotypes
 - Transgene
 - Promoter
 - Guidance/Teachings Provided by the Specification



Examination Issues in Animal Patents-Written Description

- **Identify disclosed distinguishing characteristics as they relate to the scope and content of the claims**
 - **Genus of Nucleic Acid Molecules (Transgenes) Embraced by the Claims**
 - identify essential structural elements
 - Identify species explicitly or implicitly disclosed
 - reconcile with the level of skill in the art



Examination Issues in Animal Patents-Written Description (cont.)

Sample Claim:

- A transgenic non-human animal whose genome comprises a disruption in an endogenous gene, wherein the endogenous gene is not expressed and the animal exhibits the ability to do back-flips.



Examination Issues in Animal Patents-Written Description (cont.)

■ Considerations

— Scope of the disrupted gene?

- Genus
- Species
- Definitions
- Structure/Function
- Written Description Guidelines
 - <http://www.uspto.gov/web/patents/guides.htm>



Examination Issues in Animal Patents-35 USC 103

- **What's in a Claim?**
 - **Broad limitation to animal comprising mutation or transgene?**
 - **For “known” genes**
 - **“routine” to make transgenic or mutant**
 - **Specific Limitation to Phenotype?**
 - **Is phenotype “expected”?**
 - **Is phenotype required?**



Examination Issues in Animal Patents-35 USC 103 (cont.)

- **Sample Claim:**
- **A transgenic mouse whose genome comprises a transgene encoding a human qrt gene operably linked to a promoter, wherein expression of human qrt results in liver cancer.**



Examination Issues in Animal Patents-35 USC 103 (cont.)

■ Considerations

- Routine to make a transgenic mouse?
- What is Known About the *qrt* gene?
 - Specification
 - Art
 - Correlation to Liver Cancer?
 - Predictability of Liver Cancer Phenotype?
 - Known *qrt* mutation correlated with liver cancer in humans?



Examination Issues in Animal Patents-35 USC 102

- **What's in a claim?**
 - **Broadest Reasonable Interpretation of Claimed Invention Consistent with the Teachings of the Specification**

- **Prior Art**
 - **Invention Known?**
 - **All Claimed Embodiments Taught?**
 - **Inherent Properties?**
 - **Same transgene-different phenotype**
 - **Claimed and prior art mice appear structurally the same**



Examination Issues in Animal Patents-35 USC 102 (cont.)

- Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a *prima facie* case of either anticipation or obviousness has been established. *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977).
- MPEP 2112.01



Examination Issues in Animal Patents-35 USC 102 (cont.)

- [Therefore,] the *prima facie* case can be rebutted by evidence showing that the prior art products do not necessarily possess the characteristics of the claimed product. *In re Best*, 562 F.2d at 1255, 195 USPQ at 433.



Questions

Thank You!

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