Patent Landscape Report on

Animal Genetic Resources

2014

PATENT LANDSCAPE REPORTS PROJECT

in cooperation with the Food and Agriculture Organization of the United Nations

WIPO
WORLD INTELLECTUAL PROPERTY ORGANIZATION

Patent Landscape Report on Animal Genetic Resources

A patent landscape report prepared
for the

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Report Summary

This patent landscape report provides an overview of international patent activity for animal genetic resources for food and agriculture. The research focused on identifying patent activity for 17 animals from 15 species of global importance in food and agriculture. The research covered cattle, buffalo, pigs, sheep, goats, horses, donkeys, bactrian and dromedary camels, llamas and alpacas along with chickens, ducks and turkeys. The research did not include fish.

The research involved:

- Text mining over 14 million patent documents from the European Patent Office, the United States Patent and Trademark Office and the Patent Cooperation Treaty for animal names and breed names;
- Mapping technology clusters involving animals;
- Identifying patent documents involving animal genetic resources of relevance to food and agriculture;
- Reviewing patent documents for references to breed names and traditional knowledge.

The main outcomes of the research are:

- A quantitative indicator of trends in patent activity for animal genetic resources that can be updated and refined over time to respond to policy needs;
- Analysis of the key features of the patent landscape for animal genetic resources of relevance to food and agriculture;
- A detailed set of examples of important patent documents involving animal genetic resources to provide evidence to inform policy debates.

The report concludes that:

- Key technologies relating to animal breeding have a long history and breakthroughs typically involve new methods or technologies rather than depending on genetic material *per se*;
- Developments involving transgenic animals now focus on recombinant proteins and medical markets rather than products for human consumption;
- Phenotypic selection is being replaced by genomic selection and the rise of genomic indices;
- The completion of major livestock genome sequencing projects has important implications for food and agriculture. However, the patent environment for genetic inventions is less permissive than in the past;
- Emerging developments in synthetic biology, metabolic engineering, genome engineering and genome editing have potentially important implications for food and agriculture and merit further investigation;
- Following a surge of patent activity in the late 1990s the dominant trend in

patent filings involving animal genetic resources of relevance to food and agriculture has been downwards. This reflects a combination of factors external and internal to the patent system. Future trends may change following the completion of major genome sequencing projects and the rise of new technologies such as synthetic biology, genome engineering and genome editing;

- The majority of patent activity focuses on dominant breeds and does not involve genetic material from rarer breeds from specific countries or the use of traditional knowledge. This reflects the nature and orientation of existing technologies directed to animal breeding;
- Patent data could potentially provide a useful source of information for farmers and animal breeding organizations to address issues such as disease resistance and control or adaptation to climate change;
- The research detected an emerging trend towards the combination and integration of genetic information with software and business methods that merits further investigation in the context of the completion of genome sequencing projects for major livestock animals.

The report provides the following options for consideration:

1. Further work to refine the patent indicator to respond to policy needs;
2. Improvements to the coverage of animals in the Cooperative Patent Classification in consultation with WIPO and the EPO to facilitate the analysis of quantitative trends for animal genetic resources for food and agriculture;
3. Examine the nature of patent claims and their implications for developments in food and agriculture;
4. Expand research on animal breeds in patent data;
5. Monitoring of patent activity and related activity in the field of animal genomics;
6. Further analysis of patent activity for methods, software and business methods of relevance to animal genetic resources for food and agriculture;
7. Analysis of the implications of technologies appearing in patents for the conservation and sustainable use of animal genetic resources in both developed and developing countries;
8. Identification of the potential utility of technologies appearing in patents for improving livestock breeding in developing countries;
9. Further research on the implications of emerging areas of science and technology such as synthetic biology, metabolic engineering, genome engineering and genome editing for animal genetic resources for food and agriculture.

Executive Summary

This patent landscape report provides an overview of international patent activity for animal genetic resources, in particular those relating to food and agriculture.

The empirical analysis of patent activity for animal genetic resources for food and agriculture has received remarkably little attention in the scientific literature. Indeed, in conducting the present research we found no example of a quantitative analytical study of patent activity for animal genetic resources with respect to food and agriculture.

This study presents large-scale quantitative analysis of patent activity across a range of animal species that are important for food and agriculture. As such, its main focus is addressing the challenges involved in identifying patent activity for animal genetic resources in general and activity relating to animal genetic resources for food and agriculture in particular.

The research focuses on identifying patent activity in relation to 17 animal species and subspecies of global importance to food and agriculture. The research covered cattle, buffalo, pigs, sheep, goats, horses, donkeys, bactrian and dromedary camels, llama and alpaca species along with chickens, ducks and turkeys. The research did not include fish. These species, and the diverse breeds associated with them, are central to global agriculture and food security.

The present research has been undertaken in the context of growing concern about the proper management of the world's diverse animal breeds to ensure the health and integrity of the genetic pool upon which agriculture depends for its long-term ability to adapt and respond to changing environmental and market conditions [1,2]. There is growing concern that large-scale industrial livestock production directed to meeting the demands of modern food markets is irreversibly narrowing the global livestock gene pool at the expense of humanity's future welfare. In approaching these issues and the patent landscape report, it is important to understand the key technological developments involved in animal breeding and animal biotechnology. Table 1 (below) outlines the historical development of key technologies in these areas and we highlight five key points for consideration:

1. *Animal breeding technologies have a long history*. Technologies such as Artificial Insemination (AI), Multiple Ovulation and Embryo Transfer (MOET), superovulation, sex-selection and freezing sperm, have a considerable history stretching back to the early and mid 20th Century. Breakthroughs in this area typically involve the application of new methods or technologies to improve fertility (e.g. flow cytometers for sperm sorting or the use of Follicle Stimulating Hormone (FSH) for superovulation) rather than the use of genetic material *per se*. As such, patent activity involving animal genetic resources typically focuses on methods.

2. Developments in transgenic animals presently focus on recombinant proteins and medical markets. The creation of transgenic animals using techniques such as somatic cell nuclear transfer have increasingly shifted from an initial focus on production for possible human consumption to production for medical markets, notably in connection with the production of recombinant proteins in animals (biopharming or the use of animals as bioreactors) [42,51]. This is presently the dominant trend in research and development involving transgenic animals and is likely to continue for the foreseeable future in the absence of markets for transgenic meat and other products from transgenic animals [26]. New and emerging developments such as synthetic biology, metabolic engineering, genome engineering and genome editing could potentially transform existing trends.

3. *Phenotypic selection is being replaced by genomic selection and the rise of genomic indices.* Methods directed to selection based on predicted economic value, such as BLUP (Best Linear Unbiased Prediction) using phenotypic data, have been augmented thanks to the availability of genetic markers, notably Single Nucleotide Polymorphisms or (SNPs), and ultimately overtaken by a focus on genetic Quantitative Trait Loci (QTLs) and Genomic Estimated Breeding Values (GEBV) in the form of genomic indices. However, the genome sequences of the majority of large livestock animals and birds were only completed in the last 5 years.

4. The completion of major livestock genome sequencing projects has important implications for food and agriculture. However, the environment for patent protection of genetic inventions is less permissive than in the past. The ongoing completion of genome sequencing projects for major livestock animals in recent years is taking place in a patent environment that is considerably less permissive than that in which the human genome project was completed in 2003. More stringent criteria are being applied to the patentability of genetic material and the assessment of patents involving claims to DNA,

RNA, amino acids, polypeptides and genes. That said, it is likely that the completion of major animal genome projects will result in new patents in this area.

5. *New and emerging developments in synthetic biology, metabolic engineering, genome engineering and genome editing have potentially important implications for food and agriculture*. Synthetic biology, metabolic engineering, genome engineering and genome editing are emerging areas of science and technology with important implications for developments in food and agriculture such as the rise of mammalian synthetic biology, or the use of engineered nucleases as molecular scissors to edit the genome of an organism [3-6]. A recent report of the birth of twin macaques with edited genomes in China marks a shift from the creation of transgenic animals using alien DNA to editing native genomes without necessarily introducing alien DNA [7]. While these emerging developments are not considered in this report they represent important areas for further research in relation to their potential application in animal breeding and intellectual property.

This patent landscape report provides a snapshot of patent activity involving animals at the European Patent Office (EPO), the United States Patent and Trademark Office (USPTO) and the Patent Cooperation Treaty (PCT) between 1976 and 2013. The EPO data covers the 38 countries that are members of the European Patent Convention (EPC), and PCT data relates to international patent applications filed by applicants from up to 148 PCT member countries. By focusing on the major markets of Europe and the US, as well as international patenting activity under the PCT, the report identifies economically significant patents relating to animal genetic resources. The report does not consider patenting activity at individual national offices, such as China, India and Brazil but recognizes that national level activity merits closer attention in the future.

The patent system provides time-limited protection for inventors and companies seeking to operate in global markets; it can contribute to Foreign Direct Investment, and facilitate the international transfer and uptake of new technologies [52-56]. The patent system also provides global indicators for trends in commercial research and development for a wide range of technology fields. The patent system constitutes a technical library of information on inventions encompassing over 60 million documents in multiple languages. Thanks to the availability of database technologies, this rich pool of information is increasingly accessible in electronic form enabling statistical and analytical research that can inform policy debates on developments in science and technology.

The patent landscape report on animal genetic resources is the result of text mining 14,038,743 patent documents for references to animal species names,

mapping of the areas of science and technology that involve animals and detailed analysis of patent activity involving animal genetic resources. A five-step method for patent analysis was developed to identify and investigate the patent landscape for animal genetic resources:

1. Searching the full text of patent documents for the target animals using their Latin species names;
2. Searching the title, abstracts and claims of patent documents for animal common names and major groupings of animals (e.g. bovine, porcine, ruminant etc.);
3. Mapping major technology clusters using patent classification codes (the International Patent Classification and Cooperative Patent Classification) and co-occurrence analysis;
4. Searching the titles, abstracts and claims for key terms relating to animal genetic resources identified from the scientific literature in Web of Science and manual review of patent data;
5. Co-occurrence analysis of key terms for animal genetic resources appearing in the technology clusters for new breeds of animals and biotechnology to identify major themes.

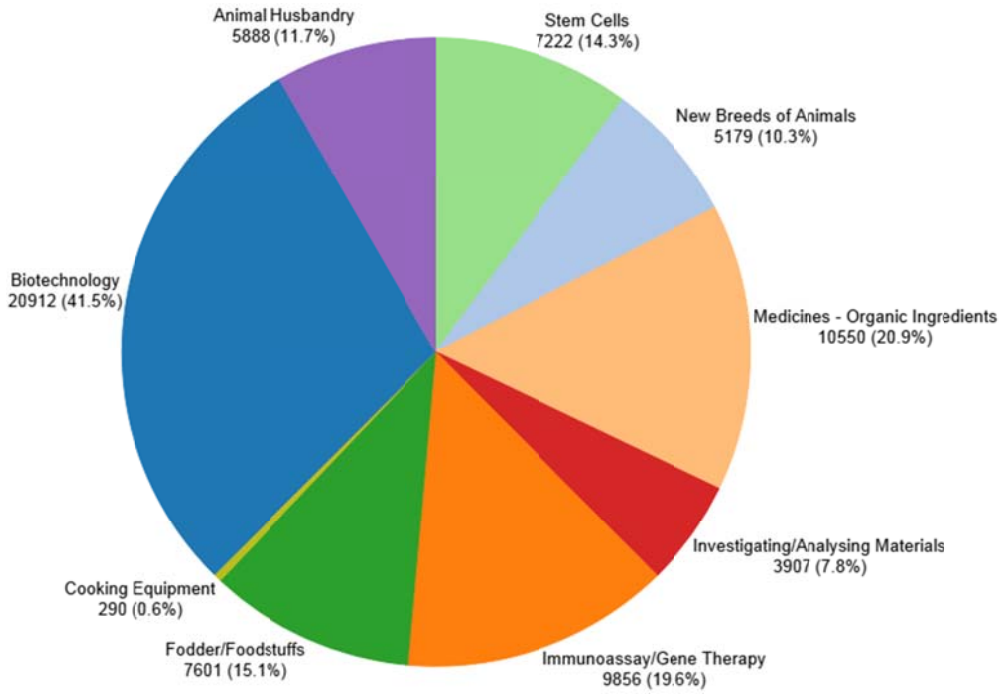
As so little research has been done on patent activity in this area, as a first step, we mapped international patent activity for animals in general. This revealed that animal-related patents permeate many different areas and underlined the important contribution that animals make to innovation across a wide spectrum of technologies. Areas in which animal-related patents occur include: foodstuffs, food and agriculture, animal husbandry, clothing, cooking equipment, toys and games, personal care products, medicines, pharmaceuticals and biotechnology in areas such as new breeds of animals (transgenic animals), gene therapy and stem cells among others.

Our research revealed 50,387 first filings of new inventions that make reference to animals using Latin species names, common names and group names (e.g. bovine, ruminant etc.). Using advanced network mapping of patent classification codes we identified eight *technology clusters* that involve animals and animal genetic resources. Figure 1 (below) displays the top areas involving animals based on the number and the percentage of filings.

Figure 1 indicates that references to animals within patent documents in a number of areas do not reflect the use of animals as genetic resources. For example, patents in the area of animal husbandry mainly relate to equipment. Similarly, references to animals or animal material, such as proteins or bovine serum albumin, are not primarily concerned with animals as a genetic resource. The research therefore focused on: a) identifying patent activity involving animals as a

genetic resource, and; b) distinguishing activity involving animal breeding for food and agriculture from other activities.

Figure 1: Technology Clusters involving Animals and Animal Genetic Resources



We manually reviewed and classified 5,179 first filings in the New Breeds of Animals cluster and 20,912 first filings in the Biotechnology cluster (see Figure 1). Patent classification systems, notably the International Patent Classification and the Cooperative Patent Classification, use the term New Breeds of Animals to refer to genetically modified or transgenic animals and related technologies. We use this term throughout this report interchangeably with transgenic animals and recognise that other uses of this term may exist outside the patent system. We identified six broad categories of patent activity of relevance to food and agriculture, namely:

1. Artificial Insemination, Sex Selection and Control of Estrus;
2. Marker Assisted Breeding;
3. Transgenic Animals;
4. Animal Cloning;
5. Xenotransplantation;
6. Animal Models.

We developed a working thesaurus of search terms and extended the analysis into the biotechnology cluster. To ensure the accuracy of data capture we reviewed 217,824 multi-word phrases from the titles, abstracts and author key words of 10,709 scientific publications on animal and livestock breeding and animal biotechnology. This enabled us to identify additional terms used in animal breeding research, such as genome wide association studies, that had not been identified during the patent review. It also expanded the range of terms available for searching the patent data. We then developed a quantitative indicator for trends in international patent filings involving animal genetic resources for food and agriculture. The advantage of this indicator is that it can be contextualised within the wider universe of activity making reference to animals and compared with approaches based on patent classification codes. The indicator can also be adjusted based on advances in understanding of the sector. Figure 2 displays the indicator and contextual information for comparative purposes.

Figure 2: Composite Patent Indicator for Animal Genetic Resources for Food and Agriculture

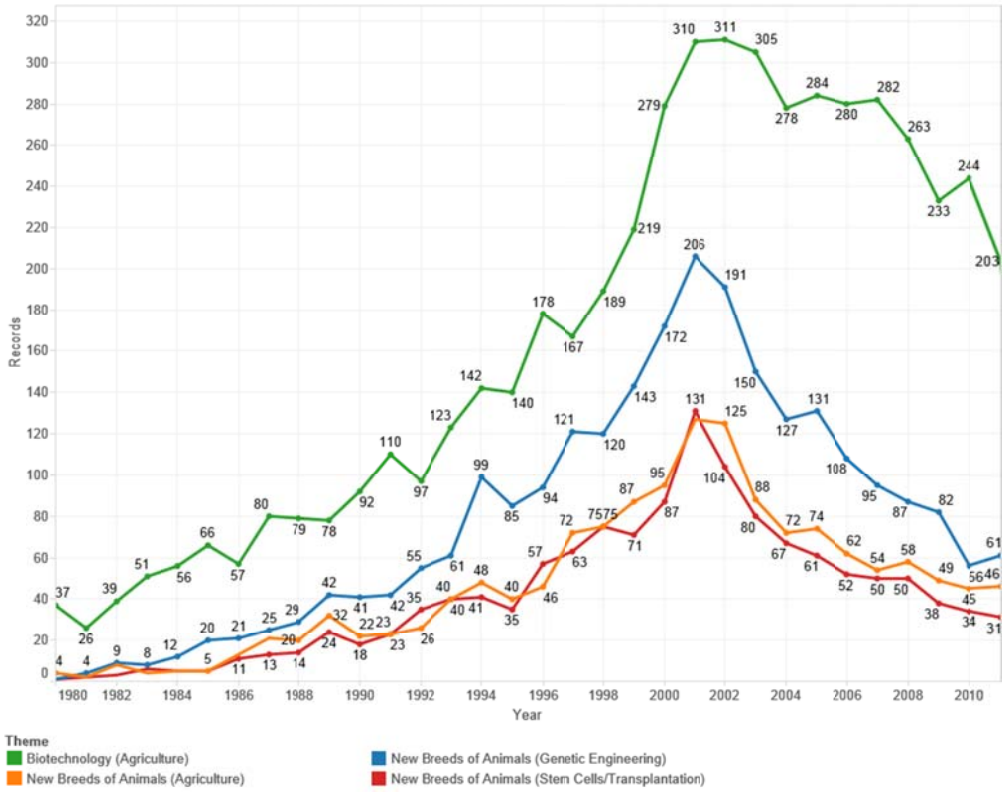


Figure 2 reveals a rapid increase in international patent applications that make reference to the 17 animals in the 1990s. This activity peaked in 2001, followed by a progressive decline in activity. This decline is attributable to a number of factors:

- Growing concern about the implications of patents on Expressed Sequence Tags (ESTs) and Single Nucleotide Polymorphisms (SNPs). As a consequence patent rules became more restrictive by requiring demonstration of the specific utility of gene fragments and polymorphisms;
- In 2001 the dot-com "bubble" burst with negative impacts on investments in biotechnology followed by a slow and partial recovery from 2004 onwards [8];
- The global financial crisis which had a temporary downward impact on patent filings worldwide [9].

While the patent system is now global in nature the rules relating to what may be patented vary from country to country. In relation to animal-related patents, Article 27.3(b) of the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS) establishes that members of the World Trade Organization may exclude, *inter alia*, animals and essentially biological processes from patentability [57,58]. Moreover, inventions may be excluded from patentability on the grounds of public policy (*ordre public)* or morality which may include protecting animal life or the environment. These provisions are relevant because a growing number of countries apply them in different ways that may lead to the rejection of patent applications on a variety of different grounds on the national level. In addition, countries vary in their interpretation and application of the substantive requirements for patentability at the national level, notably, novelty, inventive step and industrial applicability.

For example, under the European Patent Convention plant and animal varieties are not patentable under Article 53(c) of the Convention [58]. Following legal cases involving plants these exclusions have been extended by the European Board of Appeal to crossing and selection and marker assisted breeding [58]. However, inventions which concern wider classes of plants and animals are patentable provided that the application of the invention is not technically confined to a single plant or animal variety (EU Directive 98/44/EC, Rec. 29; EPC Enlarged Boards of Appeal 1999 G0001/98 Transgenic Plant/Novartis II). Rules on patent exclusions arising from *ordre public* or morality concerns (Article 53(a) EPC) are formalised in a rule that excludes processes for modifying the genetic identity of animals, and animals resulting from such processes, where they are likely to cause harm or suffering to the animal without a substantive medical benefit for humans or animals (Rule 28(d)) [58]. Rules on the patentability of

animals and animal material across different countries have not been reviewed in preparing this landscape report. However, a recent decision by the United States Court of Appeal for the Federal Circuit rejecting a claim for a cloned animal on the grounds that it is not patentable subject matter perhaps indicates a stricter approach to patentability requirements in some jurisdictions than was formerly the case [59].

Trends in patent filings involving animal genetic resources have also been influenced by the wider regulatory environment and the nature of markets for products arising from animal biotechnology. As one observer has recently remarked, increasing concerns about animal welfare have created a situation where "there is no clear end user in the food chain or in other words, an overall lack of consumer support for GM animals" [26]. It appears likely, therefore, that the decline in demand for patent rights for new breeds of animals reflects increasing recognition of an absence of markets for transgenic animals resulting from a lack of consumer demand.

Our research confirms that a consequence of this is that R&D involving animal genetic resources in countries such as the United States is directed towards medical and pharmaceutical markets rather than animal breeding for food and agriculture [26].

In addition to identifying and interrogating patent activity for animal breeding we also sought to investigate whether patent activity involves significant access and benefit-sharing issues with respect to: a) the origins of genetic material that appear in patent documents, and; b) the involvement of the traditional knowledge (TK) of indigenous peoples and local communities in the context of the Convention on Biological Diversity. The origins of genetic material and traditional knowledge are addressed in Section 5 of this report. We did not identify evidence of the use of traditional knowledge in patent applications involving animal genetic material. This is likely to reflect the orientation of technological developments reflected in the patent system. This finding does not signify that traditional knowledge is lacking in importance in animal breeding or that traditional knowledge does not have an important potential role to play in innovations in areas such as adaptation to climate change in animal breeding. Rather, it reflects the reality that traditional knowledge with respect to animal genetic resources is not presently recognised as important by patent applicants.

In the context of the Convention on Biological Diversity and debates under the Intergovernmental Committee on Intellectual Property and Genetic Resources, Traditional Knowledge and Folklore (IGC) at WIPO significant concern has been expressed about biopiracy or the misappropriation of genetic resources and associated traditional knowledge without the knowledge or consent of the

provider country, indigenous peoples or local communities and any share in associated economic benefits.

In reviewing these issues, 98,386 patent publications arising from 50,387 first filings were reviewed for references to 7,618 animal breed names from the *FAO Global Databank for Animal Genetic Resources* [1]. The results were then mined for references to countries, indigenous peoples and local communities, traditional knowledge, farmers and pastoralists in conjunction with references to animal breeds. The vast majority of references to animal breeds referred to dominant breeds, such as Holstein cattle or Merino sheep, rather than rarer breeds and did not make reference either to collection of genetic material from a specific country or to traditional knowledge. We therefore concluded that, on the balance of the available evidence, there is very limited, if any, real evidence of cases that could be considered to constitute misappropriation or biopiracy. We recognise that further research may identify such cases but the present research suggests such cases are likely to be isolated rather than characteristic of activity in the sector. This appears to be consistent with existing research suggesting that global trade in animal genetic resources is heavily dominated by North to North resource flows rather than South to North flows [60,61].

It is important to note that the cause for concern about intellectual property and access and benefit-sharing would appear to lie elsewhere. The main challenge confronted in the present research was the lack of specificity in patent applications with respect to the animal species or breed involved in the realisation or practice of an invention. Patent claims commonly include references to more than one species across a spectrum encompassing cattle, sheep, pigs, goats, mice and rats etc. Furthermore, applicants commonly use higher-level groupings, such as bovine, porcine, avian and murine or ruminant and ungulate, in framing patent claims. This lack of specificity can make it very difficult to determine the organism that is the actual source or target of the invention making it difficult to track patent trends for a single organism or group of organisms. Moreover, the broad framing of patent claims, *where granted and in force*, signifies that others seeking to make, use or offer for sale a method or product involving the spectrum of animals in the patent claims would need to seek authorisation from the patent holder to avoid infringing the claims. We emphasise here that this would only apply in jurisdictions where a patent had been granted and is in force (being maintained by the applicant) rather than in cases involving historic applications. The point is, the broad nature of patent claims in this field could constrain other innovators inside or outside the patent system and thus constrain innovation. Furthermore, the extent to which patent applicants claim the offspring or progeny arising from the use of particular genetic material or methods merits further research. We therefore recommend further research on the construction of patent

claims in this field and analysis of cases of litigation or opposition to gain a fuller understanding of the extent to which these issues are a problem.

As noted above, most genome sequencing projects involving livestock have been completed in the last 5 years. Delays in the publication of patent applications (usually 18 months from filing) limited our ability to analyse data between 2012 and 2014 [10]. However, it is reasonable to expect that patent filings will arise from the sequencing of livestock genomes and that these will become visible in the future. While it will be important to take into account the increasing restrictions on DNA-based patents, it will also be important to monitor patent activity relating to developments in livestock genomics. This applies not only to patents relating to DNA, RNA, and amino acids but extends to software and business methods patents. Modern animal breeding increasingly involves the integration of a range of technical methods with genomic and life-cycle data that is enabled by computer software into integrated systems. Individual components of these systems, and the systems themselves, may be eligible for patent protection. As such, it is important to look beyond DNA data to trends in methods, processes, software and business methods in relation to patent activity for animal breeding. At present some countries and breeding organisations may not be in a position to use biological analytical approaches arising from advances in genomics. However, the spread of particular methods, or combinations of methods and technologies, could have far reaching consequences for the livestock breeding sector.

A further consequence of the non-specific nature of patent claims relating to animals, which may relate to human and non-human animals, is that developments in human related biotechnology may spill-over into animal breeding (e.g. assisted reproduction techniques). This may have positive and negative implications for developments in the field. Positive, in the sense that new methods and techniques may be applicable to animal breeding and negative if patent activity restricts the application of such methods and techniques for animal breeders.

Finally, it is important to consider the implications of patent activity for economic development [62-64]. The patent system provides public access to new and useful inventions. The information contained in patent applications is publicly available and can be accessed through a growing number of publicly available patent databases which are free to use. For example, WIPO's Patentscope hosts over 37 million patent applications (October 2014). As examples in this report show, this information could potentially be useful for farmers and animal breeders in developing countries. As examples in this report also show, many patent applications do not survive the examination process while granted patents may not be maintained by patent holders thus releasing the technical information to the

wider public. This information could potentially prove to be a useful source of information for farmers and animal breeders in developing countries and merits greater attention than it presently receives. In particular, research disclosed in patents on disease resistance or disease control (e.g. the tsetse fly or specific animal viruses) and climate change technologies could have wider applicability in developing countries and contribute to innovative breeding practices and husbandry adapted to local conditions and challenges.

The potential concentration and reduction of the global gene pool for animal genetic resources for food and agriculture is a growing concern. Of equal concern is the ability of small-scale livestock keepers and breeders organisations to retain control over breeding processes and decision-making adapted to local needs and priorities. The patent system reflects and informs, rather than drives, developments in science and technology. The present research maps the patent landscape for animal genetic resources and highlights areas of research and development that may merit further attention. For example, we propose that developments in technologies such as multiple ovulation and embryo transfer (MOET) merit fuller attention in terms of their impacts on the wider gene pool. We also propose that the potential consequences of the increased integration of animal breeding technologies with genomic selection data merits fuller investigation. The consequences of a particular technology or integration of technologies will rarely be simply positive or negative. Balanced assessment of the positive and negative implications of a particular technology or integration of technologies is required to advance food security and economic development while conserving and promoting the diversity of the underlying gene pool of animal breeds and related breeding systems.

Options for consideration

1. Further work to refine the patent indicator to respond to policy needs;
2. Improvements to the coverage of animals in the Cooperative Patent Classification in consultation with WIPO and the EPO to facilitate the analysis of quantitative trends for animal genetic resources for food and agriculture;
3. Examine the nature of patent claims and their implications for developments in food and agriculture;
4. Expand research on animal breeds in patent data;
5. Monitoring of patent activity and related activity in the field of animal genomics;
6. Further analysis of patent activity for methods, software and business methods of relevance to animal genetic resources for food and agriculture;

7. Analysis of the implications of technologies appearing in patents for the conservation and sustainable use of animal genetic resources in both developed and developing countries;
8. Identification of the potential utility of technologies appearing in patents for improving livestock breeding in developing countries;
9. Further research on the implications of emerging areas of science and technology such as synthetic biology, metabolic engineering, genome engineering and genome editing for animal genetic resources for food and agriculture.

Table 1: Landmarks in Animal Breeding & Biotechnology

(Adapted and updated from Vàsquez-Salat and Houdebine 2013: 6)

Event	Year
First experiments in embryo transfer in rabbits [11]	1890
Development of modern Artificial Insemination techniques [12]	1920s
Limited advances in detection and control in estrus [12]	1950s onward
Semen successfully frozen in chickens and then in bulls. Emergence of markets for bull semen [12]	1949-1968
Success in long distance transport of pig and sheep embryos [11]	1970
L. E. A Rowson predicts that the combination of Artificial Insemination with superovulation, synchronisation of estrus, and embryo manipulation would lead to major advances in livestock production [11]	1971
Demonstration of transportation of frozen mice embryos [11]	1974
First successful use of freeze dried sperm reported [12]	1974
First report of successful superovulation in cattle and sheep using gonadotropins in advance of estrus [13,14]	1975
Successful long-distance transport of frozen cattle embryos [11]	1976
Fertilization of oocytes matured in vitro in cattle [11]	1978
Advance in superovulation reported using Follicle-stimulating hormone [14]	1978
Transgenic Mouse created using DNA microinjection [15]	1980
Advances in superovulation in cattle to produce ten live calves makes the front page of Science magazine [11,16]	1981
Development of Best Linear Unbiased Prediction (BLUP) selection based on phenotypic information [17,18]	1984
Breakthrough in sexing sperm using DNA quantification with flow cytometry [12,19]	1985
Transgenic rabbits, pigs and sheep using DNA microinjection [20]	1985
First cloned lambs by nuclear transfer [11]	1986
Transgenic fish – trout and goldfish [21-23]	1986
Gene replacement with embryonic stem cells and homologous recombination [24,25]	1986
First recombinant protein produced in milk in mice (recombinant tissue plasminogen activator or rtPA) [26]	1987
Routinisation of embryo production in vitro accompanied by better methods for retrieving follicular oocytes [11]	1990s
Transgenic rat [26]	1990
Transgenic cow (Herman the Bull) [27]	1990
Transgenic chicken [26]	1991
Human lactoferrin produced in cow's milk [26]	1994
Maps of Quantitative Trait Loci (QTL) become available for milk production in cattle [18,28]	1995
Gene knock out using Cre recombinase induced by oestrogen or tetracycline [26]	1997
First animal clone using Somatic Cell Nuclear Transfer in sheep (Dolly the sheep) [29]	1997
Wakayama and Yanagimachi report improved method for use of freeze dried sperm in mice [12,30]	1998

Table 1: Landmarks in Animal Breeding & Biotechnology (Continued)

Event	Year
World survey of artificial insemination for 1998 in 109 countries reveals 20 million semen doses exported and 110.4 million first inseminations, mainly in the Far East [11,31]	1998
Improvements in sexing sperm [12,32]	1999
Gene replacement through homologous recombination and Somatic Cell Nuclear Transfer in sheep and pigs [26]	2000
Pigs expressing salivary phytase (Enviropig™) [33]	2001
Approximately 500,000 cattle embryo transfers worldwide [11,31]	2001
The rise of genome wide markers for selecting breeding values [18]	2001
Spider silk in mammalian cells [34]	2002
Use of lentiviral vectors for gene transfer in mice [26]	2002
Animal Quantitative Trait Locus Database (Animal QTL) initiated with pig QTL data at NAGRP – Bioinformatics Coordination Program [35]	2003
Genome of the chicken sequenced [36]	2004
Creation of pigs for xenotransplantation of cells and organs into humans [26]	2004
Embryonic germ cells used to create transgenic chickens [26]	2006
Recombinant Antithrombin (ATryn) produced in goats approved by USFDA [37]	2006
Gene knockout using small interfering RNA (siRNA) in pigs [26]	2008
Gene targeting using Zinc Finger Nucleases and Non-homologous end-joining in rats [26]	2008
Cow (*Bos taurus*) genome sequenced [38]	2009
Horse (*Equus ferus caballus*) genome sequenced [39]	2009
Recombinant human C1 esterase inhibitor (Ruconest™) produced in rabbits enters market [26]	2009
Gene targeting using Zinc Finger Nucleases in mice [26]	2009
Increasing use of Single Nucleotide Polymorphism (SNPs) maps and the rise of genomic selection and genomic indices	2009-2012
Dromedary camel Expressed Sequence Tags Library published as a prelude to sequencing [40]	2010
Genome of the domesticated turkey (*Meleagris gallopavo*) sequenced [41]	2011
Gene targeting using Transcription activator-like effector nuclease (TALEN) in mice [26]	2011
Recombinant C1-esterase inhibitor produced in rabbits approved by European Medicines Evaluation Agency [42]	2011
Llama Bacterial Artificial Chromosome library published [43]	2012
Draft genome sequence of wild and domestic bactrian camels (*Camelus bactrianus*) published [44]	2012
Pig (*Sus scrofa*) genome sequenced [45]	2012
Yak (*Bos grunniens*) genome sequenced [46]	2012
Zebu (*Bos primigenius indicus*) genome sequenced [47]	2012
Mallard Duck genome (*Anas platyrhynchos*) genome sequenced [48]	2013
Genome sequence of the domestic goat (*Capra hircus*) completed [49]	2103
Completion of the DNA sequence for water buffalo announced by Lal Teer Livestock Limited (Bangladesh) and the Beijing Genomics Institute (BGI, China). Source: EurekAlert 24/01/2014	2014
Complete mitochondrial genome of the Muscovy Duck (*Cairina moschata*) published [50]	2014
Alpaca (*Vicugna pacos*) sequence assembly project underway at the Genome Institute at Washington University with funding from the US NHGRI and NIH. Source: NHGRI and Genome Institute at WU	2014

Section 1: Policy Background

Section Summary

- There is growing concern among international policy makers about the loss of animal genetic diversity. This concern is reflected in the 2007 *Interlaken Declaration on Animal Genetic Resources* and the *Global Plan of Action for Animal Genetic Resources*;
- The FAO report on *Status and Trends of Animal Genetic Resources 2012* reveals that data on the conservation status of animal and avian breeds worldwide is limited [2];
- Two core principles have emerged in international agreements and debates on access and benefit-sharing: a) fair and equitable sharing of benefits arising from the utilization of genetic resources; b) facilitating access to genetic resources for wider research and development.
- These principles are increasingly linked with the knowledge, innovations and practices of indigenous peoples and local communities embodying traditional lifestyles or traditional knowledge;
- The two main instruments addressing access and benefit sharing are the 2001 *International Treaty on Plant Genetic Resources for Food and Agriculture* (the Plant Treaty) and the 2010 *Nagoya Protocol on Access to Genetic Resources and the Fair and Equitable Sharing of Benefits Arising from their Utilization* of the United Nations Convention on Biological Diversity;
- The Plant Treaty includes provisions on Farmers Rights while the Nagoya Protocol includes provisions on indigenous and local communities;
- The Nagoya Protocol does not make direct reference to intellectual property rights with the exception of potential joint ownership of IPRs. It also mentions the establishment of checkpoints that may potentially include intellectual property offices;
- Access and benefit-sharing is being debated within the framework of the United Nations Convention on the Law of the Sea for marine genetic resources. In connection with the Human Genome, UNESCO adopted the Universal Declaration on the Human Genome and Human Rights in 1997. The 2007 United Nations Declaration on the Rights of Indigenous Peoples includes provisions on intellectual property and the rights of indigenous peoples;
- The WIPO Intergovernmental Committee on Intellectual Property and Genetic Resources, Traditional Knowledge and Folklore, is considering whether, and to what extent, the IP system should be used to ensure and track compliance with access and benefit-sharing systems in national laws established pursuant to the CBD, its Nagoya Protocol and the FAO Treaty.

Introduction

Human societies around the world depend upon animals and animal genetic resources for a wide range of services ranging from livelihoods and welfare to social and cultural needs. Animals are also an important focus of innovation in science and technology across a wide range of sectors from agriculture to pharmaceuticals, biotechnology and emerging areas of science and technology such as synthetic biology and technologies to address climate change.

The 20th Century was marked by growing concerns about the status of conservation of the world's biological diversity and resulted in the establishment of the 1992 United Nations Convention on Biological Diversity. The status of the world's animal genetic resources for food and agriculture falls within the mandate of the Food and Agriculture Organization of the United Nations. In 2007, building on 169 Country Reports, the Food and Agriculture Organization published the first global assessment of livestock biodiversity in The *State of the World's Animal Genetic Resources for Food and Agriculture* [1]. The FAO has identified 7,616 livestock breeds of which 20 per cent were classified as at risk [2]. Between 2001 and 2007 an estimated 62 breeds are thought to have become extinct representing a broader underlying trend of erosion of the genetic diversity of livestock animals.

Key drivers of the loss of animal genetic diversity have been identified as:

1. Marginalisation of traditional production systems and local breeds due to intensive livestock production.
2. The growing concentration of meat, milk and egg production in high-output breeds that are well suited to industrial production systems.
3. The increasing ease of transportation of animal genetic material along with production technologies and inputs than can be transported and diffused around the world is increasing the narrowness of genetic diversity in the livestock sector.
4. Threats such as disease and epidemics or other impacts (such as drought or conflict) may have significant impacts on geographically concentrated breed populations.
5. Policy frameworks within the livestock sector may not favour the sustainable utilization of animal genetic resources and may favour large-scale production over small scale systems utilizing a wider variety of animal genetic resources.
6. Development and disease control interventions involving livestock may have impacts on the conservation of genetic diversity and rare breeds.

In response to these issues Member States of the Food and Agriculture

Organization adopted the 2007 *Interlaken Declaration on Animal Genetic Resources* and associated *Global Plan of Action for Animal Genetic Resources*. The Interlaken Declaration "recognises the essential role and values of animal genetic resources for food and agriculture, in particular, their contribution to food security for present and future generations." In response, Member States committed themselves "... to achieving the sustainable use, development and conservation of animal genetic resources for food and agriculture." Furthermore, Member States committed themselves "to facilitating access to these resources and the fair and equitable sharing of the benefits arising from their use..." with the objective of enhancing world food security, improving human nutritional status and contributing to rural development [1]. The Interlaken Declaration further recognised that Member States are not making use of the existing diversity in animal species for increased food production, human nutrition and sustaining livelihoods. In parallel with the Interlaken Declaration member states also established the *Global Plan of Action for Animal Genetic Resources*.

The main aims of the *Global Plan of Action for Animal Genetic Resources* are:

- To promote the sustainable use and development of animal genetic resources, for food security, sustainable agriculture, and human well-being in all countries;
- To ensure the conservation of important animal genetic resource diversity, for present and future generations, and to halt the random loss of these crucial resources;
- To promote a fair and equitable sharing of the benefits arising from the use of animal genetic resources for food and agriculture, and recognize the role of traditional knowledge, innovations and practices relevant to the conservation of animal genetic resources and their sustainable use, and, where appropriate, put in place effective policies and legislative measures;
- To meet the needs of pastoralists and farmers, individually and collectively, within the framework of national law, to have non-discriminatory access to genetic material, information, technologies, financial resources, research results, marketing systems, and natural resources, so that they may continue to manage and improve animal genetic resources, and benefit from economic development;
- To promote agro-ecosystems approaches for the sustainable use, development and conservation of animal genetic resources;
- To assist countries and institutions responsible for the management of animal genetic resources to establish, implement and regularly review national priorities for the sustainable use, development and conservation of animal genetic resources;
- To strengthen national programmes and enhance institutional capacity

– in particular, in developing countries and countries with economies in transition – and develop relevant regional and international programmes; such programmes should include education, research and training to address the characterization, inventory, monitoring, conservation, development and sustainable use of animal genetic resources;

- To promote activities aimed at raising public awareness and bringing the needs of sustainable use and conservation of animal genetic resources to the attention of concerned governments and international organizations.

These objectives are being pursued through activities identified under four Strategic Priority Areas. These are:

1. Strategic Priority Area 1: Characterization, Inventory and Monitoring of Trends and Associated Risks
2. Strategic Priority Area 2: Sustainable Use and Development
3. Strategic Priority Area 3: Conservation
4. Strategic Priority Area 4: Policies, Institutions and Capacity-building

The present project falls under Strategic Priority Areas 1, 2 and 3 and with particular attention to Strategic Priority 16 under Strategic Priority Area 4 directed to "Strengthen international cooperation to build capacities in developing countries and countries with economies in transition", for: a) characterization, inventory and monitoring of trends and associated risk; b) sustainable use and development; and c) conservation of animal genetic resources.

The latest available information on the status of animal genetic resources is provided by the 2012 report of the Commission on Genetic Resources for Food and Agriculture entitled *Status and Trends of Animal Genetic Resources 2012* based on information in the Global Databank for Animal Genetic Resources from 182 countries and 37 species [2]. A total of 8,262 breeds (including avian breeds) have been reported of which 7,202 are local breeds and 1,060 are transboundary breeds. 509 of transboundary breeds are regional transboundary breeds (i.e. for Europe, the Caucasus, Asia and Near and Middle East). A total of 628 breeds were classified as extinct with variations in extinction rates from previous years reflecting improved reporting.

Figure 1.1: Existing Knowledge of the Distribution of Animal Breeds

Species	Africa	Asia	Europe & Caucasus	Latin America & the Caribbean	Near & Middle East	North America	Southwest Pacific	World
Ass	20	39	48	23	15	5	3	153
Bactrian Camel	0	8	3	0	0	0	0	11
Buffalo	2	90	12	11	8	0	2	125
Cattle	172	241	351	148	43	17	32	1004
Dromedary Camel	46	13	1	0	23	0	2	85
Goat	96	182	200	28	33	7	11	557
Guinea Pig	4	0	0	12	0	0	0	16
Horse	38	138	306	76	14	22	24	618
Pig	51	211	197	68	1	13	15	556
Rabbit	11	16	175	17	5	0	0	224
Sheep	114	259	567	52	52	24	38	1106
Yak	0	25	2	0	0	0	0	27
Total	554	1222	1862	435	194	88	127	4482

Note: Excludes extinct breeds. Not shown: alpaca, deer, dog, dromedary x Bactrian camel, guanaco, llama, vicuña. Source: CGRFA/WG-AnGR-7/12/Inf.4.

Figure 1.2: Existing Knowledge of the Distribution of Avian Breeds

Species	Africa	Asia	Europe & Caucasus	Latin America & the Caribbean	Near & Middle East	North America	Southwest Pacific	World
Chicken	126	274	702	87	35	15	30	1269
Duck	14	80	88	22	4	1	11	220
Goose	10	40	110	5	2	0	2	169
Muscovy Duck	5	9	6	1	1	0	2	24
Ostrich	6	2	4	0	0	0	1	13
Partridge	2	8	3	0	0	0	0	13
Pheasant	0	7	5	6	0	0	0	18
Pigeon	7	12	33	7	8	1	2	70
Turkey	11	11	36	11	3	11	5	88
Total	181	443	987	139	53	28	53	1884

Note: Excludes extinct breeds. Not shown: cassowary, Chilean tinamou, duck x Muscovy duck, emu, guinea fowl, ñandu, peacock, quail, swallow.
Source: CGRFA/WG-AnGR-7/12/Inf.4

1,881 or 22 per cent of the 8,262 breeds have been identified as at risk for mammalian and avian species. The main mammalian species at risk with the highest proportion of breeds at risk are cattle, rabbits, horses and pigs. However, the calculation of at risk status is heavily affected by a shortage of data. Among avian species, chickens have the highest number of breeds with 32% at risk followed by geese (37%), turkeys (34%), quail (31%) pigeons (37%) and ostrich (44%) [2]. On the global level the regions of the world with the highest proportion of breeds at risk are North America, Europe and the Caucasus. However, data on at risk status for other regions is likely to be affected by an absence of data on risk status. Because of the limitations in the data, and the confounding effects of the absence of data, the FAO has concluded that: "The current state of data availability and updating means that it is not possible to draw reliable conclusions regarding global trends in breed risk status" [2]. As such, FAO concludes that there is a need for significant improvements in the quality and frequency of reporting on animal breeds and animal genetic resources by member states.

Access and Benefit-Sharing

Two core principles have emerged in international agreements in relation to genetic resources and traditional knowledge. These are:

a) the principle of fair and equitable benefit-sharing arising from the utilization of genetic resources, and;

b) facilitating access to genetic resources for wider research and development.

These core principles are increasingly debated and applied across a spectrum of genetic resources and closely linked with the knowledge, innovations and practices of indigenous peoples and local communities embodying traditional lifestyles ("traditional knowledge").

The Convention on Biological Diversity

The main starting point for debates on these principles and their practical implementation was the 1992 United Nations Convention on Biological Diversity which introduced the concept of fair and equitable sharing of the benefits arising from the utilization of genetic resources into the third objective of the Convention. The concept of fair and equitable benefit sharing under the Convention is linked with a set of related concepts and articles under the Convention. These can be briefly summarised as follows:

1. Recognition of state sovereignty over natural resources and a corresponding requirement for prior informed consent from countries of origin when seeking access to genetic resources (Article 15.1 & Article 15.5);

2. A requirement to establish mutually agreed terms (MAT) between the provider of a genetic resource (and/or associated traditional knowledge) and those seeking access to a genetic resource (Article 15.4);

3. The creation of conditions to facilitate access to genetic resources for Contracting Parties to the Convention (Article 15.2);

4. The participation of the provider country in scientific research utilizing the genetic resource (Article 15.6);

5. "Fair and equitable sharing of the results of research and development and the benefits arising from the commercial utilization of genetic resources with the Contracting Party providing such resources" where benefit sharing will be upon mutually agreed terms (Article 15.7).

The core provisions of the Convention under Article 15 are linked with provisions on Access to and Transfer of Technology relevant for the conservation and sustainable use of biodiversity between Contracting Parties, notably developing

countries, on fair and most favourable terms under Article 16. In addition, Article 15 is linked with Article 19 on the Handling of Biotechnology and Distribution of its Benefits which establishes that Contracting Parties shall take measures to provide for the effective participation of other Contracting Parties, notably developing countries, in biotechnological research activities and priority access to the results of research based upon genetic resources provided by a Contracting Party.

The provisions of the Convention on access and benefit-sharing have increasingly been linked with the treatment of what the Convention describes as the "knowledge, innovations and practices of indigenous and local communities embodying traditional lifestyles" under Article 8j of the Convention. The reference to indigenous and local communities embodying traditional lifestyles is commonly interpreted as referring to indigenous peoples and other communities that follow traditional lifestyles (e.g. Amazonian *caboclos*) who may not identify themselves as indigenous peoples. In addition, this grouping would include farmers from indigenous and local communities embodying traditional lifestyles. Increasingly it is argued that the term indigenous should be replaced with indigenous peoples in recognition of advances in international law such as the 2007 United Nations Declaration on the Rights of Indigenous Peoples. However, the use of the term indigenous peoples in international environment and development agreements is an ongoing subject of debate. The provisions of Article 8(j) of the Convention are also linked with the provisions of Article 10 on the Sustainable Use of Components of Biological Diversity, notably Article 10(c) that aims to "Protect and encourage customary use of biological resources in accordance with traditional cultural practices that are compatible with conservation or sustainable use requirements." As such there is an increasing link under the Convention between access and benefit-sharing in relation to genetic resources and traditional knowledge and sustainable use. This is considered in more detail below in connection with the Nagoya Protocol.

Finally, intellectual property rights are addressed in three places in the Convention. First, the objectives of the Convention refers to "the fair and equitable sharing of the benefits arising out of the utilization of genetic resources, including by appropriate access to genetic resources and by appropriate transfer of relevant technologies, taking into account all rights over those resources and to technologies." Second, Article 16. 2 of the Convention on Access to and Transfer of Technology. In connection with facilitating access to technology under fair and most favourable terms Article 16.2 establishes that: "In the case of technology subject to patents and other intellectual property rights, such access and transfer shall be provided on terms which recognize and are consistent with the adequate and effective protection of intellectual property rights." However, this provision is

intended to be consistent with the provisions of Article 16.3, Article 16.4 and 16.5. Article 16.3 sets out provisions favouring access to technologies, including patented technologies, that utilize a genetic resource from a provider country. Article 16.4 promotes the transfer of technology by the private sector including joint development with the private sector in developing countries. Article 16.5 establishes that:

> The Contracting Parties, recognizing that patents and other intellectual property rights may have an influence on the implementation of this Convention, shall cooperate in this regard subject to national legislation and international law in order to ensure that such rights are supportive of and do not run counter to its objectives.

The latter provision has been a subject of extensive debate on the relationship between the Convention and the treatment of intellectual property rights under the Agreement on Trade Related Aspects of Intellectual Property Rights (the TRIPS Agreement). These debates are ongoing in the TRIPS Council and at the CBD in connection with the problem of biopiracy or the misappropriation of genetic resources and traditional knowledge.

The International Treaty on Plant Genetic Resources for Food and Agriculture (the Plant Treaty)

The second important development in the evolution of international norms on access and benefit-sharing is the 2001 *International Treaty on Plant Genetic Resources for Food and Agriculture* administered by the Food and Agriculture Organization (FAO) [65]. The International Treaty (widely known as the Plant Treaty) is closely linked with, and is intended to be harmonious with, the Convention on Biological Diversity. However, whereas the Convention can be said to take a strong stance on the subject of sovereignty over natural resources, the Plant Treaty embodies recognition by countries that food and agriculture fundamentally depends on shared genetic resources.

The objectives of the Plant Treaty are as follows:

> 1.1 The objectives of this Treaty are the conservation and sustainable use of plant genetic resources for food and agriculture and the fair and equitable sharing of the benefits arising out of their use, in harmony with the Convention on Biological Diversity, for sustainable agriculture and food security.
>
> 1.2 These objectives will be attained by closely linking this Treaty to the Food and Agriculture Organization of the United Nations and to the Convention on Biological Diversity.

The Plant Treaty focuses on a list of major food crops and forages that are

detailed in a Annex 1 to the Treaty and establishes a Multilateral System (Article 11) for food crops and forages listed in Annex 1 under the management and control of the Contracting Party (Article 11.2). Typically, this means plant genetic resources in public collections and includes the collections under the Consultative Group on International Agricultural Research. Annex 1 of the Treaty includes the major food crops such as wheat, rice and maize along with important forage crops such as the major grasses and alfalfa among others. However, it is important to note that Contracting Parties have increasingly expanded the range of plant genetic resources covered under the Multilateral System to include genetic material falling outside Annex 1.

The purpose of the Multilateral System is to promote "facilitated access" to plant genetic resources among Contracting Parties. Facilitated access under the Multilateral System is achieved through the use of a simple Standard Material Transfer Agreement (SMTA) setting out basic terms for the transfer of plant genetic material held under the Multilateral System.

Whereas the Convention on Biological Diversity deals with indigenous and local communities, the Plant Treaty contains provisions on Farmers Rights (Article 9). Specifically Contracting Parties: "…recognize the enormous contribution that local and indigenous communities and farmers of all regions of the world, particularly those in the centres of origin and crop diversity, have made and will continue to make for the conservation and development of plant genetic resources…"(Article 9.1). Furthermore, Contracting Parties to the Treaty agreed to "take measures to protect and promote Farmer's Rights, including:

> (a) protection of traditional knowledge relevant to plant genetic resources for food and agriculture;
>
> (b) the right to equitably participate in sharing benefits arising from the utilization of plant genetic resources for food and agriculture; and
>
> (c) the right to participate in making decisions, at the national level, on matters related to the conservation and sustainable use of plant genetic resources for food and agriculture."

Finally, in connection with Farmers Rights Article 9.3 specifies that: "Nothing in this Article shall be interpreted to limit any rights that farmers have to save, use, exchange and sell farm-saved seed/propagating material, subject to national law and as appropriate."

In connection with intellectual property rights the Plant Treaty focuses on material covered under the Multilateral System and specifies in Article 12.3 that:

> 12.3 (d) Recipients shall not claim any intellectual property or other rights that

> limit the facilitated access to the plant genetic resources for food and agriculture, or their genetic parts or components, in the form received from the Multilateral System.

As such, the pursuit of intellectual property rights is permitted under the Treaty provided that Plant Breeders Rights and patent rights are not pursued over the genetic material or components in the form received from the Multilateral System.

The International Treaty system is important because it has established a functioning system for the exchange of plant genetic material and has also begun to generate benefits (to date, mainly through support from countries) that have been distributed to local project initiatives for the *in situ* conservation of plant genetic resources. However, due to the long lead times for the development of commercial varieties the Treaty has not yet attracted significant benefits from the private sector [66].

The International Treaty is also important because it recognizes that in some sectors such as plant agriculture, the health of the global agricultural system depends on the ability to conserve and share plant genetic resources. That is a single new variety may contain germplasm from multiple sources. The Standard Material Transfer Agreement (SMTA) provides a straightforward means for exchanging germplasm with simple rules and thus limits transaction costs.

The Nagoya Protocol on Access to Genetic Resources and Benefit-Sharing

The third important development in access and benefit-sharing is the Nagoya Protocol under the Convention on Biological Diversity. The *Nagoya Protocol on Access to Genetic Resources and the Fair and Equitable Sharing of Benefits Arising from their Utilization* was adopted by the Conference of the Parties to the Convention in 2010 [67-69]. It will enter into force on the 12th of October 2014 following its ratification by 51 Parties to the Convention on Biological Diversity.

The Nagoya Protocol builds on and expands a set of voluntary guidelines on access to genetic resources and benefit-sharing adopted by the Convention in 2002 as the *Bonn Guidelines on Access to Genetic Resources and Fair and Equitable Sharing of the Benefits Arising out of their Utilization*. The Protocol elaborates on, and gives force to, the key articles of the Convention on access and benefit-sharing and makes the connection between genetic resources and traditional knowledge on indigenous and local communities explicit. The Protocol is intended to create conditions of legal certainty and transparency for providers and users of genetic resources and traditional knowledge in the context of long-standing concerns by developing countries about the problem of biopiracy or misappropriation of genetic resources and traditional knowledge.

The Nagoya Protocol requires that:

1. Parties to the Protocol introduce legislation on access and benefit-sharing;

2. That access to genetic resources and associated traditional knowledge is subject to the prior informed consent of the Contracting Party and, where relevant, of indigenous and local communities providing traditional knowledge associated with genetic resources;

3. That benefit-sharing shall be on mutually agreed terms between the providers and users of genetic resources and associated traditional knowledge;

4. That access and benefit-sharing agreements are supported by permits and/or an international certificate of compliance;

5. That Contracting Parties standing in the position of "users" of genetic resources and associated traditional knowledge will ensure compliance with the legislation of provider countries by users (subject to the existence of national legislation in the provider country);

6. That the Nagoya Protocol will not prevent Contracting Parties from "developing and implementing other relevant international agreements, including other specialized access and benefit-sharing agreements, provided that they are supportive of and do not run counter to the objectives of the Convention and this Protocol." (Article 4.2)

The Nagoya Protocol does not make direct reference to intellectual property rights except with respect to the possibility of joint ownership of intellectual property as part of Access and Benefit-Sharing agreements. However, Article 17 on Monitoring the Utilization of Genetic Resources refers to the designation of one or more checkpoints to monitor the utilization of genetic resources. During the negotiation of the Nagoya Protocol there was extensive debate about the inclusion of intellectual property offices as checkpoints. While no specific reference is made to intellectual property offices it is likely that some countries will include IP offices in their checkpoints for the Nagoya Protocol.

Other Developments Relevant to Access and Benefit-Sharing

Three other developments are relevant to the consideration of access and benefit-sharing issues. The first of these are ongoing discussions within the framework of the United Nations Convention on the Law of the Sea on the potential creation of a new international instrument on marine biodiversity in Areas Beyond National Jurisdiction (ABNJ) that may include an access and benefit-sharing mechanism for marine genetic resources [70,71]. Discussions are ongoing.

Second, in the field of human genetics, in 1997 UNESCO adopted the *Universal Declaration on the Human Genome and Human Rights*. Article 1 describes the human genome as follows: "The human genome underlies the fundamental unity of all members of the human family, as well as the recognition of their inherent dignity and diversity. In a symbolic sense, it is the heritage of humanity." With respect to benefit-sharing Article 12 (a) establishes that "Benefits from advances in biology, genetics and medicine, concerning the human genome, shall be made available to all, with due regard for the dignity and human rights of each individual". Article 19 (iii) goes on to establish that states should encourage measures to promote benefits in developing countries. In connection with intellectual property, the UNESCO Declaration is framed in such a way that it is "without prejudice to" international instruments in relation to intellectual property.

Outside the United Nations system the development of guidance in relation to human genome issues has focused on the ethics committee of the Human Genome Organisation (HUGO) which has developed a series of statements on issues such as DNA sampling (1998), Cloning (1999), Benefit-Sharing (2000) and Stem Cells (2004). While these statements are non-binding they are influential in identifying and framing issues to be considered in the field of genetics. They are potentially relevant to debates on animal genetic resources and intellectual property as background on potential overlaps between animal and human genetic resources in research and development in areas such as cloning (reproductive and therapeutic) and stem cells (e.g. nuclear transfer). As we will see in more detail a significant proportion of uses of animal genetic resources are directed to medical applications in humans.

The WIPO Intergovernmental Committee on Intellectual Property and Genetic Resources, Traditional Knowledge and Folklore (IGC)

In 2000, WIPO members established an Intergovernmental Committee on Intellectual Property and Genetic Resources, Traditional Knowledge and Folklore (IGC), and in 2009 they agreed to develop an international legal instrument (or instruments) that would give genetic resources, traditional knowledge and traditional cultural expressions effective protection. In particular, WIPO members

are considering whether, and to what extent, the intellectual property system should be used to ensure and track compliance with access and benefit-sharing systems in national laws and other measures established pursuant to the Convention on Biological Diversity, its Nagoya Protocol and the FAO Plant Treaty. One of the options under discussion is to develop mandatory disclosure requirements that would require patent applicants to show the source or origin of genetic resources, and also possibly evidence of prior informed consent and a benefit-sharing agreement. Another key issue is that of the defensive protection of genetic resources, so as to prevent patents, which do not fulfill patentability requirements of novelty and inventiveness, from being granted over genetic resources, and associated traditional knowledge. Defensive protection measures could include, for example, the creation of databases on genetic resources and traditional knowledge to help patent examiners find relevant prior art and avoid the grant of erroneous patents. Over the years, WIPO has developed a number of useful tools in the area of intellectual property and genetic resources, including a database of Biodiversity-related Access and Benefit-sharing Agreements, and Intellectual Property Guidelines for Access to Genetic Resources and Equitable Sharing of the Benefits arising from their Utilization.

Indigenous Peoples, Local Communities and Traditional Knowledge

The 1990s and early 2000s witnessed increasing attention to indigenous and local communities and traditional knowledge. As noted above, these terms can be interpreted in various ways but are a category that would include indigenous peoples and many small-scale agro-pastoralist and pastoralist communities around the world. In 2007 the United Nations General Assembly adopted the *United Nations Declaration on the Rights of Indigenous Peoples* (UNDRIP) [72]. In connection with intellectual property Article 31.1 of UNDRIP establishes that:

> Indigenous peoples have the right to maintain, control, protect and develop their cultural heritage, traditional knowledge and traditional cultural expressions, as well as the manifestations of their sciences, technologies and cultures, including human and genetic resources, seeds, medicines, knowledge of the properties of fauna and flora, oral traditions, literatures, designs, sports and traditional games and visual and performing arts. They also have the right to maintain, control, protect and develop their intellectual property over such cultural heritage, traditional knowledge, and traditional cultural expressions.

UNDRIP sets out the aspirations of member states with respect to the rights of indigenous peoples. The implication of Article 31.1 is that the human rights of indigenous peoples with respect to genetic resources and traditional knowledge need to be taken into account in policy developments of relevance to them.

Summary

As this discussion of existing instruments and ongoing developments makes clear, access and benefit-sharing for genetic resources and traditional knowledge is an important area of emerging international law. This field can be characterized as an emerging trend towards the international governance of genetic resources that encompasses intellectual property and benefit-sharing arising from innovation. However, in considering these developments in relation to the intellectual property system it is also important to have a sound understanding of the nature of the intellectual property system. We now turn to a brief description of patents and the patent system as a guide to readers in interpreting the intellectual property landscape for animal genetic resources.

Approaching Intellectual Property

Intellectual property encompasses a number of legal instruments including copyright, trademarks, database rights, plant variety rights and patent rights. This report focuses on patents.

In approaching the patent system there are two main issues to be considered: 1) the nature of the rights provided; 2) the patent system as an information system. This patent landscape report will mainly be concerned with the patent system as an information system.

Patent Rights and Procedures

In simple terms a patent is a temporary grant of exclusive rights to a patentee to prevent others from making, using, offering for sale, or importing a patented invention without their consent, in a country where a patent is in force. Patent rights are territorial rights, meaning that a patent is only valid in the territory of the country in which protection is granted, enabling the patent owner to enforce their rights only within that territory. Patents are typically granted for a period of 20 years from the filing date of the patent application, provided that maintenance fees are paid and that no request for invalidation or revocation has been successful during this period. During this period patent holders enjoy exclusivity over the protected invention or may licence or transfer the patent to others.

In order to be eligible for patent protection, an invention must meet various criteria: These include, in particular, that the claimed invention: 1) involves patentable subject matter; 2) is new or novel; 3) involves an inventive step (is non-obvious to a person skilled in the art), and; 4) is susceptible to industrial application or useful. In addition to these criteria, patent applicants must meet a substantive requirement for adequacy of disclosure of the invention such that it may be carried out by a person skilled in the art. In some countries, patent applicants are required to disclose the origin or source of genetic material and associated traditional knowledge in a patent application. A substantial body of legislation, rules and jurisprudence exist on each of these criteria.

The modern patent system is global in nature and includes national laws, regional patent instruments (such as the European Patent Convention) and international instruments administered by WIPO, notably the Paris Convention, the Patent Cooperation Treaty and the Patent Law Treaty. Patent applicants can submit applications through a number of routes notably, filings through national offices, filings through regional patent offices (e.g. the European Patent Office), or filings through the international Patent Cooperation Treaty (PCT-Direct).

When a patent application is filed with a patent office in one country or region,

the applicant normally has 12 months to file an application for the same invention in other countries of interest in order to benefit from the filing date of the original application. The date of the first application for a particular invention is called the "priority date" and the application is known as the "priority" or "first" filing. A patent office then examines the application and a patent will be granted if all the requirements under the applicable law are met. The examination carried out by patent offices varies from one country to another. While many countries grant patents after a full substantive examination, other offices may grant patents based on formality examination only (a registration system).

Depending on the applicable law, various costs are incurred by applicants during the process of obtaining a patent. For example, in many countries, filing fees and examination fees are requested. The applicant will then pay periodic fees to the patent office to maintain the patent or it will lapse.

It is not possible to obtain patent protection with global, world-wide effect. However, a fundamental feature of the modern patent system is that applicants can seek protection in more than one jurisdiction using regional patent instruments such as the European Patent Convention or the international Patent Cooperation Treaty (PCT). Thus, under the Patent Cooperation Treaty an applicant can submit a single application that becomes eligible to go forward as an application in up to 148 Contracting States. An international PCT application that designates a Contracting State of the PCT has the same effect as a national application filed in each Contracting State of the PCT. PCT international applications may be filed by anyone who is a national or resident of a PCT Contracting State.

After going through various procedures at the international level, patent applications enter what is called "the national phase" in which patent offices of designated countries decide whether or not to grant a patent with respect to an invention contained in a PCT international application. A decision on whether to grant a patent by an individual patent office is based on its substantive conditions for patentability under its respective national/regional law.

Patent applications that are submitted in more than one country, and any later patent grants, become part of the patent family of the original priority application (first filing). This allows inventions to be traced around the world.

The Patent System as an Information System

The patent system is a highly organised information system that operates in multiple languages. This information system consists of over 60 million documents that are increasingly freely available online through services such as the PATENTSCOPE database operated by the World Intellectual Property

Organization, or esp@cenet database operated by the European Patent Office as main repositories for electronic patent data.

The nature of the patent system as an information system is important because it provides the basis for the patent landscape analysis provided in this report. The key elements of patent documents are well-defined fields as summarised in Figure 1.3.

Figure 1.3: Key Patent Information Fields

Field	Description
Publication Number, Application Number, and Priority Numbers.	These numbers describe different levels of the document history and consist of a two letter country code, the year, a unique number and a kind code (e.g. A1 or B1) describing the type of document (e.g. application or grant). The easiest number to locate in patent databases is the publication number.
Assignees (Applicants)	The legal entities seeking patent rights protection.
Inventors	Individuals who invented the invention.
International Patent Classification (IPC)	A set of alphanumeric classification codes setting out the technical content of the document. Animal related technology is often found under code A01K.
Cooperative Patent Classification (CPC)	A more detailed version of the IPC used by major patent offices to more precisely describe the content of documents.
Publication Date, Application Date, Priority Date.	The publication date is the date of publication of the document. The application date is the filing date of the underlying application. The priority date is the date of the original first filing.
INPADOC Patent Family	This field provides a link to all patent documents linked to the original underlying filing (the priority filing). INPADOC stands for International Patent Documentation Centre and is part of the European Patent Office. This allows related documents to be tracked around the world.
Title	The title of the invention.
Abstract	A short summary of the content of the document.
Description	A detailed disclosure of the claimed invention.
Claims	The subject matter for which patent protection is sought

	organised numerically from Claim 1 onwards.

The basic patent fields described above are important for understanding the patent landscape because they provide access to the following information:

1. The Title, Abstract, Description and Claims fields can be text mined for animal Latin and common names using large scale text mining. The results can be explored using text mining and qualitative data analysis tools. The analysis can be further refined by examining the title, abstract or claims (TAC) to identify documents that are fundamentally about a particular animal.

2. Patent classification codes can be used to identify technology areas within the global system where animals appear. Advanced network mapping can visualise clusters of technology around animals.

3. Patent dates allow statistical trends to be graphed using a variety of counting measures such as first filings, publications (applications and grants) in the main jurisdictions and family members (global trends).

4. Applicant and Inventor data provides the answer to who is active in the patent system for animal genetic resources.

5. INPADOC Family data allows global activity to be mapped for inventions in a particular technology area.

Understanding Existing Limitations

In considering the patent system as an information system it is also important to recognise the limitations of the existing system in relation to emerging policy needs for information. Thus, the principal means of identifying relevant patent documents is through the patent classification system, notably the International Patent Classification (IPC) and the new Cooperative Patent Classification (CPC). However, this system is presently oriented around the description of technology rather than a particular animal of interest. The new Cooperative Patent Classification (CPC) includes a set of classification codes that are directly relevant to animals (e.g. A01K227/00 for animals characterised by species or A01K2267/00 for animals characterised by purpose). However, according to the CPC description of these codes and the public patent database esp@cenet they are "not used" and it appears that they will be discontinued.[1]

A second limitation of the patent system from the point of view of the identification of information on specific animals of interest to policy makers

[1] Cooperative Patent Classification, Sheme A01K. CPC-A01K-2014.09. http://www.cooperativepatentclassification.org/cpc/scheme/A/scheme-A01K.pdf. Accessed 22/09/2014.

working in food and agriculture relates to the way in which patent documents are written and, in particular, the way in which patent claims are written.

As we will see below, patent applicants have a number of choices in the use of terms when writing patent documents and constructing patent claims. Figure 1.4 provides a simple guide to these options based on the research conducted for this report.

Figure 1.4: The Use of Animal Terms in Patent Claims

Level	Significance in Patent Claims
1. Mammals, Animals, Vertebrates	Patent claims encompass the use of specified genetic material from any of these organisms in practising the invention or an invention can be applied to any organisms in these groupings. This framing includes humans.
2. Ungulates, Artiodactlya, Avians	Patent claims use specified genetic material from animals with hooves as a general class or avians as a general class or the invention can be applied to any animals in these groupings. This framing excludes humans from the scope of the claimed invention.
3. Bovine, porcine, caprine, ovine, camelids etc.	Patent claims apply to specified genetic material from animals in these groups or the invention can be applied to animals in these groups.
4. Family (e.g. Bovidae) or genus level (e.g. Bos)	Patent claims apply to the use of specified genetic material from animals in this taxonomic family or genus or the invention can be applied to animals within these groupings.
5. Cattle, Pigs, Sheep, Chickens, Ducks, Turkey	Patent claims apply to the use of specified genetic material from one or more of these animals or the invention can be applied to them.
6. Sus scrofa (wild boar, pigs)	Patent claims only apply to the use of specified genetic material from this species and associated breeds or the claims are restricted to application of the invention only in this species and breeds and not to other animal species.

Figure 1.4 reveals that patent applicants have choices in framing patent documents that move from the general (e.g. mammals) to the particular (e.g. *Sus*

scrofa). Applicants frequently frame patent claims by beginning with a general statement (e.g. mammals) and moving to the particular further down in the list of patent claims as they focus in on the main target for the invention (e.g. pigs, cattle or mice).

The reason that patent applicants adopt this approach is to protect the claimed invention from efforts by competitors to "invent around" the claimed invention.

However, this creates significant problems in identifying patent activity that focuses on specific animals for use in food and agriculture and identifying statistical trends. The key question becomes at what level should patent activity involving animals be counted? We now turn to the methods used to identify animal genetic resources in the patent system and to develop a quantitative indicator as a basis for detailed analysis of the patent landscape.

Section 2: Defining the Landscape

Section Summary

- Following discussions with FAO and upon their request, the research focused on 17 animal and avian names from 15 species of livestock animal. The research did not address fish;
- Large scale text mining of 14 million patent documents allows for the precise identification of animal names in the texts including in the claims;
- Patent documents are mainly classified using the International Patent Classification (IPC) codes and increasingly using the Cooperative Patent Classification (CPC) codes. Patent classification systems consist of alphanumeric classification codes such as A01K67/00 for Rearing or Breeding Animals and New Breeds of Animals in the IPC. [2] These codes provide different levels of detail that describe the technical content of a document. The Cooperative Patent Classification (CPC) is a highly detailed classification that is used by the European Patent Office, the United States Patent and Trademark Office and the State Intellectual Property Office of the People's Republic of China.[3]
- Mapping of networks of IPC and CPC classification codes allows technology clusters to be identified that involve animals and animal genetic resources;
- Animals appear in nine main technology clusters in the patent system. The research focused on the New Breeds of Animals (transgenic animals) and Biotechnology clusters;
- Patent applicants commonly refer to multiple animals as individual species, genera or wider groupings (e.g. bovine) in the patent claims;
- Patent claims are often broadly constructed to refer to mammals, ungulates, bovines etc.;
- Animals may be the source of material used in an invention or they may be the target of an invention. For example, animals may be the *source* of a product such as a recombinant protein or milk with particular properties. In other cases animals may be the *target* of an invention such as an animal feed or therapeutic veterinary product.

Introduction

This patent landscape report focuses on a set of 17 mammalian and avian species

[2] WIPO International Patent Classification. http://www.wipo.int/classifications/ipc/en/. Accessed 08/08/2014.
[3] European Patent Office/United States Patent and Trademark Office. Cooperative Patent Classification. http://www.cooperativepatentclassification.org/index.html. Accessed 08/08/2014.

and subspecies that are important in food and agriculture. Table 2.1 displays the species covered by the report.

Table 2.1: Target Species

Common Name	Latin Name	Taxonomic Status
Duck	Anas platyrhynchos	Accepted name
Zebu cattle	Bos indicus	(syn. of Bos taurus)
Auroch Cattle	Bos primigenius	(syn. of Bos taurus)
Taurine Cattle	Bos taurus	Accepted name
Water Buffalo	Bubalus bubalis	Accepted name
Muscovy Duck	Cairina moschata	Accepted name
Bactrian camel	Camelus bactrianus	Accepted name
Dromedary camel	Camelus dromedarius	Accepted name
Goat	Capra hircus	Accepted name
Donkey	Equus asinus	Accepted name
Horse	Equus caballus	Accepted name
Chicken	Gallus gallus	Accepted name
Llama	Lama glama	Accepted name
Turkey	Meleagris gallopavo	Accepted name
Sheep	Ovis aries	Accepted name
Pig	Sus scrofa	Accepted name
Alpaca	Vicugna pacos	Accepted name

The aim of this report is to work towards the identification of quantitative trends in patent activity for these species and to explore issues relating to animal breeds in patent data.

This depends on three main factors:

1. The accurate identification of the target animals in patent data;
6. The ability to discriminate technological innovations that relate to animal genetic resources of relevance to food and agriculture from other areas of invention;
7. The identification of animal breeds in patent data.

In practice, this involved significant challenges for two main reasons:

a) Animal names, particularly common names, may have a very wide variety of uses that do not refer to the animal as such or to animal genetic resources;

b) Animals appear in a wide range of technology areas such as animal husbandry, sporting equipment and games among others. It is therefore important to be able to identify references to actual animals and to be able to discriminate between different areas of technology.

Methods

As a starting point we used a collection of 14 million full text patent documents from the collections of the United States of America, the European Patent Office and the Patent Cooperation Treaty between 1976 and October 2013. This collection focuses on international patent activity and is therefore more likely to capture economically important patent documents. It does not capture patent documents that are only filed in one country.

We then used large-scale text mining and a pattern-matching algorithm to identify all references to Latin species names in the patent data [73]. One known issue with Latin species names in patent data is that when species are well known applicants will often use common names for animals. To address this we reviewed the words and phrases used in the titles, abstracts and claims to identify common terms used by applicants to describe animals in the target group. The search criteria were then expanded to identify additional documents.

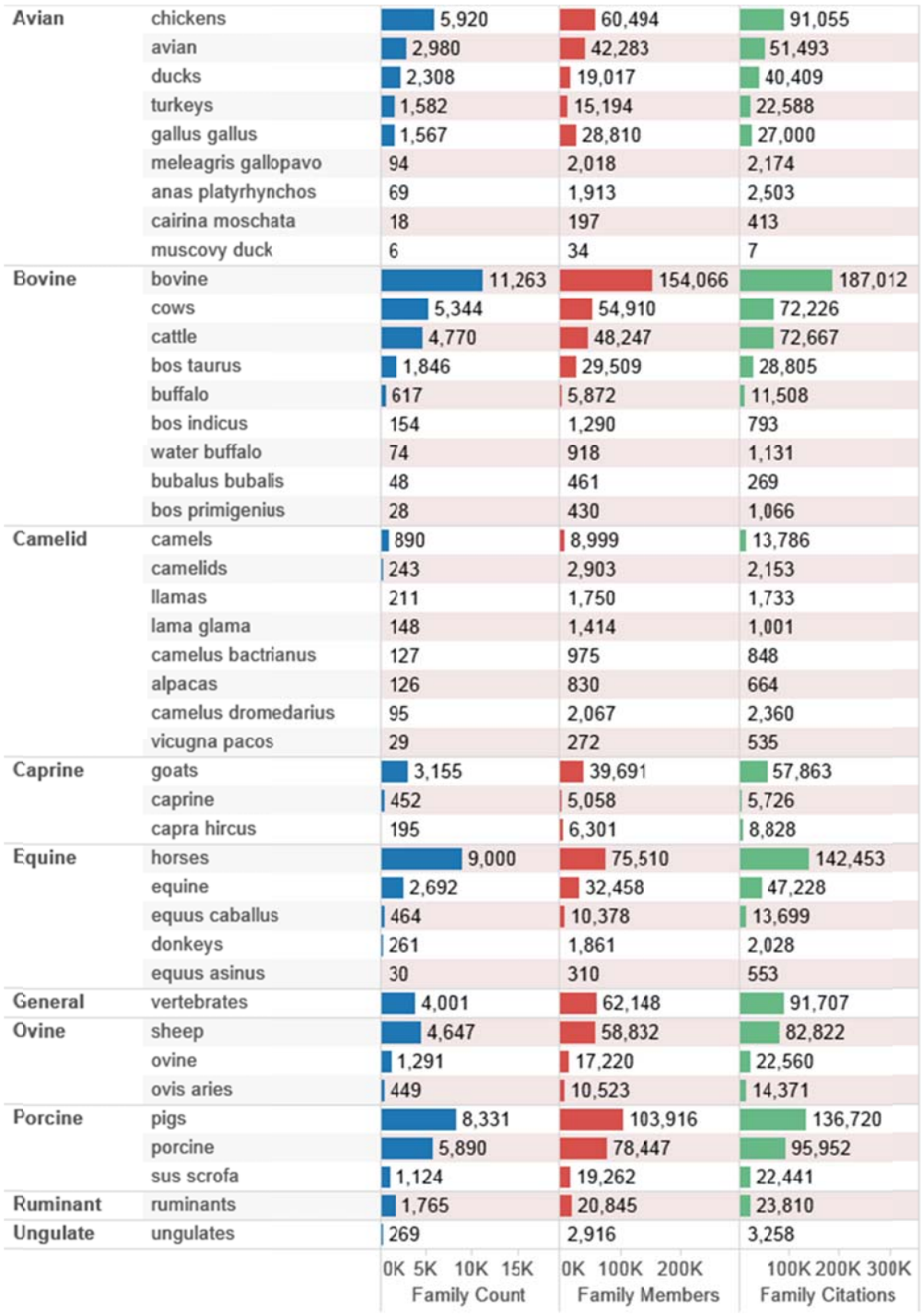
Figure 2.1 displays the results of patent searches by species names. The column family count refers to the number of first filings that reference the species and family members refers to global applications and grants linked to the first filings. Family Citations refers to the number of later patent filings that cite a member of a family for a species adjusted to remove self-citations. Because a cited patent limits the scope of a later patent filing for the same or a similar invention, patent citations indicate the impact of a patent family or set of families within the wider patent system [74,75].

The Latin species name data suggests that patent activity for animal genetic resources is most likely to be concentrated in 10,651 patent families. However, the review of patent claims for these documents also revealed that patent applicants are very likely to use common names. Figure 2.1 also sets out the results of searches of patent documents for common names. In this case searches were confined to the Title, the Abstracts and the Claims of patent documents to reduce the levels of noise on common terms.

In total the patent universe making reference to animals based on Latin species names and common names based on data from the main patent jurisdictions consists of 98,368 patent publications arising from 50,387 first filings (patent families) linked to 510,595 patent family members worldwide.

Figure 2.1 makes clear that the data radically expands when common names are taken into account. This reflects the very wide range of technology areas that involve animals or animal products and the range of different uses of animal names in the patent system that have no relevance to animal genetic resources. These irrelevant names can include types of viruses, equipment, sporting goods and a whole host of non-obvious uses of animal names that are difficult to predict.

Figure 2.1: Patent Search Results by Latin and Common Species Name



To address these issues patent landscape analysis typically relies on patent classification codes drawn from the International Patent Classification or the new Cooperative Patent Classification to focus the analysis of patent activity on a relevant area. Unfortunately, in the case of animals, in depth analysis of patent classification codes did not reveal a clear concentration of animal related codes

that could be used for statistical indicators. Annex 1 provides an extended analysis of this problem. This differs markedly from the situation with plant genetic resources for food and agriculture where a small number of classification codes capture the majority of activity [76].

This raised the question of how the patent data on animal genetic resources for food and agriculture could be more easily targeted. To address these issues we initially focused on using a variety of approaches, such as additional searches of the data to identify biotechnology terms from an FAO thesaurus of biotechnology terms. However, this did not have a major impact on the data because, as will be seen below, the majority of patent activity involves some reference to biotechnology across a wide range of sectors. We also identified those patent documents containing an animal name and sequence listing which we discuss in further detail below.

In response to the complexity of the presence of animals in the patent system we developed a new method that focuses on mapping networks of technology clusters using patent classification codes that focus on animal genetic resources.

Mapping Technology Clusters

Network mapping depends on the mapping of the relationships between nodes (such as authors, inventors or applicants) within a landscape and the clustering and description of nodes based on the strength of the linkages between the nodes relative to other nodes in the landscape. Typically, this approach is used to map networks of authors in scientometrics for emerging areas of science and technology [4].

In this case we focused on using patent *classification codes* from the International Patent Classification and Cooperative Patent Classification as the nodes in the landscape and mapping the landscape using co-occurrence analysis to cluster and distribute nodes in the landscape based on the strength of the linkages between the nodes.

As noted above the patent system uses a sophisticated hierarchical classification system to classify the technical content of patent documents. These alphanumeric codes are organised into classes, sub-classes, groups and sub-groups with increasing levels of technical detail. Typically, patent documents are awarded between 3 and 5 classification codes to describe the contents of documents. Table 2.2 displays a selection of the top classification codes for the raw patent universe referencing animal names.

Table 2.2: Top CPC Codes for Animal Names

Records	Cooperative Patent Classification (CPC)
9,198	A61K38/00: Health; amusement -> preparations for medical, dental, or toilet purposes -> Medicinal preparations containing peptides
3,833	C07K14/005: Organic chemistry -> Peptides -> Peptides having more than 20 amino acids; Gastrins; Somatostatins; Melanotropins; Derivatives thereof -> from viruses
3,503	A61K39/00: Health; amusement -> preparations for medical, dental, or toilet purposes -> Medicinal preparations containing antigens or antibodies
3,203	C07K2319/00: Organic chemistry -> Peptides -> Fusion polypeptide
2,879	A61K48/00: Health; amusement -> preparations for medical, dental, or toilet purposes -> Medicinal preparations containing genetic material which is inserted into cells of the living body to treat genetic diseases; Gene therapy
2,800	A01K2217/05: Agriculture -> Animal husbandry; care of birds, fishes, insects; fishing; rearing or breeding animals, not otherwise provided for; new breeds of animals -> Pasturing equipment -> Genetically modified animals -> Animals comprising random inserted nucleic acids (transgenic)

Table 2.2 displays the top patent classification codes for the universe of 50,387 first filings referencing animals in the main jurisdictions. It neatly illustrates the problem that the bulk of references relate to peptides for medical use and gene therapy in the fields of health followed by genetically modified animals.

Network mapping helps to overcome this by focusing on the linkages between classification codes. This works by identifying documents that share the same codes, or sets of codes, and distributing the network map based on the strength of those links. Table 2.3 displays the co-occurrences between the documents in Table 2.2.

Table 2.3: Co-occurrence Matrix of CPC to CPC Codes

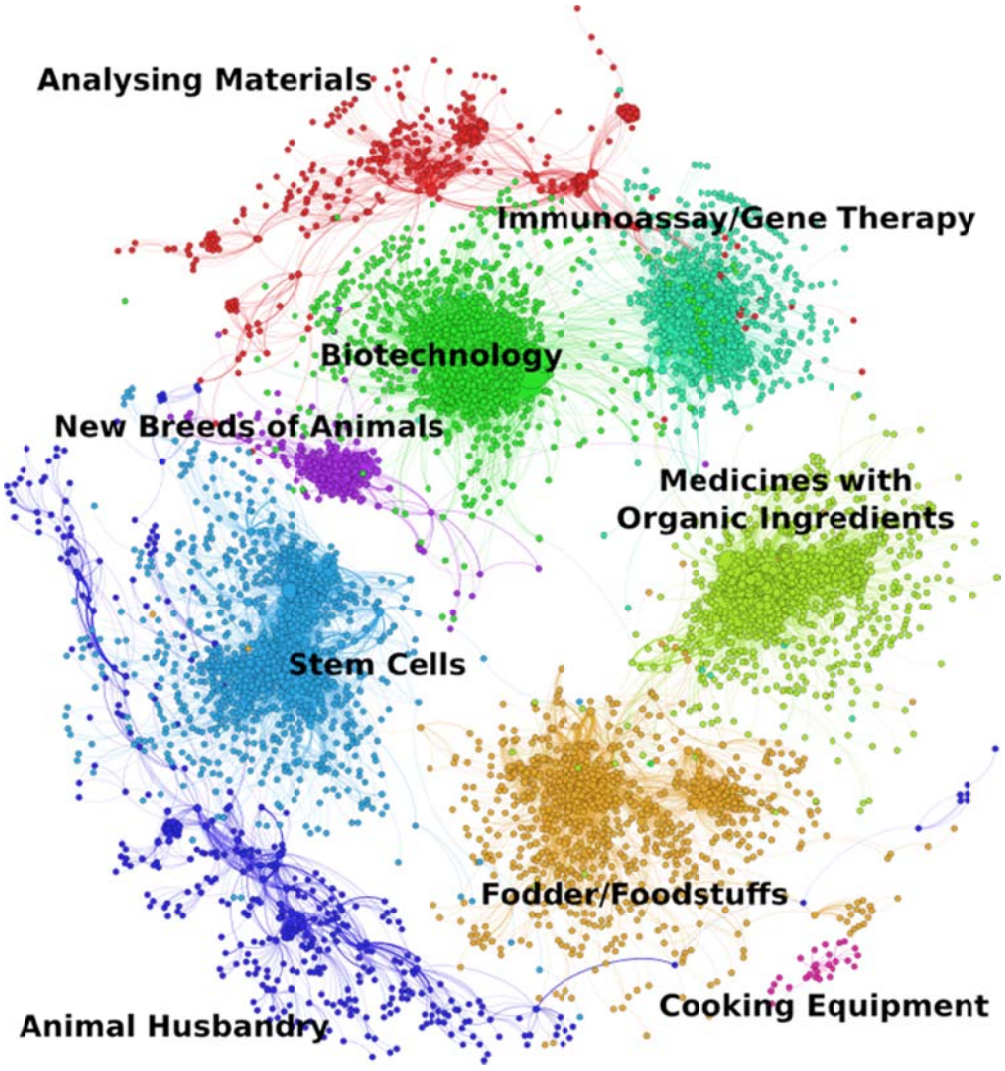
Co-Occurrence	A61K38/00	C07K14/005	C07K2319/00	A61K48/00	A01K2217/05
A61K38/00	9,198	566	1,355	1,067	892
C07K14/005	566	3,833	546	509	169
C07K2319/00	1,355	546	3,203	370	387
A61K48/00	1,067	509	370	2,879	664
A01K2217/05	892	169	387	664	2,800

In considering Table 2.3 note that the strongest linkage is always the self-reference to the same code (e.g. A61K38 to A61K38). These self-references are removed during the network mapping phase. However, note also that the patent code relating to transgenic animals A01K2217/05 is quite weakly related to the dominant code for medical peptides (A61K38/00). Network mapping assists with visualizing and clarifying these relationships.

The first step of the network mapping process involved combining the International Patent Classification and Cooperative Patent Classification codes into one complete set containing 41,167 codes consisting of 17,953 IPC codes and 34,472 CPC codes. The codes were then placed in a matrix in Vantage Point software and exported with the diagonal (self-referencing codes) excluded. The relationship between the classification codes (as nodes) is measured on document counts that form edges between the nodes. Network visualisation was performed in open-source Gephi software where each code forms a node on the map (see Figure 2.2 below). The network map was laid out using the Fruchterman-Reingold algorithm and expanded to clarify the clusters.

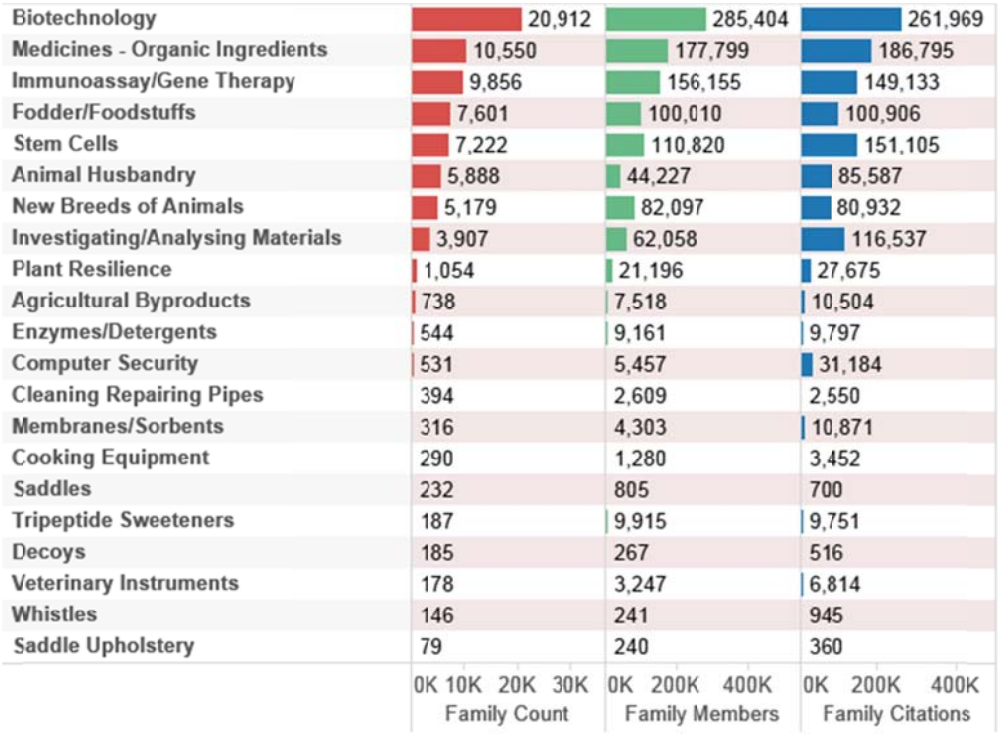
In the next step the aim is to identify major clusters in the map based on the strength of the connections between them to visualise communities of closely related clusters. To achieve this we partitioned the map by colour using a modularity class algorithm that iteratively calculates the mathematical strength of the relationships between nodes and allocates nodes to a modularity class until all nodes are allocated [77]. In practice this creates over 3,000 modules or clusters. Only the major clusters are displayed in Figure 2.2. Labels are selected based on the top ranking classification code or codes for each cluster to clearly explain the dominant content.

Figure 2.2: Major Technology Clusters for Animals (IPC / CPC Co-occurrence)



In interpreting this map note that technology areas that are closest together will cluster together and those that are least connected to each other will move to the periphery. Thus, biotechnology and new breeds of animals, immunoassays/gene therapy and stem cells are clustered towards the top of the map. In contrast animal husbandry, an area of innovation that mainly focuses on equipment and housing for animals, along with cooking equipment appear on the opposite periphery of the map. The reason for this is that they are only very weakly related with other areas of technology making reference to animals. Figure 2.3 displays the rankings for the clusters in the map. In interpreting Figure 2.3 note that a document may appear in more than one cluster.

Figure 2.3: Rankings of Technology Clusters Involving Animals



The strength of this approach is that we can see that some areas that may relate to animals such as fodder or foodstuffs, agricultural by-products, cooking equipment and veterinary instruments are displayed in distinct clusters. We can also see prominent areas such as computer security or cleaning and repair that make reference to animal names (such as a metal or plastic pig for cleaning oil pipelines), but do not in fact involve animals. The importance of this approach is that it is possible to gain an overview of the technology areas that make reference to animals and identify the best candidates for closer analysis.

Three candidate clusters stand out in the network map. The first is biotechnology, the second is new breeds of animals and the third is animal husbandry. While the third candidate, animal husbandry, may appear promising in practice analysis reveals that it focuses on equipment for caring for, working with, and housing animals. In making a decision about where to focus it is possible to zoom into the map. Figure 2.4 displays the details of the codes around the biotechnology cluster (light green) and the new breeds of animals cluster (dark green).

Figure 2.4: Detail of the Biotechnology and New Breeds of Animal Cluster

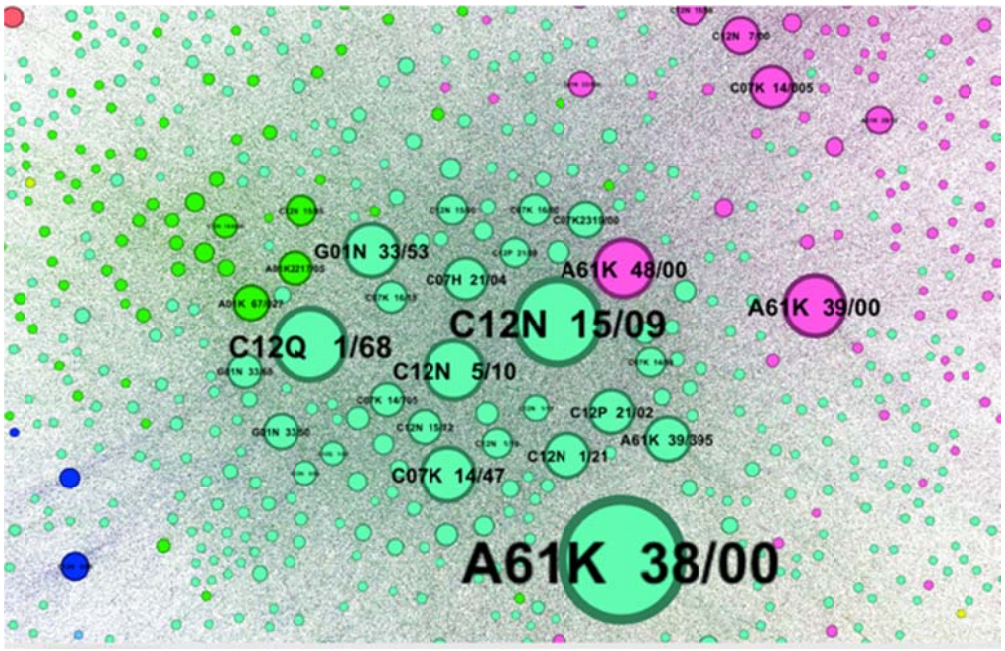


Figure 2.4 reveals the dominant classification codes in the clusters based on the combined IPC and CPC scores. We can clearly see that peptides (A61K38/00) are dominant in the biotechnology cluster. Other important classification codes include C12N15/09 for recombinant DNA technology and C12Q1/68 focusing on DNA sequencing. However, none of these classification codes relate directly to animals with peptides typically directed to health rather than to food and agriculture. The new breeds of animals cluster is smaller and focuses on classification codes in A01K67 (IPC) and A01K2227 (CPC) for genetically engineered or transgenic animals.

The contents of these technology clusters come into clearer view when they are disaggregated to reveal the network of technologies inside the clusters. We now turn to network mapping for the New Breeds of Animals and Biotechnology clusters as a basis for indicator development and close reading of patent documents in the next two sections.

Network Mapping for New Breeds of Animals and Biotechnology

We have seen above that the overall landscape for patent documents that make reference to animals can be broken down into clusters based on the use of patent classification codes (from the International Patent Classification or IPC and the Cooperative Patent Classification or CPC). We now turn briefly to mapping the two target clusters that form the basis for indicator development and analysis in the next sections. In the process we will progressively shift from using patent classification codes as the unit of analysis to the use of key terms.

New Breeds of Animals (Transgenic animals)

As a starting point the new breeds of animals cluster consists of 11,797 documents published in the main jurisdictions and 5,179 first filings (families) linked to 82,097 family members worldwide in the period 1976-2013. Figure 2.5 uses network mapping to disaggregate the underlying network for animal breeding into its component sub-clusters or communities of activity. This consists of 15 areas where the labels provide a brief summary of the dominant topics for each sub-cluster of documents based on the main patent classification codes in each sub-cluster.

The network diagram in Figure 2.5 breaks out a tightly connected cluster of activity on new breed of animals into its constituent sub-clusters and labels the sub-clusters by dominant topics based on a review of the document classification codes. It is important to emphasise that the documents are in fact tightly connected. The aim of the network visualization is to try and identify components within the cluster by deliberately forcing them apart. We then use the modularity class algorithm mentioned above to colour communities of related technologies based on the strength of the connections between them. Figure 2.6 displays the rankings for the sub-clusters relating to new breeds of animals. The network for new breeds of animals related activity can be briefly described as follows based on a review of 5,179 first filings (families).

Figure 2.5: Sub-Clusters in the New Breeds of Animals Cluster

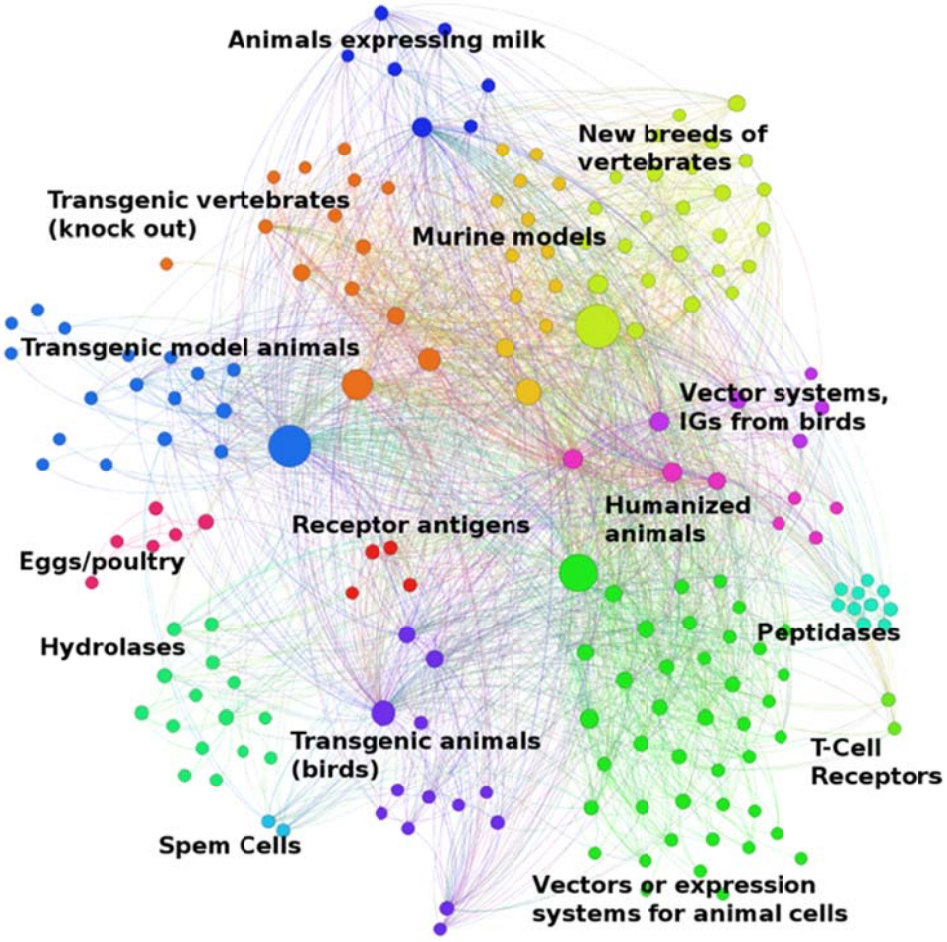


Figure 2.6: Sub-clusters Ranked on Patent Families

	Family Count	Family Members	Family Citations
New breed of vertebrates	2,237	34,413	30,973
Vector or expression systems for animal cells	2,219	42,058	48,396
Transgenic model animals with random inserted nucle..	1,366	26,803	29,559
Transgenic vertebrates (knock out)	1,139	20,968	21,696
Transgenic vertebrates (birds)	1,034	21,189	26,852
Murine models for tests/diseases	870	15,918	17,437
Vector systems, immunoglobulins from birds	563	7,921	10,017
Animals expressing milk	520	8,492	9,339
Hydrolases	467	9,705	13,742
Humanized Animals (knockin)	397	5,686	8,855
Eggs and Poultry	199	1,434	1,319
Receptor antigens from animals	188	4,327	6,327
Peptidases	146	3,112	5,988
Sperm cells	57	694	400
T-Cell Receptors	45	1,549	4,087
	0K 1K 2K 3K	0K 20K 40K 60K	0K 20K 40K 60K

When viewed in terms of the numbers of patent families the network is dominated by *New Breeds of Vertebrates* which focuses on animals with random inserted nucleic acids or transgenic animals. This is closely followed by *Vector or expression systems for animal cells* relating to the use of vectors (i.e. viruses) for

the introduction or expression of foreign genetic material to produce genetically modified animals. As such, we are in the realm of standard genetic engineering.

Transgenic animals break out into specific sub-clusters.

a) The largest of these sub-clusters is for *Transgenic model animals* for use in gene therapy and other medical applications. This sub-cluster includes an important patent grant from 1989 to the University of Ohio for the genetic transformation of zygotes (US4873191A).

b) The sub-cluster on *Transgenic vertebrates ("knock out")* focuses on animals where loss of function has been induced by knocking out specific genes. These animals are typically used as model animals for specific medical research. This sub-cluster includes the foundational patent for the Harvard Oncomouse for cancer research (US4736866A awarded in 1988). It also includes an important application originally filed in 1986 for transgenic animals that secrete desired proteins in milk from Integrated Genetics Inc. (see EP0264166A1 & EP0264166B1).

c) The sub-cluster on *Transgenic animals (birds)* is dominated by transgenic birds, notably with reference to chickens.

d) The sub-cluster on *Murine Models* reflects prominent references to genetically modified mice and rats in the wider cluster. The patent claims of these documents frequently make reference to vertebrates in general along with pigs, sheep and bovines.

e) *Vector systems, immunoglobulins from birds* focuses on documents featuring the creation of genetically modified animals with enhancer or promoter combinations that are relevant for transcription. Immunoglobulins from birds, notably chickens, are a major feature of this sub-cluster and include subjects such as avian antibodies, humanized chicken antibodies and egg white antibodies.

f) *Animals expressing milk* is dominated by genetically modified animals with a particular focus on animals expressing industrially exogenous proteins. Top ranking animals referenced in these documents include bovines, porcine, ovine and caprine animals. Topics covered in this sub-cluster include animal bioreactors, control of lactation and cattle beta-casein genes.

g) *Humanized animals* are animals that have been genetically modified to include some aspect of a human genetic component. Activity in this area includes allergen containing milk, chimeric non-human animals and humanized immunoglobulins. The top ranking animal groups in this sub-cluster are porcine, bovine, ovine and caprine animals.

h) *Hydrolases* are a type of peptide with more than 20 amino acids. Activity in this area is oriented to medicinal preparations and includes vaccines, chimeric proteins, egg hydrolases, cryopreservation of sperm, and preventing diarrhoea in pigs and calves.

i) The *Eggs and Poultry* sub-cluster is dominated by applications directed to injecting or treating eggs, focusing on chickens, turkeys and ducks. Examples of activity in this area include methods for injecting eggs in an early embryonic state, disease control by embryonic vaccination, and methods for determining the gender of a hatchling. Activity in this area frequently focuses on apparatus and methods for delivering substances into eggs.

j) *Receptor antigens from animals* is a small sub-cluster that mainly refers to cell surface determinants and links across to immunoglobulins. The top animal references in this sub-cluster are from the porcine, bovine and equine groups. Topics addressed in documents in this sub-cluster include immunoglobulins, mammalian stem cells and chimeric mammalian hosts.

k) *Peptidases* are another small sub-cluster that mainly focuses on medical preparations containing peptides. This sub cluster cross-links with hydrolases and includes blood coagulation factors. An example of activity in this area is direct gene transfer into ruminant mammary glands.

l) The *Sperm cells* sub-cluster mainly focuses on sperm cells, spermatozoa and fluids and includes preparing cells for nuclear transfer, freeze processing sperm and the preservation of sperm.

m) Finally, *T-cell receptors* are molecules found on the surface of T lymphocytes that recognise antigens and elicit an appropriate response from the immune system. Patent documents in this sub-cluster cover issues such as regulating immune response by blocking lymphocytic signals and transgenic animals with humanized immune systems.

As this brief description of the new breeds of animals cluster makes clear, the data is dominated by transgenic animals with a range of uses that include food and agriculture but also extend to a wide range of health applications.

The Biotechnology Cluster

In approaching the biotechnology cluster we identified a total of 20,912 first filings linked to 46,564 publications in the main jurisdictions and 285,404 family members worldwide. Figure 2.7 displays the network map of technology areas inside the cluster with labels chosen on the basis of the top IPC/CPC codes in a sub-cluster. Note that each dot refers to a classification code.

Figure 2.7: Inside the Biotechnology Cluster

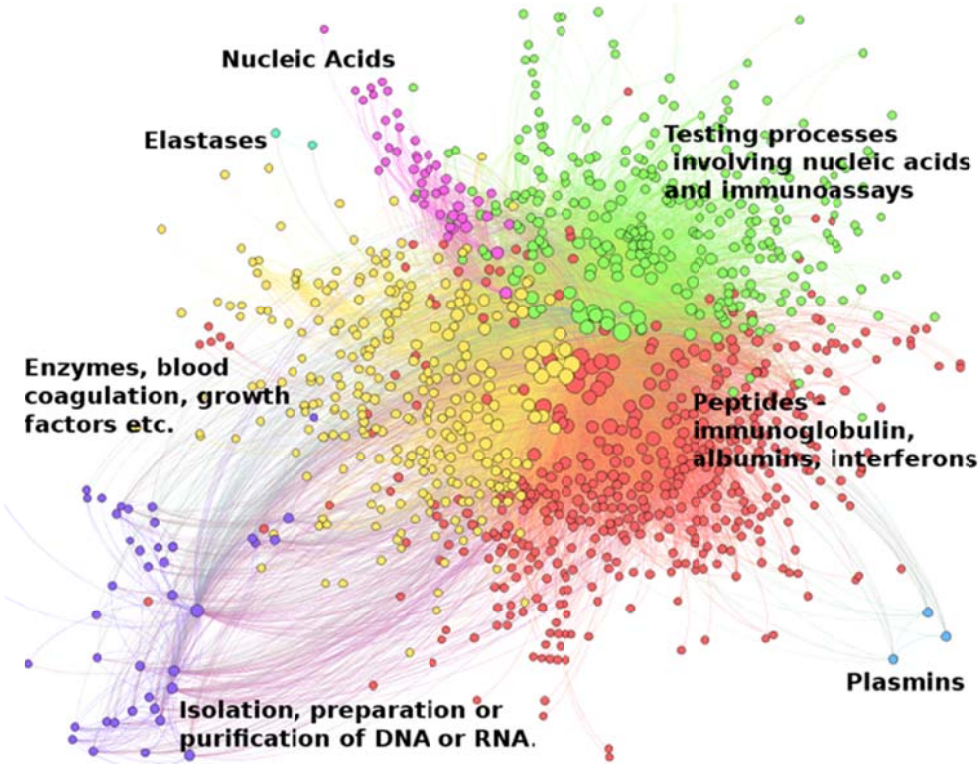


Figure 2.7 makes clear that in approaching the biotechnology cluster the main focus is on a combination of DNA and health related inventions such as blood coagulation factors, immunoglobulins etc. This comes into greater focus when we break down two of the major clusters: a) Peptides, and; b) Enzymes, blood coagulation and growth factors into their component sub-clusters. These are shown respectively in Figure 2.8 and Figure 2.9.

Figure 2.8: Peptides and Immunoglobulins (Sub-cluster)

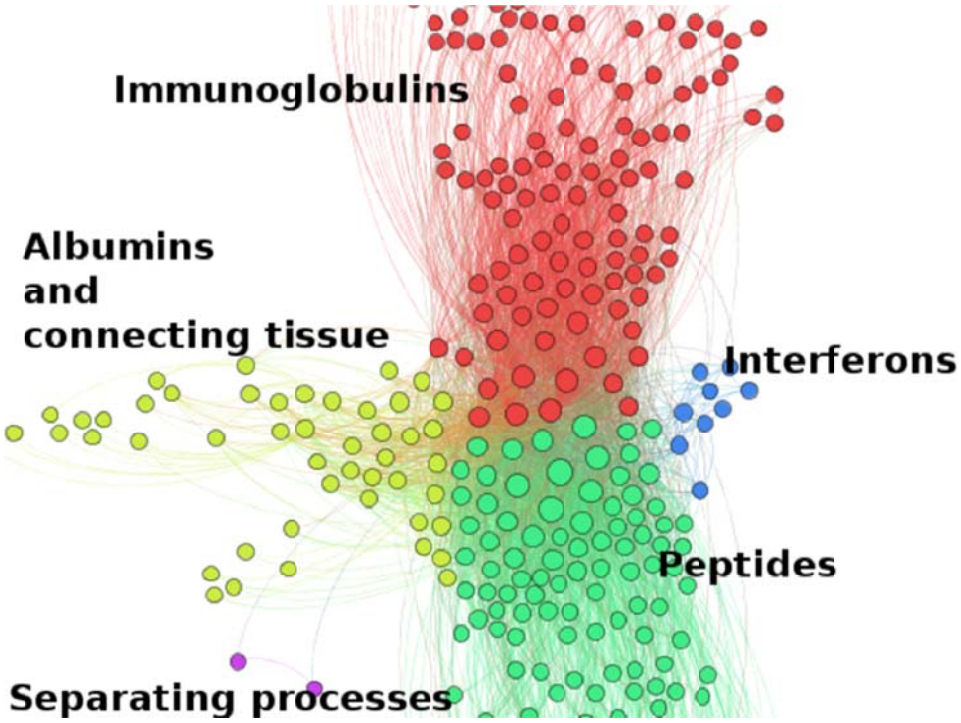
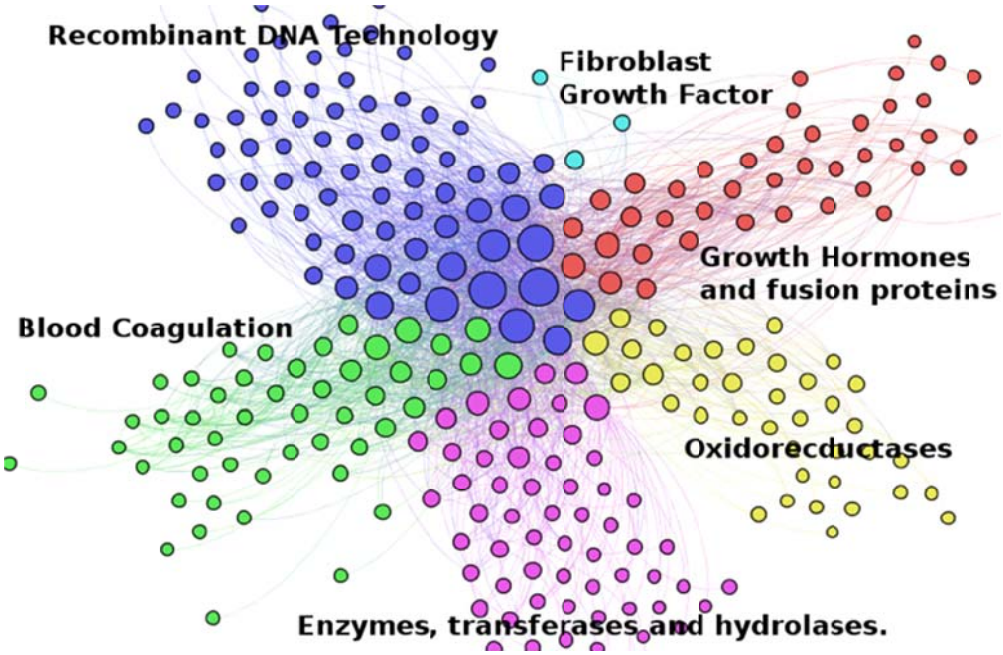


Figure 2.9: Enzymes and Blood Coagulation (Sub-cluster)



In approaching the biotechnology cluster we are therefore confronted by the reality that there is no clear indicator that specifically relates to animals as such and animal genetic resources for food and agriculture in particular. At the same time, this is the largest cluster in the wider landscape that makes reference to animals and the components of animals.

In practice, there appear to be three aspects to this. First, applicants frequently make reference to animals as the target for particular methods or applications notably with respect to health related applications. Second, the cluster contains a combination of non-transgenic related technologies and transgenic related technologies that have not been captured at the level of classification (notably in A01K). Third, components of organisms such as bovine serum albumin or viruses associated with particular animals frequently appear in this cluster.

Conclusion

This section has focused on the use of a combination of large-scale text mining for animal names in millions of patent documents and the identification of major technology clusters using network mapping of the International Patent Classification and the Cooperative Patent Classification. On this basis two main clusters have been identified for further analysis focusing on new breeds of animals (transgenic animals) and biotechnology.

In the course of this analysis it has become clear that research on patents for animal genetic resources involves significant problems.

1. Patent applicants frequently refer to multiple animals at different levels (bovine, cattle, *Bos indicus*) in constructing patent claims;
2. Patent applicants frequently refer to more than one animal in patent claims to capture the broadest possible range of animals, including humans, and subsequently narrow the claims to the actual target (e.g. mice). This makes it extremely difficult to accurately filter for livestock animals;
3. Applicants may refer to components from animals, e.g. bovine serum albumin or to viruses that are associated with animals;
4. Animals may be the target of an invention or the source of an invention.

Navigating these complexities is rendered more challenging by a lack of sufficient definitional clarity in both the International Patent Classification and the Cooperative Patent Classification on: a) types of animals, and; b) technologies directed towards food and agriculture. Improving this situation would make a major contribution to longer term monitoring of animal genetic resources for food and agriculture in the patent system.

Finally, the use of classification codes for network mapping as discussed in this section has the limitation that it is unlikely to be readily intelligible to farmers and others interested in the field. That is, the analysis needs to focus on technologies and terms that will be familiar to those interested in animal genetic resources for food and agriculture. To address this problem we begin by developing a quantitative indicator for animal genetic resources based on the clusters identified in this section using key terms. We then turn to analysis of key patent activity relating to animal genetic resources for food and agriculture.

Section 3. Developing a Patent Indicator for Animal Genetic Resources

Section Summary

- Using the scientific literature on animal breeding and transgenic animals, a thesaurus was developed to search the titles, abstracts and claims of patent documents in the New Breeds of Animals (transgenic animals) and Biotechnology clusters identified in Section 2;
- We mapped the individual clusters for New Breeds of Animals (transgenic animals) and Biotechnology to identify sub-clusters and major themes using key words from the scientific literature;
- A quantitative indicator was developed that can be updated and adapted over time to respond to policy needs;
- The dominant trend in filings for animal genetic resources is downwards from 2001 onwards. This probably reflects factors external to the patent system (availability of markets) and internal to the patent system (tightening of patent rules for genetic inventions);
- Trends in filings of patent applications that make reference to a livestock animal and contain a DNA sequence have remained relatively stable at +/- 1,200 filings per year for the last 10 years under the Patent Cooperation Treaty;
- The interpretation of patent documents containing DNA sequences is not straightforward and should be addressed in any future work. The presence of a DNA sequence in an application does not mean it is claimed;
- The downward trend in patent activity for animal genetic resources remained under any alternative definition of animal genetic resources tested using patent classification codes. The completion of genome sequencing projects and new and emerging areas of science and technology such as synthetic biology, genome engineering and genome editing may result in a future increase in activity;
- The patent indicator can be adjusted and updated as required to meet policy needs.

Introduction

In the previous section we examined the process for interrogating patent data for animal genetic resources using text mining and network mapping with patent classification codes. This involved the following steps:

1. Searching the full text for Latin species names for the target animals;

2. Searching the title, abstracts and claims of documents for animal common names and major groupings (bovine, porcine, ruminant etc.);

3. Mapping major technology clusters using patent classification codes and co-occurrence analysis.

This approach allows for the exploration of the technology clusters that are most directly related to animal genetic resources. In particular, we will now focus on the technology clusters for new breeds of animals (transgenic animals) and biotechnology (non-transgenic). However, because of the diversity of patent activity that may involve an animal genetic resource or expression product, further steps are required as the basis for the development of a quantitative indicator. In this section we describe the outcomes of two additional steps directed to indicator development.

4. Searching the titles, abstracts and claims for key terms relating to animal genetic resources identified from the scientific literature in Web of Science and manual review of patent data;

5. Co-occurrence analysis of key terms for animal genetic resources appearing in the technology clusters for new breeds of animals and biotechnology to identify major themes.

The outcome of this exercise is a scalable quantitative indicator for animal genetic resources for food and agriculture that can be expanded, contracted and refined over time in accordance with policy needs.

Based on this data we are then in a position to examine the details of the technologies involving animal genetic resources as a basis for considering their implications for food and agriculture. We begin however with discussion of the development of a thesaurus to search the technology clusters.

A Thesaurus for Animal Genetic Resources

Our aim in developing a thesaurus for animal genetic resources was to target those terms most directly related to food and agriculture for the development of a quantitative indicator and detailed review.

We approached the development of a thesaurus using three main steps:

1. Testing an FAO dictionary of 3,417 biotechnology terms;

2. Developing a classification scheme and thesaurus through manual review of patent families in the New Breeds of Animals cluster in Vantage Point focusing on the Titles, Abstracts and Claims of patent documents and the additional Derwent World Patent Index (DWPI) abstract fields from Thomson Innovation. DWPI abstract fields are written by specialists working for Thomson Reuters to provide a fuller technical description of an invention and are particularly useful for identifying the intended uses of an invention;

3. Collating scientific literature on animal breeding and animal biotechnology from Thomson Reuters Web of Science and reviewing author key words and phrases from the titles and abstracts of scientific publications.

Our tests revealed that the FAO dictionary of biotechnology terms demonstrated the feasibility of the approach but the dictionary terms were too generic to be of use in separating animal breeding from other areas of biotechnology. In contrast manual classification of patent documents and word stemming in the new breeds of animals cluster produced valuable results. However, this approach created uncertainty on whether the full range of terms relevant for animal breeding had been captured.

To address these issues we engaged in experimental searches of the scientific literature for a range of terms relating to animal breeding and animal biotechnology. The aim of this exercise was not to generate a dataset containing the complete universe of scientific literature on animal breeding but to generate a sufficiently large sample to identify key phrases used in the literature on animal breeding to sub-search the patent data. Table 3.1 sets out the search terms used in the topic field of Thomson Reuters Web of Science to generate the dataset of scientific literature.

Table 3.1: Search Queries in Thomson Reuters Web of Science

Topic Search Query	Results
("animal" or "animals") and ("biotechnology")	1,793
"animal breed" or "animal breeding"	1,503
"genetic engineering" and ("animals" or "animal")	769
"livestock" and ("breed" or "breeds" or "breeding")	2,768
"animal clone" or "animal cloning"	179
"transgenic animal" or "transgenic animals"	4,015
Total	**10,709**

The results of the searches were de-duplicated to remove copies of the same record that appeared across the different datasets to arrive at 10,709 scientific publications. These records provided access to 272,935 words and phrases from the title, abstracts, author keywords and terms from the titles of cited literature (keywords plus). A total of 217,824 multi-word phrases were reviewed and 2,213 phrases and composite terms (such as dairy-cow) were identified. These terms were then combined with the results of a manual review of patent documents to create a thesaurus of terms to sub-search the patent data to develop an indicator. Table 3.2 displays the top results for the selected terms based on publication counts in Web of Science data. The datasets of terms are provided in the Annex 2.

Table 3.2: Top Selected Terms in the Scientific Literature

Records	Keywords & Phrases
3,119	transgenic animals
1,567	transgenic mice
920	animal breeding
341	animal models
249	modified animals
213	nuclear transfer
198	livestock production
194	mouse model
183	transgene expression
178	animal welfare
172	quantitative trait loci
160	genetic improvement
160	livestock breeding
159	gene therapy
156	animal production
154	mammary gland
153	Alzheimer's disease
153	farm animals
151	animal model
142	animal health

Table 3.2 is significant because it highlights the importance of terms in the scientific literature that are not necessarily obvious to non-specialists, such as quantitative trait loci or quantitative trait locus. This approach allows for the construction of an indicator based on the appearance of terms in the title, abstract or claims of patent documents in the new breeds of animals and biotechnology cluster.

The second step in the process is to map the occurrence of these terms in the patent data focusing on the new breeds of animals and biotechnology clusters. This involves two additional steps:

1. Because there are overlaps between the New Breeds of Animals and Biotechnology clusters, any patent document appearing in the New Breeds of Animals cluster is removed from the Biotechnology cluster. This avoids double counting of the same documents;

2. Single terms may be used in inventions describing different technologies. For example, a transgenic animal may be directed to food and agriculture or the production of a recombinant protein for the health sector. To address this we place the terms into a co-occurrence matrix to identify clusters of activity (e.g. agriculture or health). Network mapping provides a basis for identifying segments for inclusion in the indicator for animal genetic resources for food and agriculture.

To identify food and agriculture using key terms we focused on analysis of two clusters:

a) New Breeds of Animals

b) Biotechnology

Text mining of patent documents was conducted using the well-known Porter Stemming Algorithm to capture any phrase containing the term in the Title, Abstract, Claims or DWPI abstract fields. Based on these results the terms were placed into a co-occurrence matrix and mapped in Gephi to identify and label major thematic areas. We now turn to the results of this exercise.

New Breeds of Animals (transgenic animals)

The new breeds of animals cluster can be subdivided into three main themes based on the use of key terms (see below). Trends in first filings based on this division are presented in Figure 3.1.

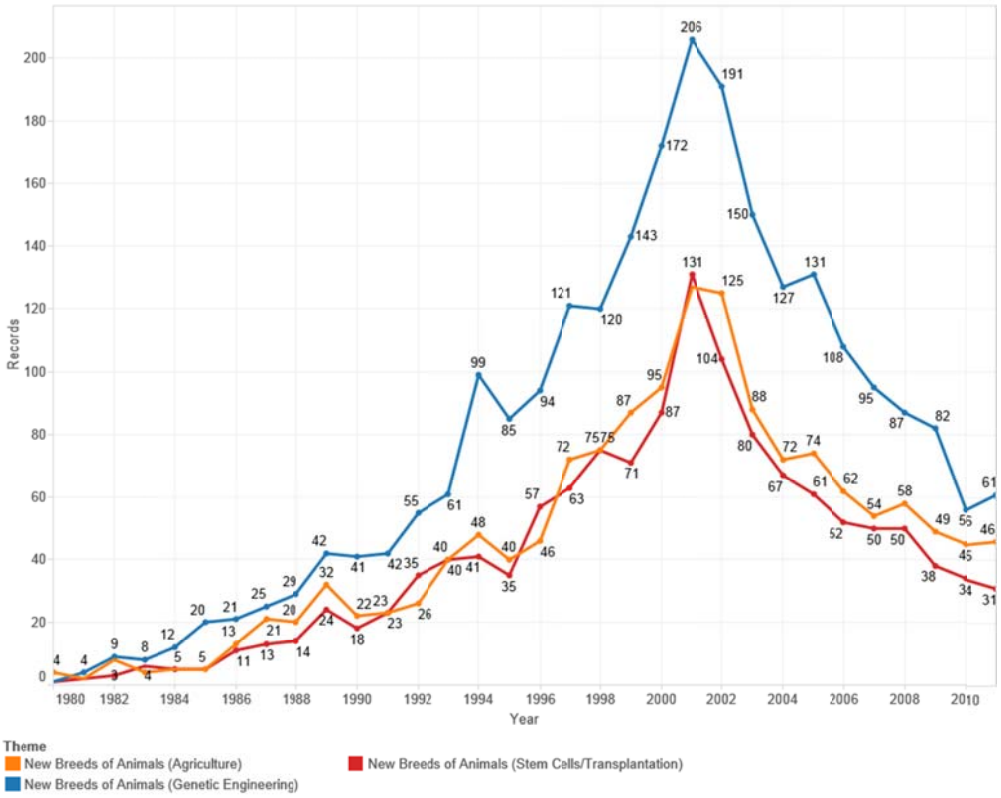
These themes are:

a) Agriculture dominated by breed and animal related terms;

b) Genetic engineering dominated by genome, transgenic and non-human animal terms, and;

c) Stem cell, embryo and transplantation related terms with a particular focus on xenotransplantation.

Figure 3.1: Trends for Themes in the New Breeds of Animal Cluster



The themes within the new breeds of animals cluster were identified using network mapping of the clusters and the application of the modularity class algorithm using Gephi (see section 2). Figure 3.2, 3.3 and 3.4 display the network maps inside the new breeds of animals cluster based on the co-occurrence of key terms in the first filings of patent documents. In considering these three network maps we would note that labels such as "food related" or "egg related" refer to groupings of related terms.

Figure 3.2: Agriculture related terms for New Breeds of Animals

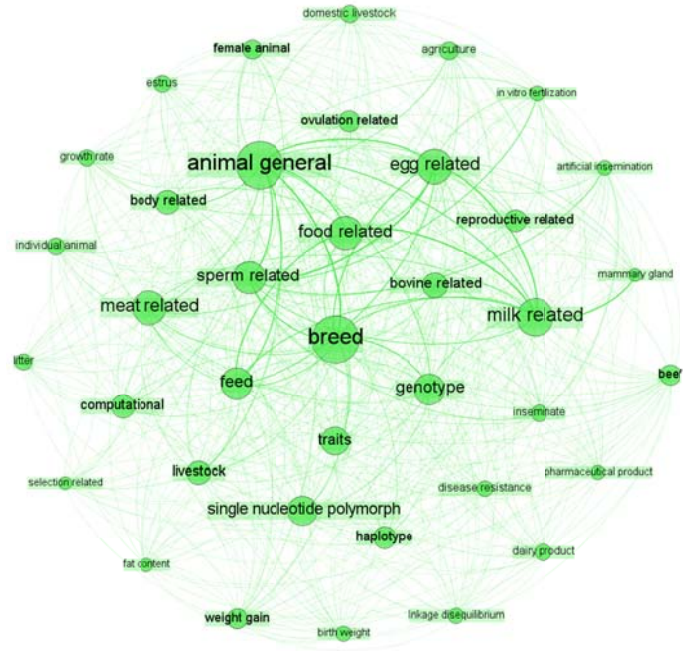


Figure 3.3: Genetic Engineering related terms for New Breeds of Animals

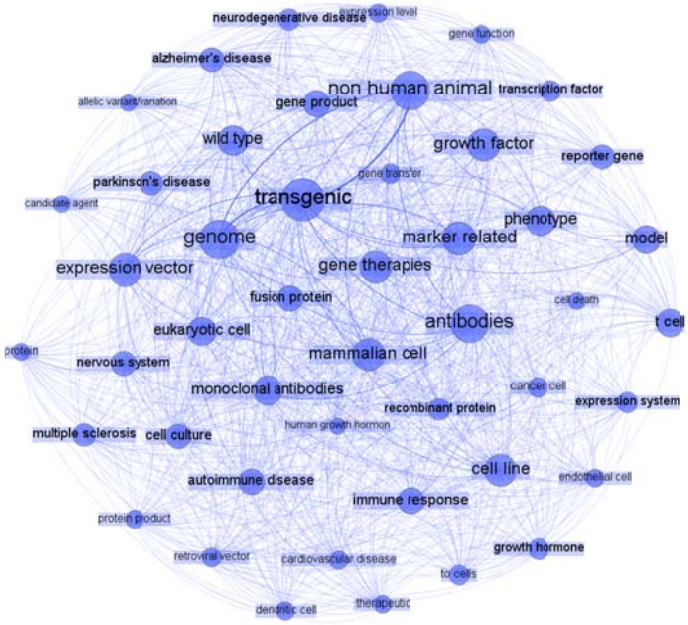
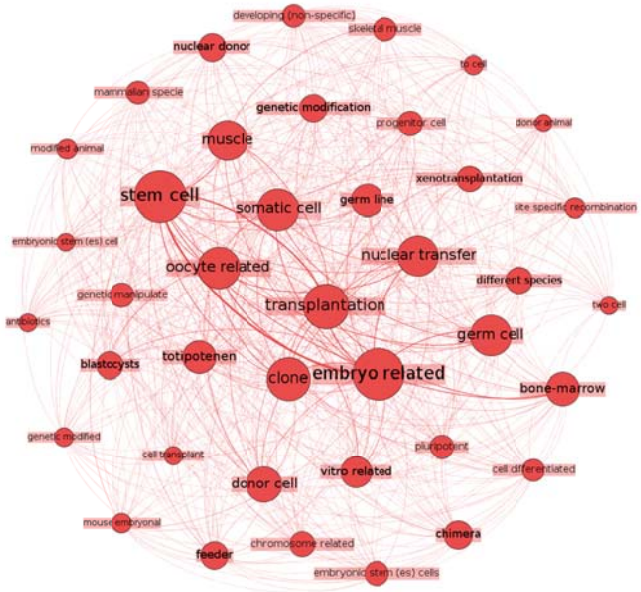
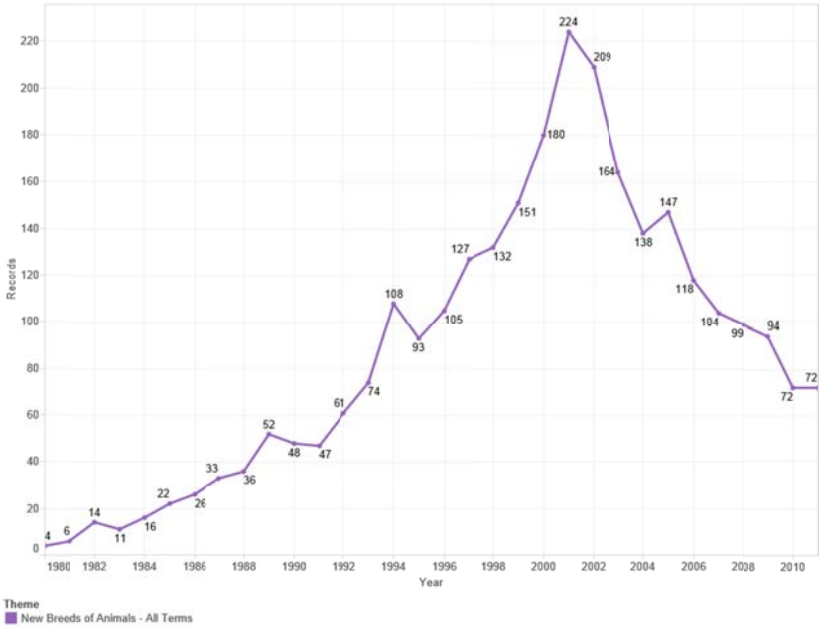


Figure 3.4: Transplantation and Stem Cells related terms for New Breeds of Animals



In considering these themes note that the terms are grouped together in thematic areas based on the strength of the connections between the terms in the underlying document set to focus the picture. This produces a final indicator for New Breeds of Animals as in Figure 3.5

Figure 3.5: Indicator within the New Breeds of Animals Cluster



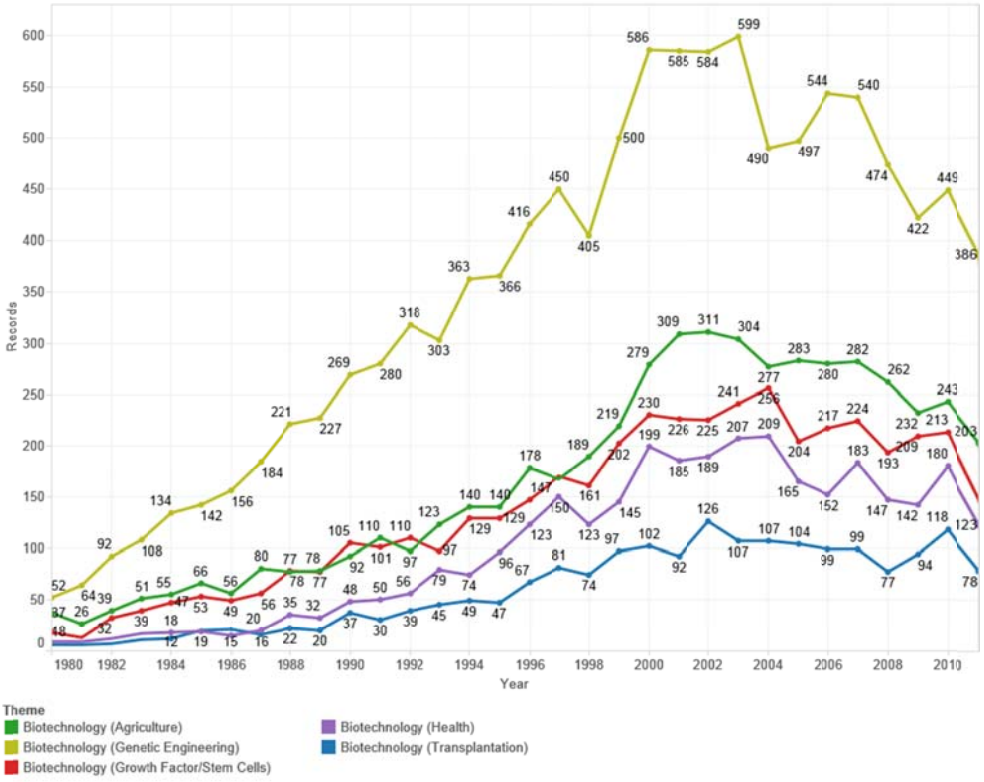
As we can see in Figure 3.5 the dominant trend for animal genetic resources

remains downwards from a peak in 2001. The importance of this figure is that it represents trends based on defined terms and can be disaggregated by major theme as required.

Biotechnology

The Biotechnology cluster can be subdivided into 5 themes based on the use of key terms. Trends in first filings based on this division are presented in Figure 3.6.

Figure 3.6: Trends for Themes of Biotechnology Cluster



The Biotechnology cluster is more diverse in its themes than the new breeds of animals cluster. Based on key terms Figure 3.6 identifies 5 major themes.

1. An Agriculture component focused around breeds, food related and animal terms;
8. Genetic engineering, dominated by references to genomics and antibodies;
9. Growth factors and stem cells;
10. Health focusing on Alzheimer's disease, Parkinson's disease, Multiple sclerosis and Bovine Spongiform Encephalopathy;
11. Transplantation, bone-marrow and t-cell terms.

The following figures display the key term networks in the thematic areas.

Figure 3.7: Agriculture Terms in the Biotechnology Cluster

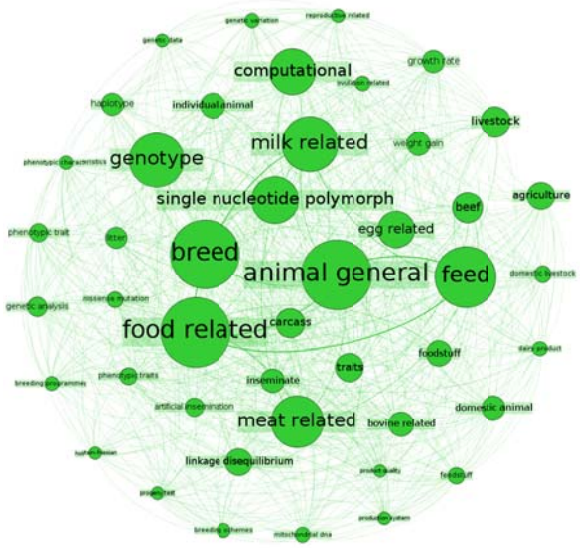
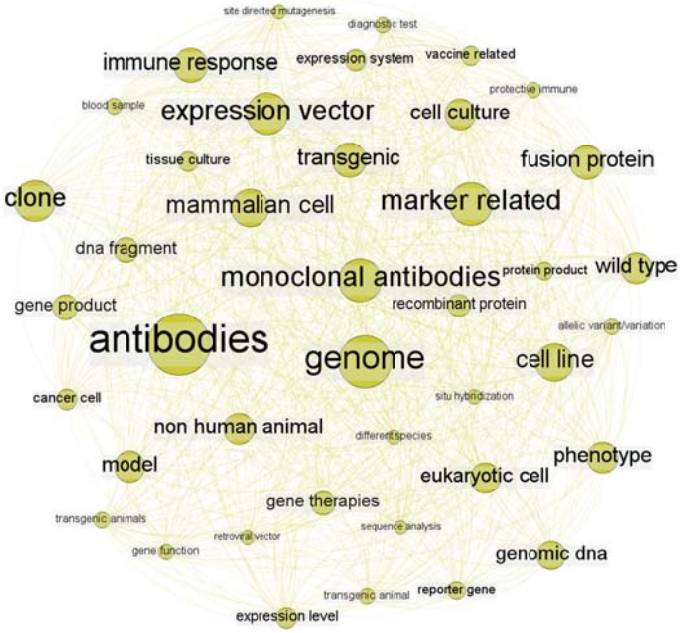
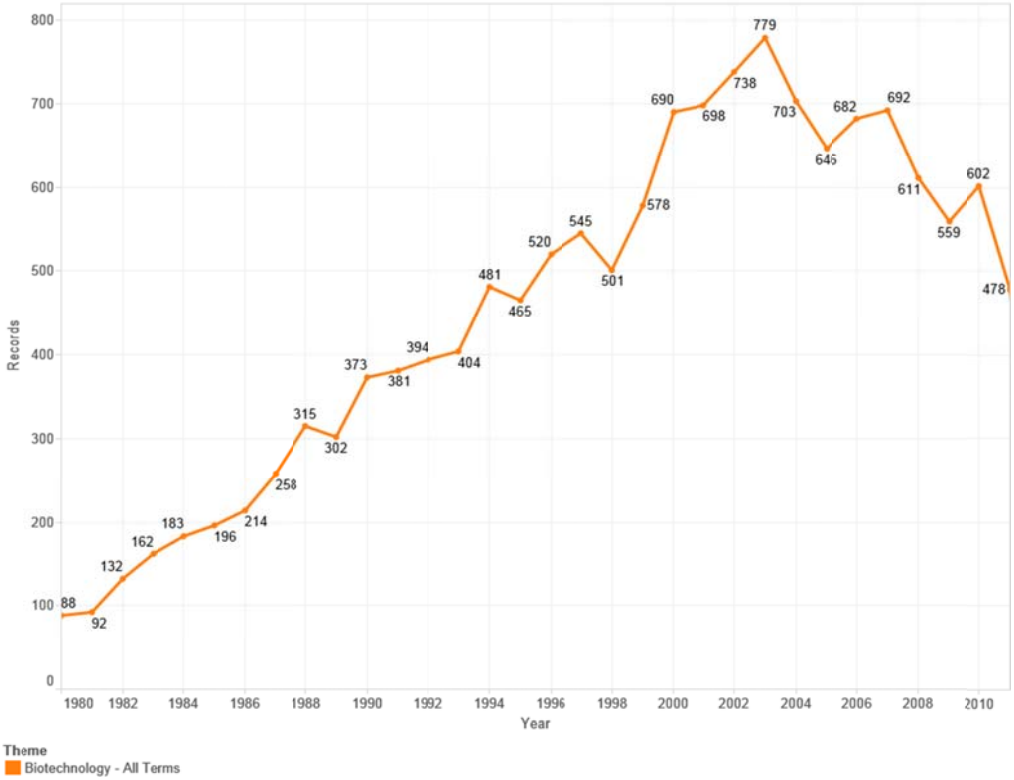


Figure 3.8: Genetic Engineering Terms in the Biotechnology Cluster



The combination of the five major themes in the biotechnology cluster produce a final indicator for Biotechnology as in Figure 3.9.

Figure 3.9: Final Indicator for Biotechnology



As we can clearly see, the biotechnology cluster also displays a downward trend in first filings. We now turn to the combined indicator from the two clusters identified in the research.

A Patent Indicator for Animal Genetic Resources for Food and Agriculture

We are now in a position to present the patent indicator for animal genetic resources for food and agriculture. As noted above there are a number of themes that could be included in the final indicator. We selected those themes from the New Breeds of Animals and Biotechnology sectors that are most closely related with the use of animal genetic resources for food and agriculture (see below). Figure 3.10 provides the indicator based on first filings.

Figure 3.10: Patent Indicator for Animal Genetic Resources for Food and Agriculture

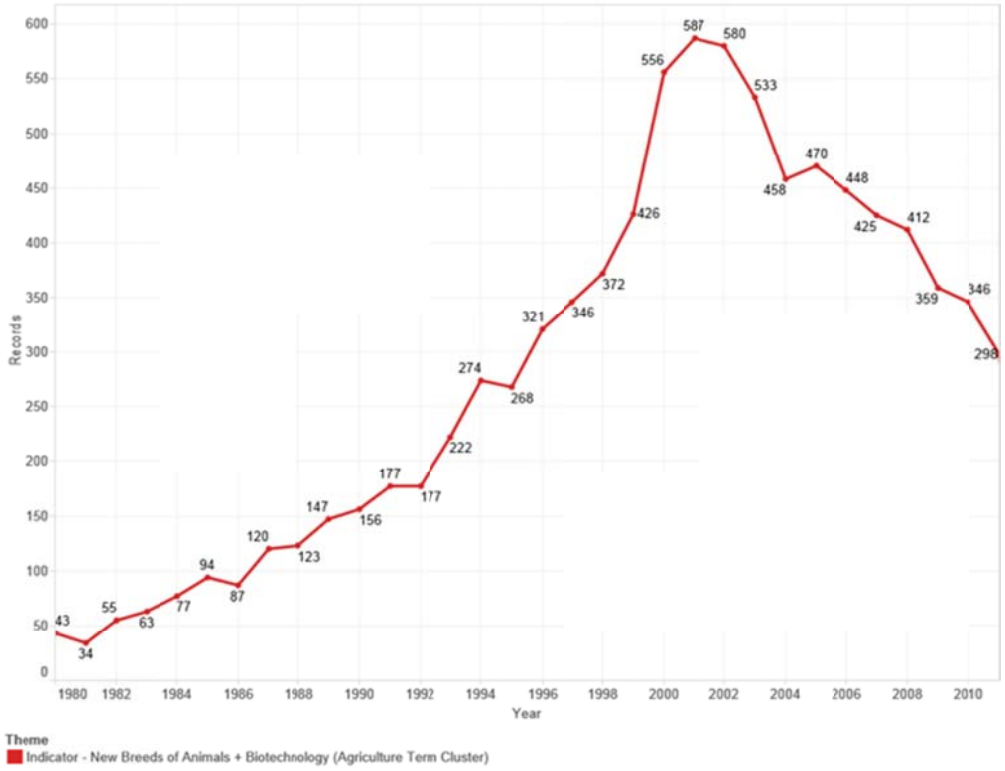


Figure 3.10 shows the patent indicator for animal genetic resources for food and agriculture. The indicator consists of four themes, three from the new breeds of animals cluster and one from the biotechnology cluster. The trends for these individual themes are shown in Figure 3.11. Figure 3.12 displays global trends in demand in the form of follow on applications and grants originating from the first filings. Data on global demand through trends in family members typically displays a delay in responding to underlying demand measured on first filings and is affected by issues such as pendency rates (time to first action by a patent office) in the processing of applications.

Figure 3.11: Themes inside the Patent Indicator

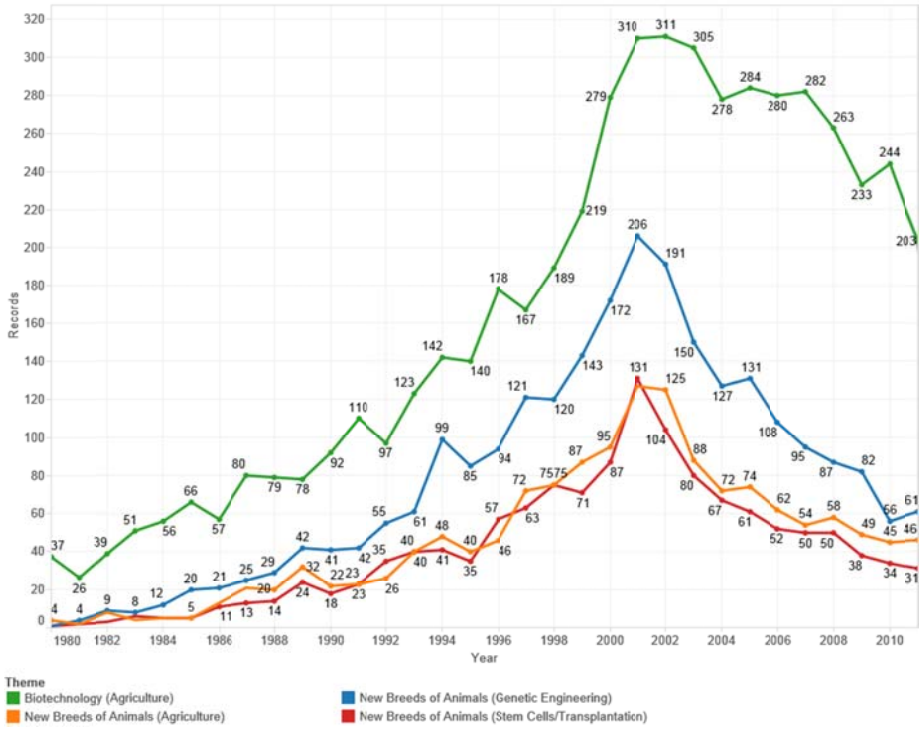
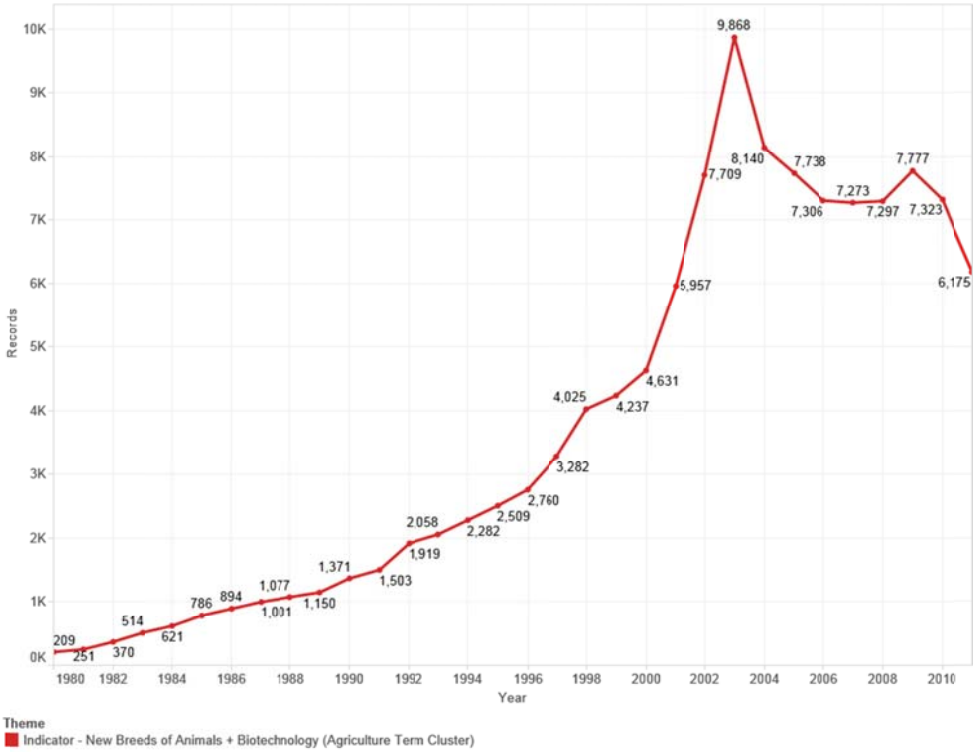


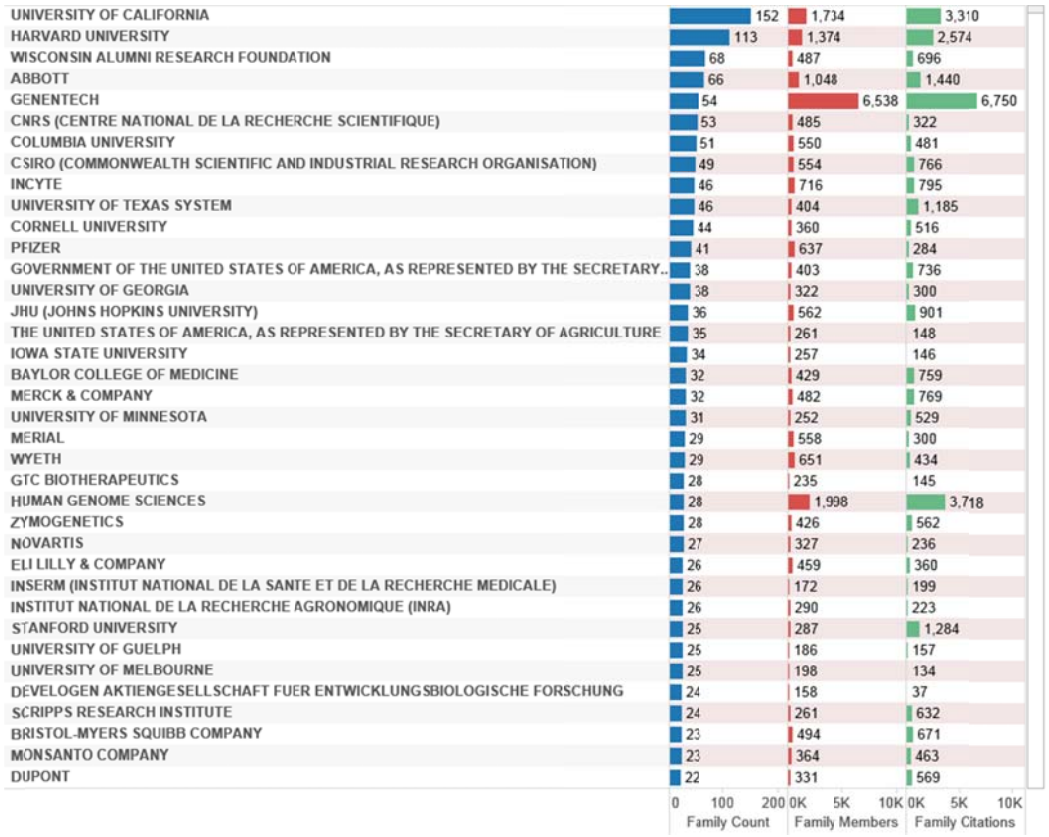
Figure 3.12: Global Family Member Trends for Patent Indicator



Based on the indicator we are now in a position to examine the major features of

the indicator and landscape. Figure 3.13 provides the top applicants for the indicator.

Figure 3.13: Top Applicants within the Patent Indicator



Data on patent applicants could as necessary be broken down in greater detail to focus on applicants addressing health issues or improvements in animal breeding. However, as we will see in more detail in the next section, there are very significant overlaps between these areas of technology with developments in relation to zygotes for both animals and plants having a major impact in the patent landscape for animals (e.g. US4873191A). As such we need to be aware of the impacts of spillovers from developments in health related activity into animal breeding and vice versa. This complicates our ability to disaggregate the patent landscape.

However, taking these overlaps into account we are now in a position to review the sources of first filings based on the number of first filings submitted through a national office (Figure 3.14). Figure 3.15 displays the data on follow on filings (family members) in the form of applications and grants originating from the first filings as an indicator of global demand.

Figure 3.14: Global Distribution of First Filings for the Patent Indicator

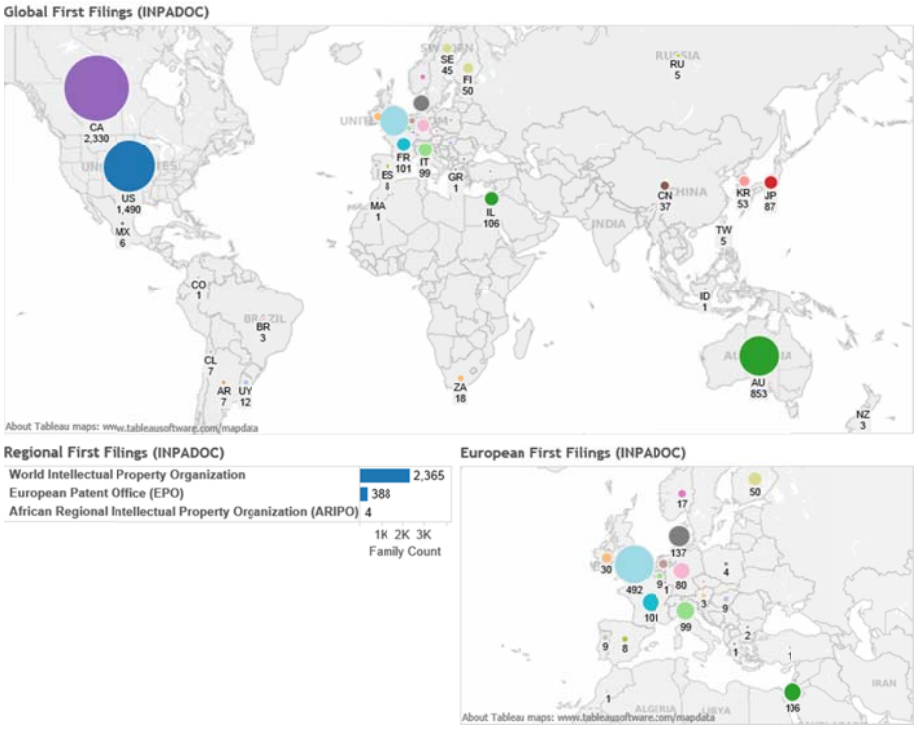
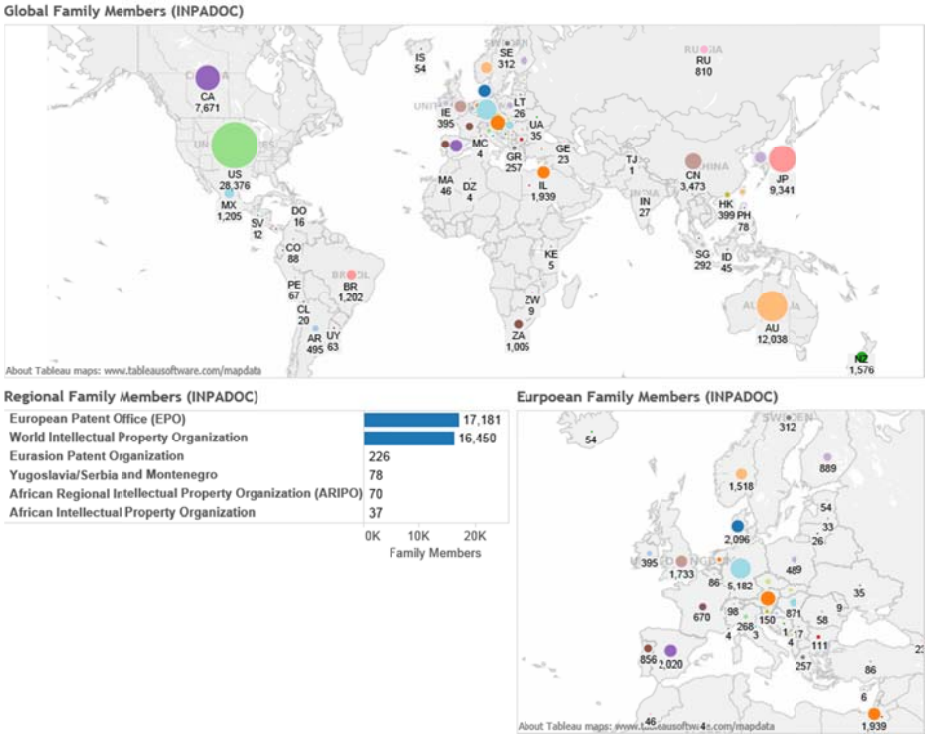


Figure 3.15: Global Distribution of Family Members for the Patent Indicator



Based on the number of first filings, Canada and the United States followed by Australia and the UK emerge prominently in the patent landscape, with limited activity from other countries in Europe and elsewhere in the world. This suggests that patent activity involving animal genetic resources is presently relatively narrowly concentrated in a small number of countries. In contrast when viewed in terms of global demand for protection, measured in follow on filings in multiple countries arising from the first filings, the United States, Canada, Australia, Japan, and Germany emerge as prominent targets for protection. Of particular interest here is the growth of demand for protection in China (3,473 family members), New Zealand (as a country with a major animal agriculture sector) along with Israel, Brazil, Mexico and South Africa. The lack of activity in India could possibly reflect a lack of available data in PATSTAT leading to an underestimate of activity while data for Australia is likely to be affected by historic over-counting of PCT designations as actual applications. However, one striking feature of global demand is the lack of demand for protection in the majority of African countries (outside South Africa) and at the two regional African patent organisations.

Figure 3.16 disaggregates the data in accordance with animal names based on Latin species names and common names. Figure 3.16 reveals that the patent data is dominated by bovine, porcine and equine animals. The challenge, as will be discussed in the next section, is moving across the range of options from specific species to larger groupings to identify the documents of greatest direct relevance for food and agriculture.

Figure 3.17 displays the top technology areas across the indicator based on the Cooperative Patent Classification on the sub-class level. Note that the term animal husbandry encompasses and is dominated by new breeds of animals (transgenic animals). Greenhouse gas reduction towards the bottom of the table represents a new and emerging area of activity for animals in the patent system that merits further investigation in any future research.

Figure 3.16: Species Names (Latin and Common) within the Patent Indicator

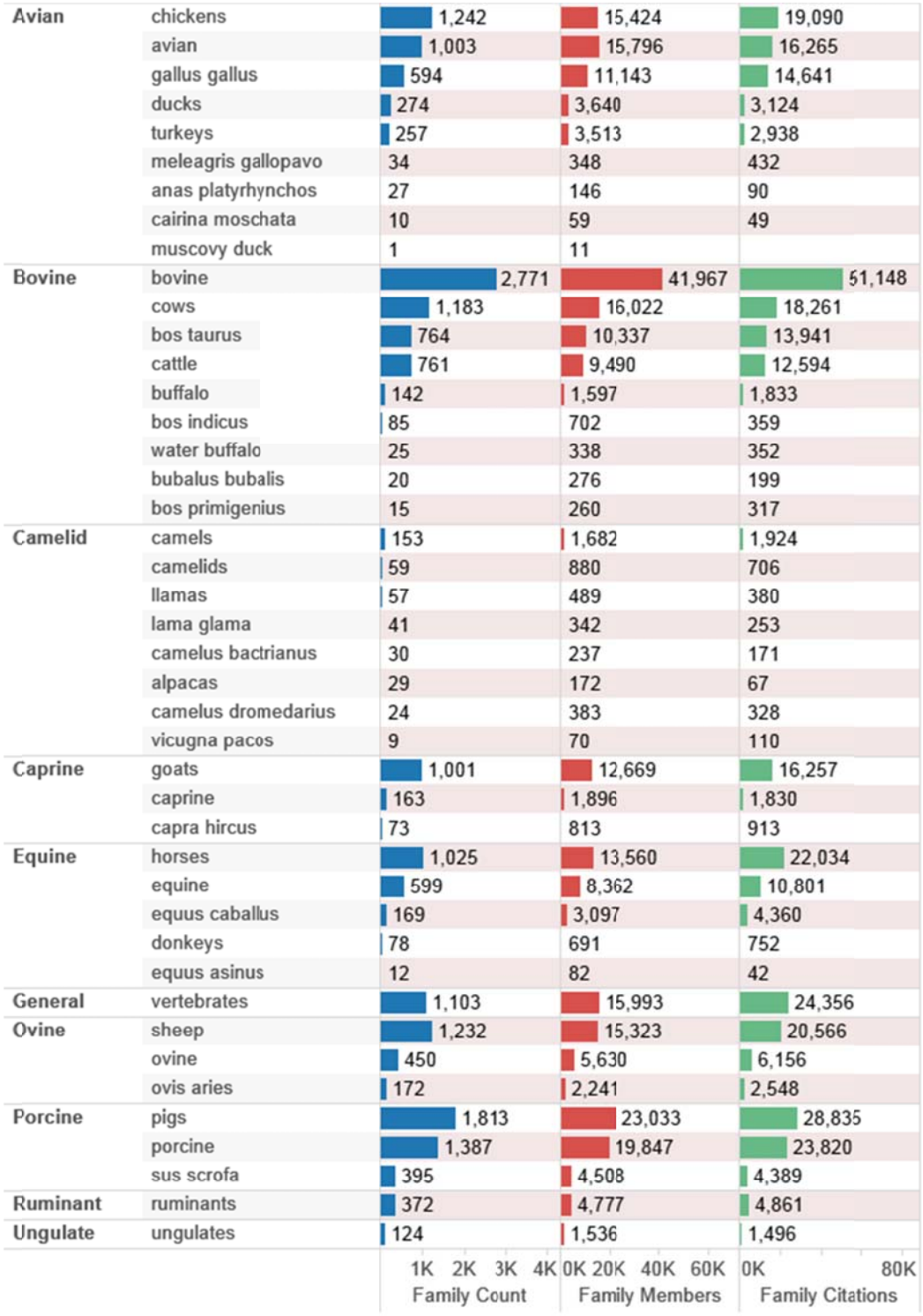
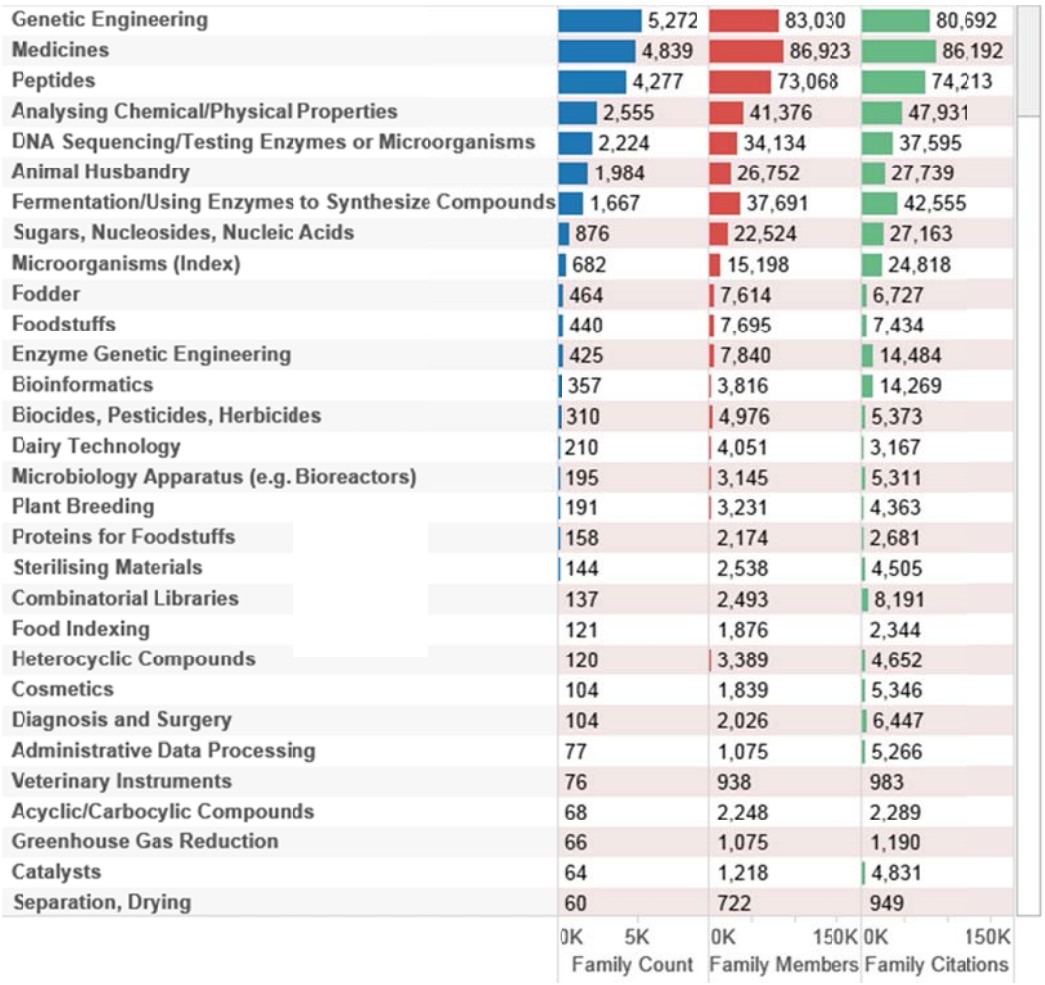


Figure 3.17: Technology Areas within the Patent Indicator



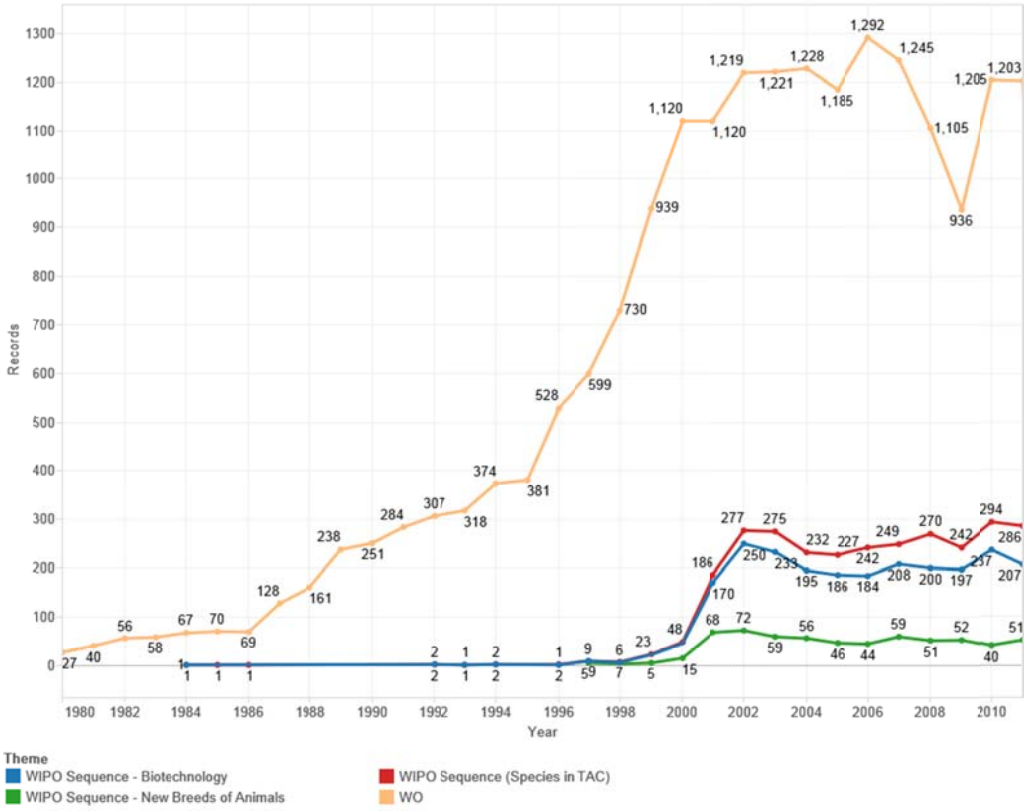
DNA and Amino Acid Sequence Data

The rise of patent applications relating to genetic sequences has been a key focus of controversy in debates on patents, patentability and the impacts of DNA patents on science and innovation [73,78-83]. In practice, debates on DNA patents typically focus on individual examples, such as the controversies over breast cancer related patents (BRCA1 and BRCA2) or are opinion based [83,84]. However, moving towards evidence based analysis of sequence data in patents poses significant challenges due to the dispersed nature of the data and the variety of options that exist for counting sequence data that have significant consequences for conclusions about the impacts of DNA related patent activity.

In approaching the issue of patent activity involving DNA sequences from animals we focused on the identification of references to animal names in the title, abstract or claims of patent filings that contained a sequence listing submitted under the Patent Cooperation Treaty at WIPO. Sequence listings include

sequences for DNA, RNA and amino acids. We use the term DNA sequences as a short-hand for the wider set of sequence data. A fuller account would expand this analysis to sequences registered in other patent offices and repositories such as GenBank [84]. Figure 3.18 displays over-all trends in filings with sequence listings under the Patent Cooperation Treaty and then displays trends for sequences containing an animal name in the title, abstract or claims for the New Breeds of Animals cluster and the Biotechnology cluster.

Figure 3.18: Trends for PCT Publications containing DNA Sequences



From this data we can see that trends in PCT filings with sequences has, with the exception of 2009, remained steady over the last ten years at +/-1200 filings per year. The line in red displays trends in WIPO filings with sequence data that contains a reference to a target animal (either Latin, common, or group name) in the title, abstract or claims of a Patent Cooperation Treaty filing. On balance this is approximately +/- 260 filings per year and is dominated by the biotechnology cluster rather than the new breeds of animals cluster.

However, recent research on patent activity relating to the human genome demonstrates that the interpretation of this data must be approached with considerable caution for the following reasons [84].

1. A reference to a DNA sequence in the patent claims does not automatically mean that the applicant is claiming the sequence. Thus, in the case of analysis of human genome related sequences research reveals that two thirds of the documents referenced the sequence in a claimed method, or made claims to the sequence in combination with other sequences, but did not claim the actual sequence itself [84].

2. Patent claims do not necessarily include references to the source organism. For example, in the case of human genome related activity, approximately 20% of the sequences were unspecified, unknown, and artificial or came from other organisms. That, is it will not always be clear where DNA sequence data is from in terms of its source or origin [84].

3. Patent claims are often constructed in terms of percentages of sequence activity (e.g. 70-90%) for a specific sequence. This means that other sequences falling within this percentage range would fall within the scope of the patent claims (if granted). This makes it difficult to determine with accuracy whether a sequence comes from a particular organism in the absence of 100% sequence identity.

4. Failure to distinguish between sequences that are referenced in a patent document and those that are claimed in a patent document will lead to an exaggeration of activity. For example, a widely cited study of patent activity for the human genome estimated that 20% of the human genome was covered by patents [85]. It is now clear that this figure exaggerated activity because it failed to distinguish between referenced sequences and claimed sequences [84]. However, it is presently very difficult to distinguish between the two types of sequence references. At the time of writing publicly accessible tools to facilitate this analysis such as the free PATSeq Explorer had only recently become available [84].

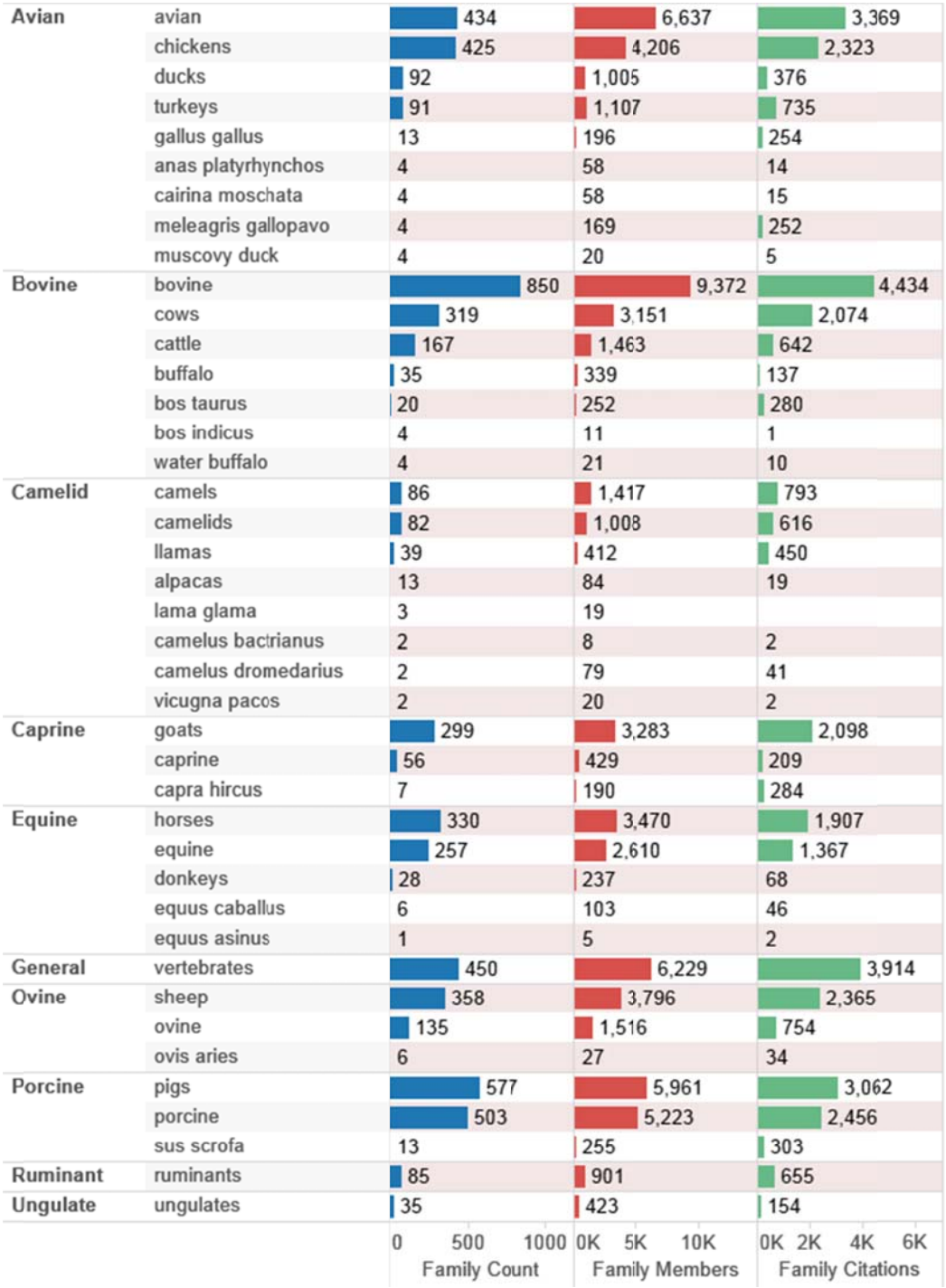
However, on the basis of the evidence provided above, and while emphasising the need for additional research, it is reasonable to argue that patent filings containing references to animals with DNA sequences under the PCT have been stable at <300 per year. In the context of the completion of a significant number of animal genome sequencing projects over the last 3-5 years, trends in this area merit careful attention in any future research as the availability of patent data for 2012-2014 improves.

As a starting point in considering this data it is worth noting that the reference to an animal in the title abstract or claims may not relate to a sequence from the animal itself. For example, one highly cited document (WO2002094989A2) with 858 citations claims a retroviral plasmid including a constitutive transport element from avian leukaemia virus with a defined sequence but the focus of the claims is actually the cell containing the retroviral vector plasmid. A second example for a

bioactive assembly (WO2007046893A2) with 398 citations includes a cytokine that may, among other possibilities, include bovine growth hormone. As such, there is a need for considerable caution in interpreting the data.

However, we do observe activity relevant to the target animals. For example, WO2005037989A2 from Trubion Pharmaceuticals focuses on novel binding domain-immunoglobulin fusion proteins from the llama CH2 and CH3 domains (IgG1 CH2 and IgG2 CH3) for use in immunotherapeutic applications. Interest in antibodies originating from llamas (and other camelids) reflects the fact that llama antibodies differ from other natural antibodies in that they lack light chains in their structure providing advantages over other antibodies because of their small size and efficiency. In other cases, an invention involving a claimed sequence may actually target delivery of a composition, such as an enzyme to a ruminant through consumption of a genetically modified plant (WO2002095003A2). In other cases applicants may make claims to sequences for fusion proteins that fuse with human, cattle, pig, chicken or fish albumins (WO2009058322A1). As these brief examples make clear, interpretation of patent data requires a very close reading and classification of patent texts. The data presented here should therefore be considered purely as a basis for further work in advancing understanding of patent activity for animal genetic resources. Figure 3.19 presents the scores for animal names appearing in the titles, abstracts or claims of WIPO documents containing sequence listings.

Figure 3.19: Species Appearing in Title, Abstract or Claims with Sequence Listings (PCT)



In practice we suspect, but cannot presently demonstrate, that patent documents containing sequences involving animal genetic resources are likely to be lower than the raw results presented above when issues such as reference sequences, viruses and other factors are taken into consideration. Any future work in this area could usefully focus on clarifying actual claims over sequences from animals and the extent to which these claims have given rise to high citation scores or litigation that would indicate problems for other users of sequences inside or outside the patent system. In particular, as we have previously noted, trends in patent activity involving animal sequences merit greater attention in light of the recent completion of livestock genome projects. Furthermore, account must also be taken of the increasingly restrictive environment for DNA patents in the United States and elsewhere and its impact on rates of patent grants.

Conclusion

This section has focused on presenting a quantitative indicator for patent trends involving animal genetic resources. We have focused on creating a structured approach to indicator development that can be expanded or contracted and refined to respond to policy needs based on the use of a thesaurus of key terms from the scientific literature and manual review of patent data.

However, while recognising the need for further refinement it is also important to recognise that the dominant direction of patent activity involving animal genetic resources in recent years has been downwards. This reflects a surge in activity around human activity and animal genetics in the period to 2001. This declining trend will not be removed by any conceivable alternative definition for international patent activity for animal genetic resources. However, what may change is that patent activity related to animal genomics will increase with the completion of genome sequencing projects and new areas of attention such as greenhouse gas reduction to address climate change may begin to become more prominent in the patent data. As such, there is a continuing need to monitor trends in activity for animal genetic resources while recognising that it is highly unlikely that activity will return to the peak observed in the early part of the century in the near future. We now turn to the analysis of key technologies for animal breeding for food and agriculture inside the patent landscape.

Section 4. Key Technologies in Animal Breeding

Section Summary

- We identified six main themes in the patent data for animal genetic resources:
    - Artificial Insemination, Sex Selection and Control of Estrus
    - Marker Assisted Breeding (including Quantitative Trait Loci)
    - Transgenic Animals
    - Cloning Animals
    - Xenotransplantation
    - Animal Models
- Patent documents that are highly cited by later patent applicants are a key indicator of important inventions involving animal genetic resources that have an impact in the patent system;
- Patent applications that are pursued in multiple countries creating large patent families are a key indicator of the importance of inventions to applicants;
- We provide 69 summary examples of important patent documents addressing the six themes to inform policy discussions.

Introduction

This section provides a review of important patent documents that focus on animal genetic resources for food and agriculture. Our purpose is to provide a broad range of examples of important filings that cover the spectrum of key technologies and in the process highlight technologies involving specific animal groups.

The identification of patent activity relating to a specific species or grouping is challenging because patent applicants frequently construct patent claims in broad terms to include multiple animals. Thus, a patent applicant may make reference to a mammal, a vertebrate, ruminants, ungulates, mice, bovines, porcine animals and others. Patent applicants use this broad approach because it addresses the possibility that a claimed invention could be applied in a range of animals. The main issue that is encountered here is identifying whether a target animal is the actual focus of the invention or a potential focus of the invention.

The identification of patent activity relating to animal breeding for food and agriculture requires a very close reading of patent documents to move past the ambiguities created by the framing of patent claims to identify activity directed to food and agriculture. To achieve this, following an initial review of the data and consultation with the specialist literature, we performed a series of sub-searches within the new breeds of animals cluster and biotechnology cluster for terms such as breed, breeding, agriculture, markers, cloning and so on. This was augmented by the key terms thesaurus from Web of Science publications related to animal breeding provided in Annex 2. Manual review of the documents permitted the identification of six major themes of relevance to food and agriculture within the patent data.

1. Artificial Insemination, Sex Selection and Control of Estrus
2. Marker Assisted Breeding (including Quantitative Trait Loci)
3. Transgenic Animals
4. Cloning Animals
5. Xenotransplantation
6. Animal Models

Within each of these major themes we identify sub-themes of particular relevance to food and agriculture such as superovulation, litter size, meat quality or milk production. Within each of the themes we also identify important patent documents within the patent landscape based on citation counts. These are typically older documents and we seek to balance this with examples of more recent patent filings to identify more recent developments. Descriptions of patent documents are based on the reading of the documents and use of the Derwent World Patent Index (DWPI) abstract fields in Thomson Innovation. Counts of

family members and citations are based on INPADOC family member scores and document citation counts in Thomson Innovation.

Artificial Insemination, Sex Selection, and Control of Estrus

Artificial Insemination is the most important, and best known, of biotechnologies applied in animals. It principally involves sire selection, testicular evaluation, sperm collection, storage, management and transfer to a receptive female animal. Technical developments in Artificial Insemination include the use of microscopes, flow cytometry and computer assisted semen evaluation [12]. Semen storage for shipping and, with the advent of frozen semen, post-freezing survival of sperm represented important technical developments for this technology [12]. Increasingly the technology has moved into sex selection of sperm prior to insemination and the use of freeze-drying [12]. However, developments in the detection of estrus (oestrus) prior to insemination and delivery techniques for insemination are also important.

In this section we provide a small selection of the most important patent documents in the new breeds of animals cluster that address these technical issues. While clearly focusing on the transmission of the genetics of an animal for breeding purposes we would note that these technologies do not always involve genetic research or manipulation as such. Table 4.1 presents a summary of these documents. Note that citations are counted by individual documents (citations) and the total score for citations within a complete family (family citations).

Table 4.1: Artificial Insemination, Sex Selection and Control of Estrus

	Number and Year	Title	Applicant	Family Members	Citations	Family Citations
1	US4474875A 1984	Method and means for controlling the sex of mammalian offspring and product therefor	Shrimpton Wallace	12	63	82
2	US5135759A 1992	Method to Preselect the Sex of Offspring	US Secretary of Agriculture	16	155	87
3	US6149867A 2000	Sheath fluids and collection systems for sex-specific cytometer sorting of sperm	University of Colorado State and XY Inc	136	89	105
4	US6140121A 2000	Methods and compositions to improve germ cell and embryo survival and function	Advanced Reproduction Technologies Inc	20	69	57
5	US20020119558A1 2002	Multiple sexed embryo production system for mammals using low numbers of spermatozoa	XY INC	136	34	105
6	US5542431A 1996	Heat Detection For Animals Including Cows.	DDX Inc	16	43	38
7	US7732408B2 2010	Reproductive management	Iversync II LLC	9	1	1
8	WO2007116410A2 2007	Livestock management for improved reproductive efficiency	Mileutis Ltd et. al.	14	0	2
9	US6372422B1 2002 (family member of US20020119558A1)	Multiple sexed embryo production system for animals	University of Colorado State and XY Inc	136	36	105

1 Sex Selection – Sorting Sperm. In 1984 Shrimpton Wallace was awarded US patent US4474875A for a *Method and means for controlling the sex of mammalian offspring*. The patent received 63 citations and is part of a patent family with 12 members. The patent describes a method of controlling the sex of a mammal by separating spermatozoa into fractions with the desired sex characteristics and artificially inseminating an animal. The key feature of the patent is separation of the spermatozoa by applying a buoyant force to a nutrient medium with the spermatozoa in a vertical separation column leading to separation by the differing density of the sperm. The patent claims "A composition of matter consisting essentially of deep frozen viable sperm genotypically having predominantly all X chromosomes in a nutrient medium." This appears to be a foundational patent for the separation and sorting of sperm to enable sex selection and is cited by later patent grants involving technical developments such as cryopreservation of sperm (i.e. EP1257168B1).

2 Sex selection - DNA Staining. US patent grant US5135759A was awarded in 1992 to the US Secretary of Agriculture for a *Method to Preselect the Sex of Offspring*. The document has attracted 155 citations and forms part of a family with 16 members. The patent claims a method of sorting intact, viable sperm into X and Y chromosome bearing populations based on the DNA content. This works by staining viable sperm with a fluorescent dye that is capable of selectively staining DNA by incubating the sperm at a temperature between 30-39° C. The sperm is passed through a sheath fluid to form a suspension that is then passed across a light source that causes the DNA to fluoresce. This allows the sperm to be sorted by sex.

The subsidiary claims in this patent reference rabbits, swine, and bovines as the focus for the invention (claims 2-4) and extend to a general claim for a method for the preselection of the sex of a mammalian offspring (claim 19). The citing patent landscape for this document is dominated by applications from XY LLC and XY INC for sex specific insemination of mammals with a low number of sperm cells (see below).

3 Sex-Selection by Sorting. US6149867A awarded in the year 2000 to the University of Colorado State and XY Inc focuses on *Sheath fluids and collection systems for sex-specific cytometer sorting of sperm*. The patent grant has received 89 citations in a wider family with 136 members. The patent focuses on sex-specific artificial insemination for breeding bovine or equine livestock and describes a method for producing a mammal with a pre-determined sex by collecting male sperm, determining its sex characteristics, sorting the sperm based on sex and then inseminating the female mammal.

The main advantage of the invention is that it involves a lower number of sperm cells than normal artificial insemination dosages. This has clear commercial applications. The patent claims entirely focus on a flow cytometer system for isolating the desired sperm cells rather than claiming the sperm cells themselves or research on the genetic level. However, this is an important patent family. WO1999033956A1 is related to the above and involves the same applicants with 64 citations and 27 family members for Sex Specific Insemination of Mammals with Low Number of Sperm Cells. In addition US6524860B1 granted in 2003 for the same or similar invention has received 51 citing patents within the same family. This is also linked with a System for improving yield of sexed embryos in mammals US6071689A granted in the year 2000 with 27 family members and 46 citations.

4 Isolating Sperm. An important document for isolating sperm in animals is by Advanced Reproduction Technologies Inc (US6140121A) for *Methods and compositions to improve germ cell and embryo survival and function* granted in

2000 with 69 citations and 20 family members. The patent focuses on enhancing fertilization in animals including humans, bovines, canine, porcine, avian and rodent species. The invention involves a method for the isolation of sperm through contact with a hexuronic acid monomer or acid solution and mixing the solution to separate and isolate the sperm. The relatively high number of citations may relate to the scope of the organisms to which the method can be applied.

5 Selection by Sperm Sorting. One of the highest-ranking families for the target animals in the patent landscape is US20020119558A1 with 136 family members and 34 citations from XY INC for *Multiple sexed embryo production system for mammals using low numbers of spermatozoa*. This application is directed to sex-specific artificial insemination that is useful for breeding bovine and equine livestock. The application claims:

> 1. An improved flow cytometer system for isolating desired cells comprising: a. a cell source which supplies cells to be analyzed by the flow cytometer, b. a sheath fluid source which creates a sheath fluid environment for said cells which contains about 2.9% sodium citrate; c. a nozzle through which said cells pass while subjected to said sheath fluid environment; d. an oscillator which acts upon said sheath fluid as it passes through said nozzle; e. a cell sensing system which responds to said cells; f. a sorter discrimination system which acts to sort cells having a desired characteristic; and g. a collector into which cells having a desired characteristic are placed.

The applicants make specific reference to bovine and equine sperm cells. However, the patent claims are oriented to methods for producing an animal with the desired sex rather than claims to specific genetic material *per se* (as such).

Control of Estrus:

Control of Estrus involves the identification and regulation of estrus in animals, with cows as a major focus in the patent data [86,87].

6 Control of Estrus. US5542431A granted in 1996 to DDX Inc focuses on *Heat Detection For Animals Including Cows*. The patent has been cited 43 times and forms part of a family with 16 members. The patent claims "1. An apparatus for use in making a determination related to the occurrence of estrus in a subject animal" that consists of sending heat mount data to dedicated software. As such this patent focuses on the use of apparatus and computer software to identify and control estrus.

7 Control of Estrus. A second patent grant from 2010, US7732408B2, to Iversync II LLC is concerned with *Reproductive management* in cattle. It claims: "a method for breeding dairy cattle that increases breeding efficiency with a

reduction in the number of months in the breeding cycle without the need for detecting standing estrus of a dairy cow prior to insemination". The method involves administering progesterone to the cow, followed by insemination nine days later and administering a second dose of progesterone nineteen days later. An ultrasound scan is then performed to determine if the animal is pregnant. The patent has been cited by 1 later filing and forms part of a family with 9 members.

8 Estrus Synchronization – Various Animals. WO2007116410A2 is a 2007 PCT application from Mileutis Ltd and the Israel Ministry of Agricultural and Rural Development for *Livestock management for improved reproductive efficiency*. The application forms part of a family with 14 members and has received zero citations. The application focuses on estrus induction in lactating livestock animals at set periods using a casein derived peptide with a claimed sequence from the sub-groups of αS1 -casein, αS2-casein, or β-casein. The peptide is administered to the herd as a whole with the aim of synchronizing estrus across the herd prior to insemination. The applicants claim: "1. A method for estrus induction in a lactating livestock animal comprising administering to the animal an effective amount of at least one peptide derived from casein." No patent grants are presently observed in this family.

Superovulation:

Superovulation involves a means of stimulating a female animal to produce a greater number of ova than would naturally be the case. The resulting ova are then fertilized (*in vivo* or, increasingly, *in vitro*) and transplanted into other females who become surrogate mothers.

9 Superovulation. Patent grant US6372422B1 from University of Colorado State and XY Inc dating to 2002 with 136 family members and 36 patent citations focuses on *Multiple sexed embryo production system for animals* and focuses on sex-specific artificial insemination as with the method described above. However, this family member claims:

> 1. A method of producing multiple, sexed embryos from a non-human female mammal comprising; a. creating superovulation in said female mammal to create at least two eggs comprising the step of using an ovulatory pharmaceutical to cause multiple eggs to be produced; b. determining a sex of a sperm cell of a male mammal; c. sorting according to said sex of said sperm cells; d. inserting at least a portion of said sorted sperm cells into a uterus of said female mammal after an onset of estrus; and e. fertilizing a plurality of said eggs to produce at least two sexed embryos of the desired sex from said female mammal.

The same patent applicants also hold a 2009 patent grant US7629113B2 for

Multiple Sexed Embryo Production System for Bovine Mammals.

Other relevant documents in this cluster include *Compositions comprising reproductive cell media and methods for using such combinations* by Minitube America (US6849394B2) with 19 citations and 10 family members which focuses on the collection, processing, sexing, culturing, storing (including cryopreservation) and in vitro fertilization of mammalian, avian or fish cells.

Marker Assisted Breeding

References to markers feature prominently throughout patent documents linked with animal breeding and in closely related areas in the biotechnology cluster. We focus here on marker related patent activity directly relevant to breeding for food and agriculture. Table 4.2 presents a summary of these documents.

Table 4.2: Marker Assisted Breeding

	Number and Year	Title	Applicant	Family Members	Citations	Family Citations
10	WO1992013102A1 1992	Polymorphic DNA Markers in Bovidae	Genmark	3	31	25
11	WO1995012607A1 1995	Single nucleotide polymorphisms and their use in genetic analysis	Molecular Tool Inc	83	50	578
12	WO1995021271A 1995	Ligase/polymerase-mediated genetic bit analysis of single nucleotide polymorphisms and its use in genetic analysis	Molecular Tool Inc	15	77	223
13	WO2004061616A2 2004	Computer systems and methods for associating genes with traits using cross species data	Rosetta Inpharmatics	5	12	22
14	US20100185047A1 2010	Methods and Compositions for Testing and Breeding Cattle for Improved Fertility and Embryonic Survival	Wisconsin Alumni Research Foundation	3	2	1

Table 4.2: Marker Assisted Breeding (Continued)

	Number and Year	Title	Applicant	Family Members	Citations	Family Citations
15	WO2003102199A1 2003	New GDF-9 and GDF-9B (BMP-15) Sequences for Altering Mammalian Ovarian Function and Ovulation Rate	Individual applicants linked with Agresearch Ltd, National University of Ireland at Galway and Ovita Ltd	9	9	7
16	US5292639A 1994	Association of bovine mitochondrial DNA with traits of economic importance	University of Iowa State Research Foundation	3	17	18
17	WO2002036824A1 2002	Marker Assisted Selection of Bovine for Improved Milk Production using Diacylglycerol Acyltransferase Gene DGAT1	Individual Inventors	16	22	28
18	WO1993004165A1 1993	Dna sequence encoding bovine alpha-lactalbumin and methods of use	Wisconsin Milk Marketing Board	18	16	35
19	US5351644A 1994	Method of Bovine Herd Management	Cornell Research Foundation	12	45	52
20	WO2005078133A2 2005	Marker Assisted Best Linear Unbiased Prediction (MA-BLUP): Software Adaptions For Practical Applications For Large Breeding Populations In Farm Animal Species	Monsanto Technology	7	7	7
21	EP1633889B1 2010	Gene expression profiles that identify genetically elite ungulate mammals	Univ Illinois Foundation	13	8	8
22	US20100162423A1 2010	Methods and Systems for Inferring Traits to Breed and Manage Non-Beef Livestock	Metamorphix Inc	8	3	13
23	EP1845159A1 2007	Method of Determining Gene Relating to Favourable Beef Taste and Texture	New Ind Res Organisation and Zh Shinsangyo Sozo Kenkyu Kiko	9	2	3

Table 4.2: Marker Assisted Breeding (Continued)

	Number and Year	Title	Applicant	Family Members	Citations	Family Citations
24	US20080183394A1 2008	Polymorphisms in mitochondrial transcription factor A ("TFAM") gene and their associations with carcass traits	B Woodward	1	1	1
25	WO2002020850A2 2008	Novel Prkag3 Alleles And Use Of The Same As Genetic Markers For Reproductive And Meat Quality Traits	University of Iowa State Research Foundation	20	27	8
26	WO2007129219A2 2007	Polymorphisms In Growth Hormone Receptor, Ghrelin, Leptin, Neuropeptide Y, And Uncoupling Protein 2 Genes And Their Associations With Measures Of Performance And Carcass Merit In Beef Cattle	University of Alberta	10	1	1
27	WO2000036143A2 2000	Selecting Animals for Parentally Imprinted Traits	University of Liege	32	19	10
28	WO2007070965A1 2007	Quantitative Trait Loci for Bovine Net Feed Intake	Adelaide Research and Innovation	1	1	0
29	WO1998030689A1 1998	Selection for dwarfism in poultry	Euribrid BV	4	3	2
30	US5374526A 1994	Method for determining genetic marker for increased pig litter size	University of Iowa State Research Foundation	19	12	22
31	WO2002020850A2 2002	Novel Prkag3 Alleles And Use Of The Same As Genetic Markers For Reproductive And Meat Quality Traits	University of Iowa State Research Foundation	20	27	8
32	WO1989011545A1 1989	Detection of the Susceptibility to Scrapie	Institute for Animal Health Limited	11	6	8

Mapping:

10 Genetic Markers – Mapping (Velogenetics). WO1992013102A1 is a 1992 PCT application from Genmark and focuses on *Polymorphic DNA Markers in Bovidae*. The document begins by discussing the existing use of biometric evaluation of individual breeding values as a basis for selection but argues that this largely takes place within a "black box" that does not permit identification of the underlying genes or Economic Trait Loci. The applicants then explain that they will use DNA Sequence Polymorphisms (Reverse Genetics) for the

identification of economic trait loci and introduce the concept of Velogenetics or the combined use of Marker Assisted Introgression and germ line manipulation of domestic species, specifically cattle. The patent application claims a set of nucleic acid fragments that hybridize polymorphic loci in bovids leading to the creation of a synteny map of microsatellite markers (Variable Number or Tandem Repeats – VNTRs). These in turn permit the claimed mapping of quantitative traits in bovids. Finally, the patent application claims a process for introducing a desired gene into a bovid. The primary focus of the application is thus upon quantitative trait mapping directed towards accelerated selection. This application forms part of a family with 3 members and has attracted 31 citations including a number of those listed in this section. As such it appears to be a key patent application in marker assisted breeding of cattle but also links to a *Genetic test for strabism in cattle* (EP1659184B1), *Calving characteristics* (WO2007090401A2) and a *Method for determining genetic traits of improved breed animal embryos prior to implantation* (WO0214544A1).

11 Traits – Horses and humans. WO1995012607A1 is a 1995 PCT application for *Single nucleotide polymorphisms and their use in genetic analysis* from Molecular Tool Inc. The application describes nucleic acid molecules and methods for identify SNPs in the genome of an animal, notably a human or a horse. The genotyping is useful for determining identity, ancestry or predisposition to genetic diseases or can be used to establish a linkage between two genetic traits. The patent claims reference the use of a "A nucleic acid molecule: (i) having a nucleotide sequence capable of specifically hybridizing to the invariant proximal or invariant distal nucleotide sequence of a single nucleotide polymorphism, and (ii) being used to specifically detect the single nucleotide polymorphic site (X) of the single nucleotide polymorphism." While referencing a range of animals including humans and cattle the patent claims focus on horses using specified DNA sequences. This patent family contains 83 members, including patent grants EP0726905B1 and US6537748B1. The individual document has been cited 50 times and the patent family has been cited 578 times.

12 Mapping Traits – Horses. WO1995021271A1 is a PCT application from 1995 for *Ligase/polymerase-mediated genetic bit analysis of single nucleotide polymorphisms and its use in genetic analysis* from Molecular Tool Inc. The patent application describes a method for the analysis of genetic identity, ancestry or genetic traits (e.g. brittle bones) through the creation of genetic maps of species notably horses, sheep or bovines among others and genotyping. The patent claims focus on methods for carrying out the invention. The description describes sequences generated from horses using PCR and a sequence listing is provided. However, specific sequences are not referenced in the claims. The patent

application forms part of a family with 15 members including patent grants EP0754240B1 and JP3175110B. The document has been cited 77 times and the family has received 223 citations.

13 Computer Systems – Cross Species. WO2004061616A2 from Rosetta Inpharmatics LLC is a PCT application published in 2004 focusing on *Computer systems and methods for associating genes with traits using cross species data*. The patent application focuses on a method for associating a gene in the genome of a species (gene G) with a clinical trait (T) from another species where T is a complex trait. The complex trait is a phenotype that does not exhibit Mendelian recessive or dominant inheritance arising from a single gene locus. The main focus of the invention relates to disorders such as asthma, bipolar disorder and others such as Alzheimer's disease. Claim 44 of the method focused claims reference chickens, horses, cows and pigs. The patent application forms part of a family with 5 members and has received 12 citations with a total of 22 citations for the patent family. No patent grants were observed in this family.

Ovulation:

14 Genetic Markers – Superovulation. US20100185047A1 is a 2010 patent publication from the Wisconsin Alumni Research Foundation which is best known for earlier work on primate embryonic stem cells [89]. In this case the patent application refers to *Methods and Compositions for Testing and Breeding Cattle for Improved Fertility and Embryonic Survival*. This involves genotyping a bovine cell (an adult, embryo, sperm, egg etc.) using defined sequences to selectively breed cattle using multiple ovulation (super ovulation) to collect eggs from suitable female animals, in vitro fertilization from a suitable male and embryo transfer into other female animals to produce the desired traits. Pregnancy is terminated if a pregnancy test does not reveal the uterine milk protein gene claimed in the invention. This is described by the applicants as the Multiple Ovulation and Embryo Transfer (MOET) procedure, a term first coined in the 1980s. The patent application claims:

> 1. A collection of at least two of isolated polynucleotide molecule species selected from the group consisting of (1) an isolated polynucleotide comprising at least 12 consecutive nucleotides surrounding position of 1296 of SEQ ID NO:1; (2) an isolated polynucleotide comprising at least 12 consecutive nucleotides surrounding position of 213 of SEQ ID NO:2; (3) an isolated polynucleotide comprising at least 12 consecutive nucleotides surrounding position of 8504 of SEQ ID NO:3; (4) an isolated polynucleotide comprising at least 12 consecutive nucleotides surrounding position of 154963 of SEQ ID NO:4; (5) an isolated polynucleotide comprising at least 12 consecutive nucleotides surrounding position of 577 of SEQ ID NO:5; (6) an isolated

polynucleotide comprising at least 12 consecutive nucleotides surrounding position of 23 of SEQ ID NO:6; (7) an isolated polynucleotide comprising at least 12 consecutive nucleotides surrounding position of 11646 of SEQ ID NO:6; and (8) an isolated polynucleotide comprising at least 12 consecutive nucleotides surrounding position of 12195 of SEQ ID NO:7

This patent application illustrates a common feature of embryo transfer approaches which is the use of non-maternal line female animals as surrogate hosts for in vitro fertilized eggs from the super ovulated maternal animal. The application forms part of a patent family with 3 members and has been cited in two later filings, including patent grant US8067171B2 to the Wisconsin Alumni Research Foundation for *Methods and compositions for improved fertilization and embryonic survival* focusing on a new bovine fibroblast growth factor for use in progeny testing and selective breeding in cattle.

15 Genetic Markers – Ovulation. WO2003102199A1 is a 2003 PCT application for *New GDF-9 and GDF-98 (BMP) Sequences for Altering Mammalian Ovarian Function and Ovulation Rate* submitted by a number of individual applicants/inventors linked with Agresearch Ltd, the National University of Ireland at Galway and Ovita Ltd in the patent family. The application focuses on the identification of a DNA mutation that is useful for identifying a mammal carrying a genetic marker encoding Growth Differentiation Factor 9B or 9 (GDF-9B or GDF-9). The marker can be used for marker assisted selection of an animal with a genotype associated with enhanced ovulation or sterility and is therefore useful for altering mammalian ovarian function or enhanced ovulation or inducing sterility. The patent claims 6 defined sequences, functional fragments or variants of the sequences along with the antisense sequences. The application cross-links to transgenic animals where the desired sequences have been introduced. The patent application forms part of a patent family with 9 documents including in Europe, South Africa, New Zealand, and Australia with a small number of grants, a refusal in Brazil and lapses in other jurisdictions (i.e. Australia). The application has attracted 9 citations including from Neocodex for a *Method for the In Vitro Detection of a Predisposition to the Development of Alterations in Ovarian Function* (e.g. EP1947195B1) and Ovita Ltd for the *Modulation of Ovulation* (WO2006059913A1).

Milk:

The modification of animal milk is a significant focus of patent activity. Here we focus purely on patent documents that illustrate selection using genetic markers for milk with respect to quantity and its particular natural properties.

16 Genetic Markers – Milk. US5292639A from the University of Iowa State Research Foundation was granted in 1994 and focused on the *Association of bovine mitochondrial DNA with traits of economic importance*. The patent is concerned with "A method of evaluating the material mitochondrial phenotypic contribution to economic traits of milk production and reproduction efficiency of a dairy cow comprising: assaying for the presence of one or more genetic markers in the mitochondrial D-loop of said cow." In particular the patent focuses on the identification of a group of mutations at D-Loop positions on the mitochondrial genome forming polymorphisms associated with increased milk production, decreased milk production or increased or decreased fat content. The patent concludes with a claim focusing on "A method of evaluating inheritable milk production and reproduction efficiency traits in dairy cattle by partitioning effects of mitochondrial lineages from nuclear effects." This patent forms part of a family with 3 members and has been cited 17 times by other applicants including the Pig Improvement Company for a *System for tracing animal products* (US7229764B2), Micro Beef Technologies for *Livestock management system and methods* (US20080059534A1) and Purdue Research Foundation for *Incorporation of Competitive Effects in Breeding Program to Increase Performance Levels and Improve Animal Well Being* (WO2002076190A2).

17 Genetic Markers – Milk. WO2002036824A1 from a range of individual inventors addresses *Marker Assisted Selection of Bovine for Improved Milk Production using Diacylglycerol Acyltransferase Gene DGAT1* and has a family of 16 members with 22 citing documents. The patent application claims a method for identifying a bovine possessing a genotype indicative of altered milk production traits by obtaining a sample from the animal and identifying a polymorphism selected from 13 sequences linked to the bovine DGAT1 gene. However, the patent application also claims a bovine selected using the method, semen produced using the method and milk produced by the bovine. The applicants then go on to claim milk with specified properties, such as increased protein and decreased fat content, produced by the bovine. Later patent filings that cite this patent application include the University of Wageningen for a *Method for selection of non-human mammal producing milk with improved fatty acid composition* based on the presence of a specific allele (EP2121976A2). Vialactia Biosciences from New Zealand has also filed an application for *Genotyping bovines for SCARB1 polymorphisms* that focuses on determining the genetic merit of a bovine with respect to milk or tissue colour or Beta carotene content

(GB2453254A).

18 Quantitative Trait Loci – Milk. PCT application WO1993004165A1 from the Wisconsin Milk Marketing Board published in 1993 addresses a *DNA sequence encoding bovine alpha-lactalbumin and methods of use*. The applicants claim: "1. A mammary specific DNA sequence encoding bovine a-lactalbumin and promoting quantitative differences in gene expression among mammals, wherein the DNA sequence is characterized by variations in the gene structure in the control region of bovine a-lactalbumin." The claims include short defined sequences for the control region of bovine a-lactalbumin. The patent family consists of 18 members including patent grants EP0555435B1, JP03698369B2, US5530177A and US5850000A. The document has been cited by 16 later filings and the patent family has been cited 35 times.

19 Method of Herd Management – Mathematical Modelling. US5351644A awarded to Cornell Research Foundation in 1994 is concerned with a *Method of Bovine Herd Management* and consists of twelve family members with 45 citations. The patent claims:

"1. A method of bovine herd management comprising the steps of: a) gathering test-day data on milk production for each member of a herd on a routine basis; b) using a mathematical herd management model to modify the test-day data to determine the actual productivity of each cow in the herd; c) establishing a database for each member of said herd, based upon the modified data of step (b); d) continuously updating said database; and e) making physical changes to said herd based upon information in said database, in order to increase milk productivity of said herd."

Essentially the invention provides a method for selecting cattle based on the monitoring of the quantity and quality of milk production. It allows for the monitoring of variables—such as changes in feed compositions and environmental conditions—to understand how they affect milk production. Using this data less viable individuals can be identified and removed from the herd whilst breeding can focus on the most productive cattle. Using databases from many herds across large geographical areas, genetic evaluation can be undertaken that may assist in breeding programmes to select primary A-1 bulls capable of siring daughters in many herds, raising productivity across regional and national populations of cattle. In contrast with other examples in this section, this patent document does not refer to specific markers but uses the general term genetic evaluation in a broad sense. Additional patent grants in this family include EP637200B1 and US5351644B1.

Meat Quality & Muscle:

20 Genetic Markers – Quantitative Trait Loci (QTL). WO2005078133A2 for *Marker Assisted Best Linear Unbiased Predicted (MA-BLUP): Software Adaptions For Practical Applications For Large Breeding Populations In Farm Animal Species* from Monsanto Technology is a PCT application from 2005 forming part of a family with 7 members that has received 7 citations. The application is important because it indicates a trend towards integrating genetic marker information with software to assist with breeding. The claimed invention consists of methods, systems and kits for increasing an animal populations average genetic merit by identifying molecular genetic markers providing Quantitative Trait Loci (QTL), evaluating the merit of the animal population for a defined set of traits, identifying optimal breeding pairs to improve the selected traits in the population and enhancing meat quality traits in pigs along with screening animals to identify those with improved meat quality traits. This application does not exhibit a clear patent grant but was pursued in Brazil (BR200507533A) and Argentina (AR48404A1). One feature of the application is that it appears to recognize the need for a balance between maximizing desirable traits within a population without "jeopardizing the potential for long-term genetic improvement (i.e. through excessive inbreeding under selection pressure on a limited number of genes or trait loci)." This application is also significant for later citing filings from Pfizer on *Methods of Improving a Genomic Marker Index of Dairy Animals and Products* (EP2178363A2) from 2010 and a 2011 application from Metamorphix Inc and Cargill Inc (US8026064B2) for *Compositions, Methods and Systems for Inferring Bovine Breed*.

21 Genetic Markers – Quantitative Trait Loci in Ungulates. European patent grant EP1633889B1 published in 2010 addresses *Gene expression profiles that identify genetically elite ungulate mammals* and was awarded to the University of Illinois Foundation. The patent describes methods for identifying and selecting genetically elite animals, specifically ungulates, with a desired phenotype for breeding targeting a quantitative trait such as high milk production, carcass quality and resistance to disease. The method involves constructing a Gene Expression Index where the genes are selected from GenBank accession numbers provided in the description. The method then involves correlating gene expression values of male and female cattle with a Reference Expression Profile that provides an optimal subset of the Gene Expression Index consisting of 1-100 genes. This index includes GenBank accession numbers AW461980, AW464526, AW465165, AW465571, AW466043, BF039168, BF044446, BF044893, BF046007, BF046202, BF440243, BF440261, AW466044, and BF039212, preferably AW466043, BF044446, BF039168, BF046202, and AW461980. The applicants claim: "1. A method of constructing a Gene Expression Index for

phenomic selection of a phenotype of an ungulate mammal, the method comprising: (a) selecting ungulate mammals with specific levels of the phenotype; (b) selecting a plurality of genes for which expression can be determined; (c) comparing expression levels of the plurality of genes in ungulate mammals at each level of the phenotype; and (d) determining a set of genes predictive of a specific phenotype level to create the Gene Expression Index. At the time of writing the patent family consisted of 13 members and had been cited 8 times with 8 citations recorded in the patent family. Patent grants in the family include AU2004251256B2 and US7638275B2.

22 Genetic Markers – Meat Quality. US20100162423A1 is a 2010 patent application from Metamorphix Inc for *Methods and Systems for Inferring Traits to Breed and Manage Non-Beef Livestock*. The method involves taking a DNA sample from the non-beef animal and identifying at least 2 Single Nucleotide Polymorphisms (SNPs) where the SNPs comprise a haplotype associated with a trait. This example is of interest because it specifically refers to alpacas, buffalo, cows, goats, llamas, horses, sheep and ducks within the list of target organisms in this landscape report. However, the specific focus of the invention appears to be pigs where the traits that are important include: a) age at puberty, b) number of pigs farrowed alive, c) birth weight of live piglets, d) weaning and weight performance, e) meat quality, and f) feed efficiency among others. The applicant goes on to describe similar targets in avians, notably chickens.

The patent claims are entirely constructed in terms of non-beef livestock indicating that the applicant was seeking to construct the patent claims very broadly. However, this example is interesting because it reveals the workings of the patent system. Thus, of a total of no less than 271 claims, claims 1-251 were later cancelled leaving only claims relating to nucleic acid samples from avian subjects in relation to egg production, feed efficiency, chick survival, meat yield etc. No patent grant was identified in the legal status data for this patent family consisting of 8 members. The patent application has attracted 3 citations, including from a grant to Cargill Incorporated for *Compositions, Methods, and Systems for Inferring Bovine Breed* (US8669056B2) that provides sequences and SNPs for identifying breed or breed combinations for Angus, Holstein, Limousin, Brahman, Hereford, Simmental, Gelbvieh, Charolais and Beefmaster breeds.

23 Genetic Markers – Meat Quality. A small number of patent documents in the new breeds of animals cluster make reference to improving meat quality. For example EP1845159A1 forms part of a patent family with 9 members and 2 citations for a *Method of Determining Gene Relating to Favourable Beef Taste and Texture* from the New Ind Res Organisation and Zh Shinsangyo Sozo Kenkyu Kiko. This patent document claims: “a method for evaluating the amount of the unsaturated fatty acid content in beef fat, on the basis of a genotype of sterol

regulatory element binding protein (SREBP-1) to evaluate whether or not it is a cattle, from which better quality of beef with better taste and texture can be produced." In practice this involves testing the polymorphism on the fifth intron of the SREBP-1 for a short intron of the S-type indicating good quality meat and the L-type allele indicating lower quality based on DNA samples from the cow amplified using specific primers with claimed sequences where the polymorphism is identified using a DNA chip. The method is also claimed to be useful for breeding and herd improvement directed to improving the taste of meat from cattle.

24 Genetic Markers – Meat Quality. US20080183394A1 is a patent application published in 2008 from a B Woodward that addresses *Polymorphisms in mitochondrial transcription factor A ("TFAM") gene and their associations with carcass traits*. This involves a method of identifying an animal and sub-groupings with desired genotypes where the animals have a similar polymorphism in the TFAM gene. The method involves determining the presence or absence of a Single Nucleotide Polymorphism (SNP) involving an A to C substitution at the -1220 nucleotide position of the TFAM gene, and a T to C substitution at position -1212 or T-C substitution at position -995 in a bovine.

The identification of the SNP is accompanied by a computer system for tracking the rearing of bovines linking diagnostic data with the breeding and health history of the cow, including vaccination, herd history and so on. The applicant believes that this combination of SNP data and computer based business method should give rise to predictable meat quality traits along with animal welfare, food safety and audit information. In connection with meat quality the document goes into detail on feed data, gross carcass weight, intramuscular fat and marbling and the rib eye area. In short, the document describes an SNP based system directed towards selecting for, and achieving, predictable meat quality in cattle. This example points to the increasing convergence of genetic information with software and business methods. The patent application is the sole member of its family and has attracted 1 citation.

25 Genetic Markers – Meat Quality. WO2002020850A2 from the University of Iowa State Research Foundation Inc entitled *Novel Prkag3 Alleles And Use Of The Same As Genetic Markers For Reproductive And Meat Quality Traits* is noted below in connection with pig litter size. This application for genetic markers, notably PRKAG3 alleles, is relevant both to increasing litter size and to the quality of meat by screening animals to select for the marker. The patent application forms part of a family with 20 members and has received 27 citations.

26 Genetic Markers – Beef Cattle. WO2007129219A2 from the University of Alberta is concerned with *Polymorphisms In Growth Hormone Receptor, Ghrelin,*

Leptin, Neuropeptide Y, And Uncoupling Protein 2 Genes And Their Associations With Measures Of Performance And Carcass Merit In Beef Cattle. This application claims a method for sub-grouping animals by genotype "…wherein the animals of each sub-group have a similar genotype in a GHR, ghrelin, leptin, NPY or UCP2 gene comprising: (a) determining the genotype of each animal to be subgrouped by determining the presence of a single nucleotide polymorphism(s) of interest in the GHR, ghrelin, leptin, NPY or UCP2 gene, (b) segregating individual animals into sub-groups depending on whether the animals have, or do not have, the single nucleotide polymorphism(s) of interest in the GHR, ghrelin, leptin, NPY or UCP2 gene." The purpose of the invention is to identify an animal with a desirable phenotype relating to feed intake, growth rate, body weight, carcass merit and the composition of milk yield. The application forms part of a family with 10 members and has been cited by one later filing.

27 Genetic Markers – Muscle Fat. WO2000036143A2 from the University of Liege and co-applicants is concerned with *Selecting Animals for Parentally Imprinted Traits*. The applicants focus on testing a nucleic acid sample from a pig for the presence of a parentally imprinted QTL located on chromosome 2 that is part of the insulin-like growth factor-2 (IGF2) gene which is then further specified. The sequence or its fragment is claimed to be useful for breeding animals with a desired genotype or phenotypic properties relating to muscle mass or fat deposition. The applicants also claim a transgenic animal and the sperm or embryo. The applicants do not specify the transgenic component. The document forms part of a family with 32 members and has been cited 19 times by later applicants. These include a *Method of Managing and Marketing Livestock Based on Genetic Profiles* from Genomicfx Inc (WO0202822A2) and *Sequencing the Mitochondrial DNA with reference to the fertility as a means for the optimization of sow breeding lines* (EP2027771B1).

Feed Intake:

28 Genetic Markers – Feed. WO2007070965A1 is of interest because it focuses on the identification of *Quantitative Trait Loci for Bovine Net Feed Intake*. This 2007 PCT application from Adelaide Research and Innovation focuses on the identification of a genomic nucleotide sequence associated with a particular level of feed intake or net feed intake in a bovine where the Quantitative Trait Locus is on bovine autosome 1. Bovines with this QTL are identified as useful for breeding purposes. The patent document is the only member of its family and has received 1 citation.

Dwarfism:

29 Genetic Markers – Dwarfism. WO1998030689A1 from Euribrid BV illustrates the use of markers in avians. The 1998 PCT patent application focuses

on *Selection for Dwarfism in Poultry*. The patent document describes nucleic acids useful to produce probes for detecting alleles of a gene responsible for autosomal dwarfism in chickens. The probes permit the identification of alleles of the Hmgi-c gene using a kit that can then be used to select and breed or cross-breed birds with the allele for use as broiler birds. The application forms part of a patent family with 4 members and has been cited by 3 later filings.

Litter Size in Pigs:

30 Genetic Markers – Litter Size. US5374526A from the University of Iowa State granted in 1994 provides a *Method for determining genetic marker for increased pig litter size*. This provides a method for screening sows to determine the allele of a polymorphism associated with the ability of a sow to produce above average litter size. This is achieved by running tests on the DNA of the sows to identify polymorphisms in the oestrogen receptor gene that can then be correlated with litter size to determine whether the polymorphism is associated with above average litter size. This patent forms part of a family with 19 members and has received 12 citations from later patent filings.

31 Genetic Markers – Litter Size. Patent application WO2002020850A2 from the University of Iowa State Research Foundation focuses on the use of Novel PRKAG3 alleles for use as genetic markers to screen for animals most likely to produce larger litters and with improved meat quality traits (see above). This application is significant because it forms part of a family with 20 members and has received 27 citations from later patent filings.

Disease susceptibility:

32 Susceptibility to Scrapie – DNA Analysis. WO1989011545A1 is an application by The Institute for Animal Health Limited from the UK dating from 1989 for *Detection of the Susceptibility to Scrapie*. The first claim states:

"1. A method of determining whether an ovine, caprine or bovine animal is susceptible to scrapie, the method comprising analysing material from that animal for a polymorphism linked to scrapie susceptibility."

Scrapie is an infectious disease of the central nervous system of sheep, goats and cattle. It is thought to be identical to the cattle disease more commonly known as bovine spongiform encephalopathy (BSE). In this invention a method is given for identifying animals with a genetic predisposition to susceptibility to the disease. DNA, extracted from an animal, is digested using enzymes and DNA fragments thus produced are analysed for three polymorphisms linked to scrapie susceptibility. The document forms part of a family with 11 members and has been cited 6 times.

Transgenic Animals

A transgenic animal is an animal that has received foreign or exogenous DNA from another organism of the same species or another species. As such, in simple terms, the animal is a product of genetic engineering where the animal has received DNA that would not naturally occur within its genome except through human intervention. Techniques for the creation of transgenic animals include, DNA microinjection, Vector based transfer (i.e. through the use of a virus as a host for the foreign DNA) and stem cell derived embryonic transfer.

The selection of transgenic animal related patent documents presented in this section address many of the themes identified above. However, it is important to recognise that transgenic animals rapidly cross-over into the domain of health such as the expression of proteins or antibodies in milk and also link to cloning (see below). In particular, because patent applicants frequently construct patent claims in broad terms it can be difficult to identify a specific animal in the field of food and agriculture. This is indicated by the first example for transgenic animals. Table 4.3 presents a summary of these documents.

Table 4.3: Transgenic Animals

	Number and Year	Title	Applicant	Family Members	Citations	Family Citations
33	WO1982004443A1 1982	Genetic Transformation in Zygotes	University of Ohio	5	23	578
34	WO2002085306A2 2002	Use of follistatin to increase muscle mass	John Hopkins University	76	35	107
35	US20020174449A1 2002	Method for generating cloned animals using chromosome shuffling	Individual inventors/applicants linked to Advanced Cell Technology Inc	4	18	16
36	WO2000075300A2 2000	Methods for Manipulating the Avian Genome	Tranxenogen Inc	7	15	13
37	WO2003022040A2 2003	Method for producing transgenic animals	California Institute of Technology	62	13	83
38	US5162215A 1992	Method Of Gene Transfer Into Chickens And Other Avian Species	Amgen and Arbor Acres Farm Inc	6	93	91

Table 4.3: Transgenic Animals (Continued)

	Number and Year	Title	Applicant	Family Members	Citations	Family Citations
39	US5639940A 1997	Production of fibrinogen in transgenic animals	Pharm Proteins Ltd and Zymogenetics Inc.	40	81	70
40	WO1993010227A1 1993	Transgenic animals lacking prion proteins	Individual applicants/inventors linked to Prionics AG Schlieren	10	55	53
41	US20020150577A1 2002	Use Of Antibodies Specific For Growth Differentiation Factor-11	John Hopkins University School of Medicine	37	28	99
42	US20050097627A1 2005	Transgenic ungulates having reduced prion protein activity and uses thereof.	Kirin Holdings and Kirin Brewery	99	8	44
43	US5827690A 1998	Transgenic Production of Antibodies in Milk	Genzyme Corp	23	167	219
44	WO2003060099A2 2003	Methods and apparatus for spinning spider silk protein	Nexia Biotech Inc.	10	26	43

33 Transgenic – Zygotes. One of the single most important patent documents in the new breeds of animals cluster based on citations is from the University of Ohio in 1982 for *Genetic Transformation in Zygotes* (WO1982004443A1). A zygote is the cell created from the union of male and female gamete cells at the earliest stage in the formation of an embryo. The document forms part of a family with 5 members and has received 23 direct citations (see also US6872868B1, US4873191A and EP0081570A1). However, the wider patent family has received an impressive 578 citations. This patent application is unusual because it refers to both animals and plants and can perhaps be regarded as a foundational patent in genetic engineering and transgenic animals. The applicants describe the utility of the invention as follows:

> The invention is particularly useful in the breeding of plants and animals, especially ones of agricultural value, to obtain species having a genetic makeup which results in a plant or animal having more desirable characteristics. Since the source of the exogenous genetic material can be from animals or plants, synthetic equivalents of naturally occurring genetic material or totally new synthetically produced genetic material and from the same or a different species of the zygote being transformed, the invention can be used to modify a species or create a new species. Modification of a species is obtained when the

genotype of the exogenous genetic material occurs in the genotype of the species whose zygote is being genetically transformed. A new species is obtained when the genotype of the exogenous genetic material occurs in another species and does not naturally occur in the species of the zygote being genetically transformed. For example, increased growth rate and the efficiency of feed utilization can be obtained by genetic transformation of animals used to produce meat. As an example, the genes relating to growth rate and feed utilization can be transferred from a buffalo into beef cattle which would create a new species. Dairy animals can undergo an increase in milk production and efficiency of feed utilization by transferring exogenous genetic material from species or breeds of the same species which have either or both traits. The quality and flavor of meat, for example, lamb, can also be enhanced in a similar manner. Additionally, the invention can be used as an in vivo analysis of gene expression during differentiation and in the elimination or dimunition of genetic diseases, e.g., hemophilia, Tay-Sachs disease, phenylketonuria, homocystinurea, galactosemia, thalassemia and sickle cell anemia.

The application describes a method of genetic transformation of a zygote and embryo and mature organisms resulting from the insertion of exogenous genetic material into the cell nucleus of the zygote that ultimately becomes part of the nucleus with a preference for adding the genetic material to the male pronucleus of the zygote. The resulting zygote will include the genotype of the exogenous material that will be phenotypically expressed. The applicants claim that the invention can be utilized in animal and plant breeding to create new species and for undertaking the treatment of diseases. The patent application claims:

1. A method of obtaining a mammal characterized as having a plurality of cells containing exogenous genetic material, said material including at least one gene and a control sequence operably associated therewith, which, under predetermined conditions, express said gene under the control of said control sequence in a cell of said mammal, which comprises: (a) introducing exogenous genetic material into a pronucleus of a mammalian zygote by microinjection, said zygote being capable of development into a mammal, said genetic material including at least one gene and a control sequence operably associated therewith, thereby obtaining a genetically transformed zygote; (b) transplanting an embryo derived from the genetically transformed zygote into a pseudopregnant female capable of bearing the embryo to term; and (c) allowing the embryo to develop to term; where said gene and control sequence are selected so that the gene is not activated in such manner and degree as would prevent normal development of the embryo to term.

34 Transgenic – Muscle Mass. WO2002085306A2 is a PCT application published in 2002 for the *Use of follistatin to increase muscle mass* from John Hopkins University. The application forms part of a family with 76 members and has been cited 35 times. The invention is described as being useful for tissue-specific expression of follistatin in a transgenic animal. This is achieved using an expression cassette integrated into the genome of the animal that elevates levels of follistatin resulting in increased muscle mass in the transgenic animal compared with a non-transgenic animal. The invention also focuses on in vitro maturation of an ovum and in vitro fertilization to form a zygote into which the DNA expression cassette can be introduced. The zygote is then matured for transplantation into a recipient female who then produces the transgenic animal. The applicants claim: "1. A transgenic non human animal whose genome contains a nucleic acid sequence comprising a truncated Activin Type II receptor gene and a muscle-specific promoter operably linked and integrated into the genome of the animal, wherein the nucleic acid sequence is expressed so as to result in elevated levels of truncated Activin Type II receptor and increased muscle mass in the animal as compared to a corresponding nontransgenic animal."

35 Transgenic – Chromosome Shuffling for Transgenic Animals and Clones. US20020174449A1 focuses on a *Method for generating cloned animals using chromosome shuffling* from individual applicants/inventors linked to Advanced Cell Technology Inc.. The patent application describes a method for producing cloned and transgenic animals that is also useful for correcting chromosomal abnormalities or altering autosomal genotypes. The applicants claim that the method can be used in agriculture, xenotransplantation, laboratory science and species conservation. The applicants claim:

> 1. A method of altering the sex of a cloned animal, embryo, blastocyst, fetus or cell comprising: (1) isolating a somatic or embryonic cell from an animal, embryo, blastocyst, fetus or other source of mammalian cells to be cloned; (2) removing or programming for removal at least one sex chromosome from said somatic or embryonic cell; (3) inserting at least one alternative sex chromosome from a non-isogenic animal; and (4) using nuclear transfer to create an autosomally isogenic, sexually non-isogenic animal, embryo, blastocyst, fetus or cell.

The patent application forms part of a family with 4 members but has been cited by 18 later filings by a set of filings and grants from Searete LLC for *Systems for genome selection* (e.g. US8521440B2).

36 Transgenic – Avian Genome. WO2000075300A2 is a PCT application for *Methods for Manipulating the Avian Genome* from Tranxenogen Inc. that has been cited 15 times and forms part of a patent family with 7 members. The application describes a method for transfecting avian blastodermal cells to produce transgenic avians with the desired genes. The method can be applied in both the laboratory and in agriculture to produce pharmaceuticals or for use in xenotransplantation. The applicants claim: "A method of introducing a nucleic acid molecule into the genome of an avian species, comprising contacting in vivo a blastodermal cell of a fertilized egg with said nucleic acid molecule, wherein said nucleic acid molecule is not associated with a viral coat protein and wherein said nucleic acid molecule is introduced directly into the germinal disc of said egg in a volume of greater than I microliter and less than 0.5 millilitres." Chickens and turkeys are mentioned in the application.

37 Transgenic – Non-Specific. WO2003022040A2 is a PCT application from the California Institute of Technology that describes a *Method for producing transgenic animals*. The application forms part of a family with 62 members and has received 13 citations. The document describes a method for producing transgenic animals using retroviral constructs that have been engineered to carry the transgene. The applicants claim: "1. A method of producing a transgenic animal comprising: transfecting a packaging cell line with a retroviral construct; recovering recombinant retrovirus from the packaging cell line; 5 and infecting an embryonic cell with the recombinant retrovirus, wherein the retroviral construct comprises the R and US sequences from a 5' lentiviral long terminal repeat (LTR) and a self-inactivating lentiviral 3' LTR."

38 Transgenic – Chickens. US5162215A is a patent grant from 1992 from Amgen and Arbor Acres Farm Inc. for a *Method Of Gene Transfer Into Chickens And Other Avian Species* in a patent family with 6 members that has received 93 citations. The patent claims: "A method for transferring a nucleic acid sequence of a replication-defective REV-derived vector into germ cells of a chicken in the absence of an exogenous replication-competent helper retrovirus comprising introducing the nucleic acid sequence into pluripotent stem cells of an embryo of a chicken at a stage in development wherein the stem cells are capable of being infected by the vector and providing the vector in an amount effective to transfer the nucleic acid sequence into the stem cells."

39 Transgenic – Bovine and others. US5639940A is a 1997 patent grant awarded to Pharm Proteins Ltd and Zymogenetics Inc. for *Production of fibrinogen in transgenic animals*. The patent forms part of a family with 40 members and has been cited 81 times. The main focus of the invention is the production of fibrinogen in transgenic animals through the creation of surgical adhesives or coatings, including for synthetic vascular grafts, that can be used in

human and veterinary medicine. The patent claims: “1. A method for producing biocompetent fibrinogen comprising: providing a first DNA segment encoding a secretion signal operably linked to a heterologous fibrinogen Aα chain, a second DNA segment encoding a secretion signal operably linked to a heterologous fibrinogen Bβ chain, and a third DNA segment encoding a secretion signal operably linked to a heterologous fibrinogen γ chain, wherein each chain is from the same species, and wherein each of said first, second and third segments is operably linked to additional DNA segments required for its expression in the mammary gland of a host female mammal; introducing said DNA segments into a fertilized egg of a non-human mammalian species heterologous to the species of origin of said fibrinogen chains; inserting said egg into an oviduct or uterus of a female of said mammalian species to obtain offspring carrying said DNA segments; breeding said offspring to produce female progeny that express said first, second and third DNA segments and produce milk containing biocompetent fibrinogen encoded by said segments; collecting milk from said female progeny; and recovering the biocompetent fibrinogen from the milk.”

40 Transgenic – Birds. WO1993010227A1 is a 1993 patent application from individual applicants/inventors linked to Prionics AG Schlieren for *Transgenic animals lacking prion proteins* that forms part of a patent family with 10 members, including patent grants EP0613495B1 and US5698763A, and has received 55 citations. The patent application targets the creation of animals or birds that are resistant to spongiform encephalopathy and the therapeutic administration of antisense oligonucleotides to control the disease. The applicants claim: “1. A transgenic mammal or bird having no functional prion protein.”

41 Transgenic Animals – Growth Differentiation Factor. US20020150577A1 is a 2002 patent application from John Hopkins University School of Medicine for the *Use Of Antibodies Specific For Growth Differentiation Factor-11*. The document forms part of a family with 37 members and has been cited 28 times. The applicants describe the creation of transgenic animals that are useful as food products due to high muscle and protein content but with reduced fat and cholesterol content. However the applicants also argue that the GDF-All agents, such as antibodies, can be used to treat a range of muscle or tissue disorders including AIDs. The applicants claim: “1. A transgenic non-human animal having a transgene disrupting or interfering with expression of growth differentiation factor-11 (GDF-11) chromosomally integrated into the germ cells of the animal.”

42 Transgenic Animals – Bovine Spongiform Encephalopathy. An important patent family is represented by US20050097627A1 with 99 family members and 8 citing documents from Kirin Holdings and Kirin Brewery for *Transgenic ungulates having reduced prion protein activity and uses thereof*. This provides for a cloned transgenic ungulate (bovine) where prion protein activity has been

reduced through genetically engineered mutations. In addition "Desirably, these transgenic bovines are also genetically modified to express xenogenous (e.g., human) antibodies. Because of their resistance to prion-related diseases such as bovine spongiform encephalopy (also known as mad cow disease), these bovines are a safer source of human antibodies for pharmaceutical uses and a safer source of agricultural products."

The patent application references bovine cells, fetal fibroblast, and bovine spongiform encephalopy and claims: "1. A bovine comprising a non-naturally occurring mutation in one or both alleles of an endogenous prion nucleic acid." In addition the applicant claims a method of producing the transgenic bovine where the fetus develops into a viable offspring. This patent application is important as one of a wider cluster of applications that sought to respond to the emergence of Bovine Spongiform Encephalopy (BSE or mad cow disease) in the early part of this century.

43 Transgenic Animals – Goats Milk. US5827690A from 1998 from Genzyme Corp focuses on *Transgenic Production of Antibodies in Milk*. The patent claims "A high level expression method for providing a heterologous and assembled immunoglobulin, in the milk of a transgenic mammal." The immunoglobulin to which the applicant refers is of human origin and is expressed in the milk of animals such as mice, sheep and pigs with specific claims focusing on obtaining the milk from a transgenic goat where the protein coding sequence for the immunoglobulin has been inserted into its germline such that the goat expresses the protein in the mammary gland epithelial cells. This patent document forms part of a family with 23 members but is important because it has been cited 162 times.

44 Transgenic Animals – Spider Silk in Goats Milk. WO2003060099A2 is a 2003 PCT application from Nexia Biotechnologies for *Methods and apparatus for spinning spider silk protein*. The patent application focuses on the production of recombinant spider silk fiber for a wide range of uses in goats milk. The applicants claim: "1. A method for producing a spider silk fiber, said method comprising extruding a dope solution comprising a recombinant spider silk protein, through a spinneret 5 to form said spider silk fiber." The applicants focus on claiming a recombinant dragline silk protein that is MaSpl, MaSpll or ADF-3.5 and in particular a MaSpl protein with a defined amino acid sequence. The applicants go on to specify the following claims for the expression of the silk protein:

> 10. The method of claim 1, wherein said recombinant spider silk protein is recovered from mammalian or bacterial cell culture media, the milk of a transgenic mammal engineered to express said spider silk protein in its milk, the

urine of a transgenic mammal, or an extract or exudate from a transgenic plant.

11. The method of claim 10, wherein said transgenic mammal engineered to express said spider silk protein in its milk is a goat.

As such we can see that claim ten provides a general overarching claim for the expression of the material in a range of cultures or organisms, while claim 11 focuses on the actual target animal. The patent application forms part of a family with 10 members, including patent grant US7057023B2, and has attracted 26 citations from later applicants.

Cloning

The cloning of animals is generally understood as the creation of a genetically identical copy of an animal. This has aroused considerable public and policy debate. Table 4.4 presents a summary of these documents.

Table 4.4: Cloning

	Number and Year	Title	Applicant	Family Members	Citations	Family Citations
45	WO1996007732A1 1996	Totipotent Cells for Nuclear Transfer	Roslin Institute Edinburgh	3	53	48
46	WO1997007669A1 1997	Quiescent cell populations for nuclear transfer	Roslin Institute, the Biotechnology and Biological Research Council (BBSRC) and Ministry of Agriculture, Fisheries and Food	63	199	184
47	WO1997007668A1 1997	Unactivated Oocytes as Cytoplast Recipients for Nuclear Transfer	Roslin Institute, Edinburgh	70	186	153
48	US5453366A 1995	Method of cloning bovine embryos	Two Individuals	7	29	55
49	WO1999005266A2 1999	Trans-Species Nuclear Transfer	Wisconsin Alumni Research Foundation	4	17	14
50	US20130117870A1 2013	Genetically Modified Animals and Methods for Making the Same	Individual applicants/inventors linked to the University of Edinburgh and Recombinetics Inc.	13	0	0
51	WO2012140677A2 2012	Isolation, Cloning, Sequencing And Functional Analysis Of β-Casein Promoter Along With The Regions Of Exon1, Intron1 And Exon2 Using Mammary Gland Derived Cell Line Of Buffalo (Bubalus Bubalis).	National Institute of Immunology in India	5	0	0

Table 4.4: Cloning (Continued)

	Number and Year	Title	Applicant	Family Members	Citations	Family Citations
52	WO2012071762A1 2012	Method For Preparing Transgenic Pigs Resisting Porcine Reproductive And Respiratory Syndrome	Beijing Jifulin Biotechnology Company	3	0	0
53	WO2005049788A2 2005	Reprogramming of Somatic Cell Nuclei	University of Massachusetts	2	5	3
54	WO2001018236A1 2001	Methods of Repairing Tandemly Repeated Dna Sequences and Extending Cell Life-Span Using Nuclear Transfer	Advanced Cell Technology Inc.	16	17	17
55	WO1999034669A1 1999	Cloning Using Donor Nuclei From Differentiated Fetal And Adult Cells	University of Massachusetts	117	11	224

The best known example of animal cloning arises from the creation of "Dolly the Sheep" by the Roslin Institute in 1996 using a process known as nuclear cell transfer involving the transfer of an adult or somatic cell nucleus into an empty oocyte (egg) to produce an embryo for implantation. While nuclear cell transfer predates the work of the Roslin Institute it is appropriate to begin with the influential patent documents associated with their work.

Prior to the announcement of the successful creation of a cloned sheep the Roslin Institute had submitted a set of three patent applications. The international versions of these applications are:

1. WO1996007732A1 - Totipotent Cells for Nuclear Transfer (first filed 05/09/1994). 3 family members, 53 citations.

2. WO1997007669A1 - Quiescent Cell Populations for Nuclear Transfer (first filed 31/08/1995). 63 family members, 199 citations.

3. WO1997007668A1 - Unactivated Oocytes as Cytoplast Recipients for Nuclear Transfer (first filed 31/08/1995). 70 family members, 186 citations.

We will now briefly summarise each of these applications before turning to more recent developments.

45 Cloning – Nuclear Transfer. WO1996007732A1 for *Totipotent Cells for Nuclear Transfer* claims: "1. An animal cell line derived from an embryonic disc of an ungulate blastodermic vesicle, or the equivalent tissue of an embryo at an equivalent stage in nonungulate species, cells of which cell line are totipotent for nuclear transfer." The document claims that the method may be used to clone animals of high genetic merit and to generate transgenic animals by mass

transformation techniques across a wider range of species than with embryonic stem cell technology and without relying on pronuclear microinjection. The method can be applied to all animals including birds but is of greatest relevance to placental animals. The method has the additional advantage of being able to limit births to a single sex for use in the dairy industry."

46 Cloning – Nuclear Transfer: WO1997007669A1 is entitled *Quiescent cell populations for nuclear transfer* from the Roslin Institute, the Biotechnology and Biological Research Council (BBSRC) and Ministry of Agriculture, Fisheries and Food in the UK. The patent application claims: "1. A method of reconstituting an animal embryo, the method comprising transferring the nucleus of a quiescent donor into a suitable recipient cell." The patent document makes reference to a range of target organisms including buffalo, camelids, ovine, porcine and bovine species and in the claims specifically refers to the use of the method on an ungulate (claim 2) and then narrows the claims in claim 3 to a "cow or bull, pig, goat, sheep, camel or water buffalo." The applicants then go on to claim:

> 18. An animal prepared by a method as claimed in any one of claims 1 to 13.
>
> 19. An animal developed from a reconstituted animal embryo as claimed in any one of claims 14 to 17.

The patent document describes a method in which the nucleus of the donor cells is genetically modified prior to embryo reconstitution where the recipient cell is an oocyte that is enucleated with an adult somatic or embryonic somatic cell leading to the development of the embryo to term. Following this the patent document claims that the animal may be bred on, or more than one animal may be derived from the embryo. Patent grants in this family include EP0849990B1 and GB2331751B among others. However, what appears to be an equivalent application in the United States US 09/225,233 contained the following claims:

> 155. A live-born clone of a pre-existing, non- embryonic, donor mammal, wherein the mammal is selected from cattle, sheep, pigs, and goats.
>
> 164. The clone of any of claims 155-159, wherein the donor mammal is non-foetal.

This application was rejected by the USPTO and went through a lengthy process of appeals culminating, at the time of writing, in a decision from the US Court of Appeals for the Federal Circuit *In RE: Roslin Institute (Edinburgh)* on the 8th of May 2014 that "Roslin's clones are unpatentable subject matter under §101" [59]. That is the invention is unpatentable under US patent law (USC 35 Article 101) in relation to patentable subject matter because it is a natural phenomenon that "did not possess 'markedly different characteristics than any found in nature'" [59].

This decision illustrates the changing landscape of patentability for genetic resources.

This foundational PCT family member has been cited 199 times for transgenic and cloned mammals. Examples of citing documents include BTG therapeutics (e.g. AU2003204830A1) for *Transgenic and cloned mammals*, and *Nuclear transfer with differentiated fetal and adult donor cells* (EP1808484A1) from the University of Massachusetts.

47 Cloning – Nuclear Transfer. WO1997007668A1 for *Unactivated Oocytes as Cytoplast Recipients for Nuclear Transfer* provides a method for cloning animals and for generating transgenic or genetically modified animals. The patent document claims:

> 1. A method of reconstituting an animal embryo, the process comprising transferring a diploid nucleus into an oocyte which is arrested in the metaphase of the second meiotic division without concomitantly activating the oocyte, keeping the nucleus exposed to the cytoplasm of the recipient for a period of time sufficient for the embryo to become capable of giving rise to a live birth and subsequently activating the reconstituted embryo while maintaining correct ploidy.

US patent grant US7361804B1 is one of several US patent grants in this patent family and is provided here to show how patent family members may vary from the original international filings. This patent specifically targets ungulates and claims:

> 1. A method of cloning a cow by nuclear transfer comprising: (i) inserting a nucleus of a cultured diploid bovine fibroblast in the G1 phase of the cell cycle into an Unactivated, enucleated metaphase II-arrested bovine oocyte to reconstruct an embryo; (ii) maintaining the reconstructed embryo without activation for a sufficient time to allow the reconstructed embryo to become capable of developing to term; (iii) activating the resultant reconstructed embryo; (iv) culturing said activated, reconstructed embryo to blastocyst; and (v) transferring said cultured, reconstructed embryo to a host cow such that the reconstructed embryo develops to term.

48 Cloning – Cattle. US5453366A granted in 1995 to two US individual inventors predates the Roslin Institute work on animal cloning and focuses on a *Method of cloning bovine embryos*. The patent formed part of a family with 7 members and received 29 citations. This patent claims:

> 1. A method for producing cloned bovine embryos comprising the following steps: a. removing the chromosomal material from a metaphase II stage bovine

> oocyte to form an enucleated recipient oocyte; b. maintaining the enucleated recipient oocyte in CR-1+1 mM L-glutamine maintenance medium wherein the maintenance period is approximately 6 to 18 hours; c. placing a membrane bound nucleus from a donor 2-64 cell bovine embryo adjacent to the plasma membrane of the enucleated recipient oocyte and; d. inducing cell fusion between the membranes of the donor membrane-bound nucleus and the enucleated recipient oocyte to form an embryonic single cell with a nucleus from the donor, wherein the membranes are either electrically fused or fused with polyethylene glycol.

49 Cloning – Trans-Species Nuclear Transfer. WO1999005266A2 from the Wisconsin Alumni Research Foundation focuses on *Trans-Species Nuclear Transfer*. The application forms part of a family with 4 members. The patent application from 1999 describes a method of producing cloned nuclear transfer embryos from differentiated donor cells. The claimed invention is used to produce genetically identical clones of adult animals with economically valuable traits such as enhanced milk production or pharmaceutical proteins that can be harvested from animal milk or blood. In addition the invention could be used to propagate endangered species in cases where it would be impossible to obtain enough gametes to optimise cloning procedures.

This patent document has been cited 17 times by applicants including the University of Massachusetts for *Embryonic stem cell lines* (e.g. AU1999029795A1). Importantly, this patent document also attracts a citation from the controversial research by Hwang Woo-Suk on a *Method for producing cloned cows* (AU753207B2) and other research including a *Method for producing cloned tigers by employing inter-species nuclear transplantation technique* (AU753209B2). As such, the application links through to wider efforts to apply cloning to re-introducing extinct, or near extinct, animals that has enjoyed a recent surge of interest as "de-extinction" [89,90]. The conservation merits of such proposals are a subject of significant debate.

50 Cloning – Creating Founder Animals. US20130117870A1 from individual applicants/inventors linked to the University of Edinburgh and Recombinetics Inc. is a 2013 application focusing on *Genetically Modified Animals and Methods for Making the Same*. The document focuses on compositions and methods for creating a genetic modification by exposing a primary cell in an in vitro culture or an embryo to a nucleic acid encoding a Transcription activator-like (TAL) effectors and nuclease (TALEN). The invention specifically focuses on livestock and references artiodactyls (any even-toed ungulate), swine, bovine, fish, rabbit and livestock in the claims. The abstract to the invention informs us that:

> Some of the embodiments of the invention provide for making an founder

> animal that is completely free of all unplanned genetic modifications. Some embodiments are directed to removing genetic faults in established breeds without making other alterations to the genome. Other embodiments are directed to particular tools or processes such as a TALENs with a preferred truncation.

This claimed invention therefore appears to be distinctive, according to the applicants, because it provides for a method for making transgenic animals that only have changes at intended sites of the genome in founder generation animals and this offers apparent advantages in levels of precision. The patent application forms part of a family with 13 members but has received zero citations to date.

51 Cloning – Buffalo. WO2012140677A2 from the National Institute of Immunology in India focuses on *Isolation, Cloning, Sequencing And Functional Analysis Of β-Casein Promoter Along With The Regions Of Exon1, Intron1 And Exon2 Using Mammary Gland Derived Cell Line Of Buffalo (Bubalus Bubalis)*. The claimed invention is useful for isolating and cloning the promoter sequence of buCSN2 to generate transgenic buffaloes expressing therapeutic proteins in milk, expressing genes to provide resistance to microbes, and generating transgenic mammals to produce large quantities of milk. The patent application forms part of a family with 5 members and zero citations.

52 Cloning – Transgenic Pigs. WO2012071762A1 is a patent application from the Beijing Jifulin Biotechnology Company in China for a *Method For Preparing Transgenic Pigs Resisting Porcine Reproductive And Respiratory Syndrome*. As such this example illustrates the use of genetic engineering to promote resistance to particular conditions affecting livestock. The patent application describes: "A method for preparing transgenic pigs resisting porcine reproductive and respiratory syndrome (PRRS)" by "preparing transgenic cells containing DNAs encoding shRNAs which target ORF1b, ORF5, ORF6 or ORF7 of porcine reproductive and respiratory syndrome virus (PRRSV); using the transgenic cells and isolated oocytes as donor cells and recipient cells respectively, obtaining cloned embryos by nuclear transplantation surgery; grafting the cloned embryos into uteri of domestic animals to initiate pregnancy by non-surgery method, and obtaining transgenic pigs." The patent application forms part of a family with 3 members and zero patent grants and citations.

53 Cloning – Reprogramming Somatic Nuclei. WO2005049788A2 from the University of Massachusetts is entitled *Reprogramming of Somatic Cell Nuclei* and "provides methods for cloning mammals that allow the donor chromosomes to be reprogrammed prior to insertion into an enucleated oocyte. The invention also features methods of inserting chromosomes or nuclei into recipient cells." This is achieved by purifying condensed chromatin from a claimed extract before

insertion into the enucleated oocyte. The method is useful for cloning mammals useful as a source of material for medical applications, such as the treatment or prevention of disease in humans and as a source of cartilage, bone marrow, or any other tissue or organ used in agricultural or medical applications. The applicants claim that the invention can be practised in a wide range of animals including cows, sheep, rabbit, pig, mouse, rat, goat, cat, dog, or buffalo. The patent application is part of a family with 2 members and has been cited by 5 later filings.

54 Cloning – Re-cloning. WO2001018236A1 is a 2001 patent application from Advanced Cell Technology Inc. entitled *Methods of Repairing Tandemly Repeated DNA Sequences and Extending Cell Life-Span Using Nuclear Transfer*. In contrast with other documents relating to cloning it focuses on re-cloning. Specifically the applicants explain that the "invention relates to methods for rejuvenating normal somatic cells and for making normal somatic cells of a different type having the same genotype as a normal somatic cell of interest. These cells have particular application in cell and tissue transplantation. Also encompassed are methods of re-cloning cloned animals, particularly methods where the offspring of cloned mammals are designed to be genetically altered in comparison to their cloned parent, e.g., that are "hyper-young". These animals should be healthier and possess desirable properties relative to their cloned parent. Also included are methods for activating endogenous telomerase, EPC-1 activity, and or the ALT pathway and/or extending the life-span of a normal somatic cell, and other genes associated with cell aging of proliferation capacity." In particular, the re-cloning methods could be useful for making transgenic animals that express more than one heterologous gene or with more than one gene knocked out. The patent document forms part of a family with 16 members.

This patent document has received 17 citations primarily from Searete LLC and Invention Fund I LLC for a group of applications and grants entitled *Systems for genome selection* (e.g. US7947455B2). This patent claims: "1. A method comprising: decondensing one or more male germ line haploid genomes; determining one or more genetic characteristics of the one or more male germ line haploid genomes; and selecting one or more of the one or more male germ line haploid genomes based at least partially on the one or more genetic characteristics of the one or more male germ line haploid genomes."

55 Cloning – Fetal Adult Cells. WO1999034669A1 is a 1999 PCT application from the University of Massachusetts entitled *Cloning Using Donor Nuclei From Differentiated Fetal And Adult Cells* and forms part of a patent family with 117 members and has attracted 11 citations. The invention focuses on cells for use in cell transplantation therapy in humans or other animals with a particular focus on Parkinson's, Alzheimer's or Huntington's diseases and a range of other disorders.

The transgenic animals of the invention are used to produce proteins in milk (such as collagen) and are sources of organs for xenotransplantation. The method can also be used to clone animals with higher value agricultural traits for meat or milk production or with greater disease resistance etc. The applicants claim: “A method of cloning a cow, comprising: (i) inserting a desired differentiated cow cell or cell nucleus into an enucleated cow oocyte, under conditions suitable for the formation of a nuclear transfer (NT) unit to yield a fused NT unit; (ii) activating said fused nuclear transfer unit to yield an activated NT unit; and (iii) transferring said activated NT unit to a host mammal such that the activated NT unit develops into a fetus.”

Xenotransplantation

Xenotransplantation involves grafting or transplanting tissues or organs between species [98]. Typically xenotransplantation means transplantation from animals to humans to meet health needs. However, it need not be confined to animals to humans. The main focus of activity is meeting human needs for donor organs in light of a shortage of organ donors [99]. The main issues involved in xenotransplantation include the risks of organ rejection and transmission of viruses across species boundaries [93-95]. Xenotransplantation has also raised ethical issues relating to the treatment of animals and societal responses to those who receive such transplants. In this section we focus on the most important patent documents in the new breeds of animals cluster that focus specifically on breeding animals for Xenotransplantation. Typically, inventions focus on pigs [96,97]. However, it is important to note that other animals also appear in patent data. Table 4.5 presents a summary of these documents.

Table 4.5: Xenotransplantation

	Number and Year	Title	Applicant	Family Members	Citations	Family Citations
56	US6166288A 2000	Method Of Producing Transgenic Animals For Xenotransplantation Expressing Both An Enzyme Masking Or Reducing The Level Of The Gal Epitope And A Complement Inhibitor	Nextran Inc.	13	51	64
57	WO1995020661A1 1995	Materials And Methods For Management Of Hyperacute Rejection In Human Xenotransplantation	St. Vincent's Hospital and Bresatec Ltd	22	36	148
58	WO1999019469A1 1999	Porcine Stem Cells Comprising A Marker Under An Oct-4 Promoter	Biotransplant Inc.	3	29	22
59	WO2001030992A2 2001	α1-3 Galactosyltransferase Gene And Promoter	University of Pittsburgh	6	21	6
60	WO2001073107A1 2001	Prion-Free Transgenic Ungulates	University of Massachusetts	15	17	12
61	WO2000075300A2 2000	Methods For Manipulating The Avian Genome	Tranxenogen	8	17	13

Table 4.5: Xenotransplantation (Continued)

	Number and Year	Title	Applicant	Family Members	Citations	Family Citations
62	US20050260176A1 2005	Tissue Products Derived From Animals Lacking Any Expression Of Functional Alpha 1,3 Galactosyltransferase	Revivicor Inc.	41	13	20
63	WO2009069986A2 2009	Genetically-Modified Cell Line For Producing Cloned Miniature Pigs For Xenotransplantation And Method For Preparing The Same	Korea Research Institute of Bioscience and Biotechnology	4	0	0

56 Xenotransplantation – Pigs. US6166288A is a patent grant from 2000 to Nextran Inc. for a *Method Of Producing Transgenic Animals For Xenotransplantation Expressing Both An Enzyme Masking Or Reducing The Level Of The Gal Epitope And A Complement Inhibitor*. The patent forms part of a family with 13 members and has been cited 51 times. The patent describes the creation of transgenic animals that have tissue and organs with a reduced risk of rejection by humans. The applicants claim:

> 1. A method of preparing organs, tissues, or cells for xenotransplantation into human patients with reduced rejection comprising the steps of: (a) providing a transgenic pig which is a source of transplant material which is anatomically and physiologically compatible with a human patient, said material selected from the group consisting of organs, tissues, or cells, said pig expressing (i) at least one transgenically encoded enzyme, functional in said pig, and in particular in said organs, tissues, or cells, that masks or reduces the level of a zenoreactive antigen of said transplant material, said at least one enzyme being a fucosyltransferase, and (ii) at least one transgenically encoded complement inhibitor functional in humans; and (b) isolating said transplant material from said transgenic pig, said material having been modified by said enzyme, wherein said modification results in a masking or a reduction in the level of a zenoreactive antigen thereof, said material further being associated with said complement inhibitor.

57 Xenotransplantation – Pigs. WO1995020661A1 is a 1995 PCT patent application from St. Vincent's Hospital and Bresatec Ltd that forms part of a family with 22 members and has been cited 36 times. The patent application is entitled *Materials And Methods For Management Of Hyperacute Rejection In Human Xenotransplantation*. The patent application describes polypeptides and xeno-Abs that help to reduce or eliminate epitopes in donor organs that are

recognized by humans. The patent application claims: “1. A purified and isolated nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of (1) the porcine nucleic acid sequence depicted in Figure 4 (SEQ ID NO: 7), (2) a sequence corresponding to the sequence of (1) within the scope of the degeneracy of the genetic code, (3) a sequence that encodes a porcine polypeptide having a-1,3 galactosyltransferase activity and that hybridizes under standard high stringency conditions with a sequence complementary to the sequence of (1) or (2), and (4) a sequence complementary to the sequence of (1), (2) or (3).”

58 Xenotransplantation – Pigs. WO1999019469A1 is a 1999 PCT application from Biotransplant Inc. with 3 family members and has been cited 29 times. The patent application is entitled: *Porcine Stem Cells Comprising A Marker Under An Oct-4 Promoter*. The patent application describes methods to isolate and enrich or selectively propagate porcine pluripotent stem cells. These cells can be altered so that they do not express a cell surface membrane protein that will be rejected following xenotransplantation. Transgenic pigs are the source of the cells and organs for transplantation. The applicants claim: “1. A method of isolating or selectively propagating porcine stem cells, wherein said method comprises introducing into a source of cells containing porcine stem cells a genetic selectable marker construct which is operatively linked to a porcine promoter polynucleotide sequence which provides differential expression of the selectable marker in stem cells and cells other than the desired stem cells, and which under appropriate culture conditions enables the selective isolation and/or propagation of the desired stem cells.”

59 Xenotransplantation – Livestock. WO2001030992A2 is a 2001 PCT application from the University of Pittsburgh forms part of a patent family with 6 members and has been cited 21 times. The patent application is entitled: *α1-3 Galactosyltransferase Gene And Promoter*. The patent document describes DNA expression cassettes that can be used to express genes or disrupt the native alpha 1-3 galactosyltransferase genomic sequence in an animal. The applicants discuss transgenic mice and then transgenic livestock that can express the growth hormone. The patent document also relates to the implantation of the tissue and a transgenic organ. The applicants claim: “A recombinant expression cassette comprising an cc 1-3 gal actosyltransferase promoter operably linked to a polynucleotide for expression, other than a polynucleotide encoding cc 1-3 galactosyltransferase.”

60 Xenotransplantation – Ungulates/BSE. WO2001073107A1 is a 2001 PCT application from the University of Massachusetts for *Prion-Free Transgenic Ungulates* forming part of a family with 15 members and has attracted 17 citations. The invention focuses on agents that may be used to screen for

spongiform encepalopathies using a therapeutic agent and monitoring of the ungulate to determine whether the encephalopathy has been prevented or treated. The applicants also claim that fetal cells or tissues can be used for xenotransplantation. The applicants claim: "A transgenic ungulate bearing a homozygous deletion or disruption of the prion gene, wherein said deletion or disruption prevents expression of a functional endogenous prion protein, and wherein lack of expression of a functional endogenous prion protein renders said bovine unsusceptible to prion-related diseases."

61 Xenotransplantation – Avians. WO2000075300A2 is a PCT application from 2000 by Tranxenogen with 8 family members that has received 17 citations for *Methods For Manipulating The Avian Genome*. This application describes a method for transfecting avian blastodermal cells to produce the avians with the desired genes. It is claimed that the invention can be used for studying human diseases or for improving agricultural livestock, the production of pharmaceuticals in milk and xenotransplantation. The applicants claim: "1. A method of introducing a nucleic acid molecule into the genome of an avian species, comprising contacting in vivo a blastodermal cell of a fertilized egg with said nucleic acid molecule, wherein said nucleic acid molecule is not associated with a viral coat protein and wherein said nucleic acid molecule is introduced directly into the germinal disc of said egg in a volume of greater than I microliter and less than 0.5 millilitres."

62 Xenotransplantation – Pigs/Ungulates. US20050260176A1 is a 2005 patent application from Revivicor Inc. for *Tissue Products Derived From Animals Lacking Any Expression Of Functional Alpha 1,3 Galactosyltransferase*. The application forms part of a family with 41 members and has attracted 13 citations. The tissues claimed in the invention can be used as a scaffold for the repair or reconstruction of a human body part, including knee repair and heart valve repair. The applicants claim: "A prosthesis comprising a tissue product derived from an animal lacking any expression of alpha-1,3-galactosyltransferase."

63 Xenotransplantation – Cloned Miniature Pigs. WO2009069986A2 is a 2009 PCT application from the Korea Research Institute of Bioscience and Biotechnology that focuses on a *Genetically-Modified Cell Line For Producing Cloned Miniature Pigs For Xenotransplantation And Method For Preparing The Same*. The document forms part of a family with 4 members and has received zero citations. The applicants describe a gene targeting vector for use in xenotransplantation and for the creation of safer donor animals. The applicants claim a: "gene targeting vector capable of deleting endogenous xenoantigenic determinant synthetic gene and targeting a gene encoding complement regulation protein or thrombosis suppressor protein, the gene targeting vector comprises sequentially (1) region 1 containing 2-4 kb long nucleic acid sequence

corresponding to the xenoantigenic determinant synthetic gene; (2) a positive selection marker gene; (3) an internal ribosome entry site (referred as 'IRES' hereinafter); (4) a gene encoding complement regulation protein or thrombosis suppressor protein; and (5) region 2 containing 6-8 kb long nucleic acid sequence corresponding to the xenoantigenic determinant synthetic gene."

Animal Models

Animals are frequently used as experimental models for medical purposes [98]. Patent applicants commonly make reference to multiple animals in claims relating to animals. However, the target model animals are normally mice or rats but expand to pigs and other organisms [99-102]. The selection below provides examples of important patent documents and also provide an indication of the spectrum of activity in this area. Table 4.6 presents a summary of these documents.

Table 4.6: Animals Models

	Number and Year	Title	Applicant	Family Members	Citations	Family Citations
64	US4736866A 1998	Transgenic Non-Human Mammals	Harvard University	11	635	646
65	US20050019260A1 2005	Animal Model for Allergy	Allergenix PTY Ltd	9	7	7
66	WO1992020790A1 1992	Transgenic non-human animal carrying a non-infectious HIV genome	Inst Rech Cliniques Montreal	8	5	11
67	US20020035736A1 2002	HER2-transgenic non-human tumor model	Genentech	123	13	231
68	US20090304595A1 2010	Animal Model and a Method for Producing an Animal Model	University of Aarhus	14	1	4
69	WO1999060108A2 1999	Transgenic Animals Produced By Homologous Sequence Targeting	Stanford Research Institute International	40	21	409

64 Animal Models – Harvard Oncomouse. The most important and best known patent involving an animal model is from Harvard University for *Transgenic Non-Human Mammals* (US4736866A) granted in 1988. This patent forms part of a family with 11 members and has attracted 635 citations. The patent claims: "A transgenic non-human mammal all of whose germ cells and somatic cells contain a recombinant activated oncogene sequence introduced into said mammal, or an ancestor of said mammal, at an embryonic stage." As such it is concerned with creating an organisms to test for carcinogens.

65 Animal Models – Allergy. One example with direct references to target organisms in the patent landscape is an *Animal Model for Allergy*

(US20050019260A1) from Allergenix PTY Ltd. which has attracted 7 citations and forms part of a family with 9 members. This document focuses on the study of asthma through chronic allergen exposure where the preferred animal is a ruminant, sheep, goat, bovine or non-human primate. The patent claims (claims 1-32 were cancelled):

> 33. An in vivo model system for an allergic condition, comprising a mammal which has been subjected to sensitisation with an antigen or administration of a cytokine involved in response to allergen, in which a) the mammal is a female, and is sensitised by repeated administration of the antigen into the mammary gland; or b) the mammal is of either sex, and is sensitised by administration of the antigen, followed by administration directly to the lung; or c) the mammal is of either sex, and blood and tissue eosinophilia is induced by administration of a cytokine involved in response to allergen, in which the mammal is a member of the order Artiodactyla, and the antigen is not one derived from a helminth parasite.

66 Animal Models – Non-Infectious Genome. WO1992020790A1 from the Inst Rech Cliniques Montreal from 1992 for a *Transgenic non-human animal carrying a non-infectious genome* that has been cited 5 times and forms part of a family of 8 documents. This patent application claims:

> 1. A non-human transgenic mammal in which the germ cells and somatic cells carry a transgene capable of expressing non-infectious HIV RNA (having the entire encoding sequence of the HIV genome) and complementary proteins in the cells, the transgene being introduced into the mammal, or an ancestor thereof, at an embryonic stage.

67 Animal Models – Tumour Models. US20020035736A1 from Genentech is a 2002 application for a *HER2-transgenic non-human tumor model* with a particular focus on breast cancer. The application is significant because it forms part of a family with 123 members and has attracted 13 citations. Patent grants in the family include US6632979B2, AU784157B2 and EP1189641B1. The transgenic animals may include, mice, rabbits, rats, pigs, sheep, goats or cattle that are used to test HER2 directed cancer therapies and identification of anticancer agents. The transgenic animals in this case may be used as the source of cells that can be immortalized in culture. The applicants claim:

> 1. A transgenic non-human mammal that produces in its mammary gland cells detectable levels of a native human HER2 protein or a fragment thereof, wherein said transgenic mammal has stably integrated into its genome a nucleic acid sequence encoding a native human HER2 protein or a fragment thereof having the biological activity of native human HER2, operably linked to transcriptional regulatory sequences directing its expression to the mammary

gland, and develops a mammary tumor not responding or poorly responding to anti-HER2 antibody treatment.

68 Animal Models – Alzheimers Disease. US20090304595A1 is a 2010 patent application from The University of Aarhus for an *Animal Model and a Method for Producing an Animal Model* that forms part of a patent family with 14 members including patent grant US8173861B2 and 1 citation. The application focuses on an animal model for hereditary autosomal diseases created through a genetic determinant or sperm-mediated gene transfer that allows for evaluation of responses to therapeutic treatments. In particular, the application focuses on Alzheimers and Parkinsons disease using pig models from a range of breeds including mini-pigs from Goettingen, Yucatan, Bama Xiang Zhu, Wuzhishan and/or Xi Shuang Banna. Claims 1-57 in the original application were cancelled leaving claim 58 as the main claim for "58. A pig model for a hereditary autosomal dominant disease, wherein the pig model expresses at least one phenotype associated with said hereditary autosomal disease obtained by a genetic determinant."

69 Animal Models – Homologous Sequence Targeting. WO1999060108A2 is a 1999 PCT application from SRI International (Stanford Research Inst Int) for *Transgenic Animals Produced By Homologous Sequence Targeting*. The application forms part of a patent family with 40 members and has attracted 21 citations. Patent grants in the family include AU772879B2, EP0672159B1, US5763240A and US6074853A. The application focuses on non-human mammals with a modified endogenous gene to produce transgenic animals including cattle, sheep, pigs, horses, goats mice and rats that are useful as models for human and veterinary diseases. The applicants claim: "1. A non-human mammal comprising a modified endogenous gene, wherein said endogenous gene is selected from the group consisting of a gene or sequence encoding an ion-channel, a G protein coupled receptor (GPCR), an immunoglobulin, a growth factor, an enzyme, or a milk protein."

5. Animal Breeds in Patent Data

Section Summary

- The available evidence for patent activity involving animal breed names and traditional knowledge was reviewed by text mining patent applications using a list of 7,616 breed names from the FAO Global Databank for Animal Genetic Resources;
- We identified 1,136 breed names in patent documents from the European Patent Office, the United States Patent and Trademark Office and at the World Intellectual Property Organization (WIPO). Many breed names are common names, such as country names, with a range of uses;
- We manually reviewed 5,454 documents containing breed names from the New Breeds of Animals (transgenic animals) and Biotechnology clusters;
- The review examined cases where a country name coincided with a breed name with the data provided in an Annex to the report;
- The dominant species in the data were pigs, cattle and sheep. Breed names were limited to a small number of dominant breeds per species. For example, data on cattle is dominated by Holsteins while pigs are dominated by Large Whites and Landrace;
- Where applicants list large numbers of breeds from multiple countries these are normally examples of breeds where the invention could potentially be applied such as the use of DNA markers for improved meat or milk production;
- Considerable care is required in interpreting patent documents to identify the actual source of genetic material. Typically, the genetic material used in an invention is taken from a well known breed rather than a rarer breed;
- We did not find evidence of patent activity that could be considered to constitute potential biopiracy in the form of misappropriation of genetic material without the knowledge or consent of a country of origin;
- We conducted specialized searches for indigenous peoples, local communities and traditional knowledge in the patent data and did not find evidence of the use of traditional knowledge in the documents reviewed in the research;
- The above conclusions do not mean that local breeds and traditional knowledge are not relevant to innovation or lacking in importance. Rather, the results illustrate that existing inventions are drawn from a narrow base of genetic material from dominant breeds;
- The wider implications of patent claims to genetic material and markers across different breeds merits fuller investigation in future research in the context of the completion of genome sequencing projects.

Introduction

In this section we present the results of research on the appearance of animal breed names in patent documents as a contribution to understanding access and benefit-sharing issues in relation to animal genetic resources and the patent system.

Analysis of the appearance of breed names was performed in the first filings of patent documents published between 1976 and October 2013 at the EPO, the USPTO and PCT under WIPO. To conduct the analysis we used a list of 7,616 breed names from the FAO Global Databank for Animal Genetic Resources [1]. Breed names are listed in the databank by country and in other cases as international breeds. Text mining of the patent data identified 1,136 raw breed names. It immediately became apparent that the breed data included a significant number of terms that would generate noise in the patent data, such as a country or region or common animal names (e.g. horse listed alongside Indonesia). To address this the raw results were manually reviewed to reduce the data to a second stage clean dataset consisting of 548 breed names in 7,328 documents for further review. We selected 2,955 documents from the new breeds of animals cluster for manual review using MAXQDA qualitative analysis software. In an additional step we identified 2,499 documents in the biotechnology cluster that contained a breed name for review in MAXQDA.

To perform the analysis the documents were computationally tagged for the country, species and breed name throughout the text (see Annex 4). Each paragraph containing the term was coded and intersections between terms in paragraphs were identified. Thus, a country name and a breed name coincided in 1,289 paragraphs in the new breeds of animals dataset. In the case of intersections between species names, breed names and country names there were 573 intersections in the new breeds of animals dataset. For the biotechnology cluster the country, breed and species names coincided in 397 paragraphs that were selected for review. All reviewed segments were marked with a short comment and the data is provided in the Annex 4.

In this section we present a range of example with the aim of providing a balanced sample of patent documents that reference animal breeds. Details of patent grants within the wider patent family are provided for each document where relevant.

The dominant species found in the patent data are pigs, cattle and sheep. The number of breed names occurring in the patent data was very low, and limited to a handful of common varieties of each species.

For pigs the dominant breeds were Large Whites, Durocs and Landrace, with research activity being dominated by agriculture and human health applications.

In the agriculture sector animal performance is the most common theme. Genetic engineering to improve and develop new varieties, to improve productivity and to increase resistance to disease all feature frequently. New varieties are developed through the manipulation of genes in embryonic cells as well the creation of transgenic breeds and genetic sequencing. The benefits sought from these breeds are improved meat quality and an increase in the litter size of sows. Disease control is tackled through the identification of genetic resistance for pathogens such as E. coli, although the testing of novel vaccines on existing breeds also features in the data. The human health applications of pig genetic material include xenotransplantation – notably the isolation of porcine proteins which can determine and monitor human rejection of transplants – and the production of pig derived immunoglobulins which are of greater utility than murine equivalents for humans due to their reduced immunogenic effect.

In the case of cattle, well known breeds such as Holstein, Friesian, Limousin, Jersey and Angus all feature prominently. Other breeds encountered include Wagyu, Sahiwal and Nellore in patent applications from outside western industrialised countries such as those from India, Brazil and Japan. Agricultural productivity dominates activity for cattle, with a large number of documents developing methodologies for the use of genetic markers for specific traits in meat, such as marbling, and for milk yields and quality. These productivity aspects are also the focus of non-genetic developments such as new feed formulations. Breeding management also has a strong presence, including methods for genetically predicting temperament and behaviour as well as fertility and productivity; markers to test for dwarfism, and remedies for breeding disorders arising from highly intensive breeding systems. Genetic technologies play a role in animal welfare by identifying resistance to tick-born diseases, but other technologies are also present such as the use of infrared thermography to detect inflammation. Beyond animal husbandry are a small number of applications: cattle have been the source of bacterial bio-inoculants for treating soils and plants, and a means of producing antibodies from cattle mammary secretions for use in medicine has been developed.

Four breeds of sheep feature in these examples: Romney, Dorset, Merino and Santa Ines. Animal husbandry is the dominant technology area involving sheep. As with pigs and cattle, the use of genetic markers to predict and improve productivity is important, as are methods to inoculate and vaccinate against disease and infection. In the field of human health, transgenic breeds of sheep have been developed and are capable of producing human bile salt-stimulated lipase (BSSL), which can be used to treat pancreatic deficiencies and aid body functions in preterm infants. In another example sheep have been used to develop cell culture systems in order to study skin cell behaviour and hair growth.

Mammal species that appear less frequently include goats and horses. Goats appear in patents for the development of transgenic varieties designed to produce increased milk yields and for methods to stimulate the growth of cashmere wool. Welsh Mountain Ponies have been used to test vaccines against bacterial infections rather than for their genetic material.

Birds appear quite regularly, but rarely for their genetic material. The White Leghorn breed and Peking duck are shown in these examples as the source of embryonic stem cells used to produce glycoproteins that are of value in treating cancers.

The examples below provide details of the origins or sources of genetic material in an invention with specific reference to breeds and have been selected to illustrate the variety of types of reference across the patent data.

Pigs

Table 5.1: Documents Referencing Breeds of Pigs

Number and Year	Title	Applicant	Family Members	Citations
EP0774510A1 1997	Ungulate EG cell	Meiji Milk Prod Co Ltd	6	9
WO1999046982A1 1999	Porcine Nuclear Transfer	Bresagen Ltd	7	9
EP1469076A2 2004	Recombinant PRRS proteins, diagnostic kits and vaccines containing said recombinant proteins	Wyeth Farma	25	1
EP1310570A1 2003	Methods and compositions to identify swine genetically resistant to F18 E. Coli associated diseases	Biotechnology Research and Development	36	0
WO2008052335A1 2008	Methods Of Determining Risk And Severity Of Disease In Pigs	University of Guelph	1	0
WO1996033288A1 1996	Gene Marker associated with swine proliferacy	Dekalb Swine Breeders Inc. and Northern Illinois University	2	4
WO1992018651A1 1992	Genetic Markers for pig Litter Size	Iowa State University Research Foundation	13	11

Table 5.1: Documents Referencing Breeds of Pigs (Continued)

Number and Year	Title	Applicant	Family Members	Citations
EP1561816A1 2005	Methods for determining genetic resistance of pigs to diseases caused by RNA viruses	National Institute of Agrobiological Sciences	6	0
EP1595447A1 2005	Transgenic animal having fatty acid desaturase and method of producing the same	University of Kinki	4	0
WO1997035878A2 1997	The porcine heart fatty acid-binding protein encoding gene and methods to identify polymorphisms associated with body weight	Dalland BV	6	8
WO1997011971A1 1997	Porcine Cell Interaction Proteins	Alexion Pharma Inc	5	17
WO1990001066A1 1990	Porcine polyclonal and monoclonal antibodies	Bio-Research Laboratories Inc	3	5

Pig breeding

France: Large White and Duroc

EP0774510A1 from Meiji Milk Prod Co Ltd focuses on porcine embryonic germ (EG) cell strains from primordial germ cell lines that can be cultured for genetic manipulation for gene targeting in pigs and the production of new swine varieties. The applicants explain that:

> Swine embryos were obtained by mating or artificially inseminating Large White x Duroc F1 females with Duroc males. Some embryos were obtained by mating or artificially inseminating Large White x Duroc F1 females with Duroc x France hybrid males. In addition, embryos were obtained by mating Duroc swine or Meishan swine among themselves. Mating and artificial insemination were performed twice, once each in the morning and afternoon of the same day or in the afternoon and in the morning of next day. (EP0774510A1).

See patent grants AU699869B2, JP03790268B2.

Australia: Large White and Landrace

WO1999046982A1 from Bresagen Ltd for *Porcine Nuclear Transfer* provides "A process for the production of nuclear transferred porcine embryonic cells". The applicants refer to breeds in an example.

> Example 4 Embryo Transfer of Nuclear Transfer Embryo Pregnant crossbred

> Large White X Landrace sows are aborted by intramuscular (IN4) injection of 1 ing prostaglandin F2 analog (Cloprostenol; Estrumate, Pittnan-Moore, NSW, Australia) between twenty five and forty days after mating followed by a second injection of 0.5 ing Cloprostenol twenty four hours later. Five hundred international units of CCG (Pregnecol, Heriot AgVet, Vic, Australia) is administered (IM) at the same time as the second injection of Cloprostenol. Ovulation is induced by an IM injection of 500 iu hCG (Chorulon, Intervet, NSW, Australia) administered approximately seventy two hours after eCG. Twenty-five to thirty, 4-cell embryos surgically transferred to the oviduct of a sow seventy two hours after the KG injection result in a litter of 5 to 8 piglets following a successful pregnancy. (WO1999046982A1).

See for example granted patent family member AU755743B2.

Pig Health: vaccines

Belgium: Landrace and Large White

EP1469076A2 from Wyeth Farma focuses on a Recombinant PRRS protein, diagnostic kit and vaccine. The patent references breeds in the following terms.

> The present invention discloses the production of recombinant proteins of the virus causing the porcine respiratory and reproductive syndrome (PRRS) […] Said recombinant proteins are appropriate to formulate vaccines capable of efficiently protecting pigs against PRRS as well as to prepare diagnostic kits appropriate to detect both the presence of antibodies which recognize PRRSV and the presence of PRRSV in a porcine biological sample.
>
> 7 to 8 week old pigs, a cross between Belgium Landrace and Large White breeds, were used. The animals, from our own farms, were seronegative to the following diseases: Aujeszky's, porcine parvovirosis, foot-and-mouth, classic swine fever, swine influenza (types H1N1 and H3N2) and transmissible gastroenteritis. (EP1469076A2).

See for example granted family members EP0717108B1, ES2078187B1 and FR2719845B1.

Pig Health: identifying genetic resistance

Switzerland and USA: Large White, Landrace, Duroc, Hampshire and Pietrain

EP1310570A1 from Biotechnology Research and Development filed in 1997 and published in 2003 focuses on *Methods and compositions to identify swine genetically resistant to F18 E. Coli associated diseases*:

> Data of the Swiss Landrace experimental population came from two pedigrees, which were built up at the Institute of Veterinary Bacteriology, University of Zurich. All other pigs of the Large White, Swiss Landrace, Duroc, Hampshire and Pietrain breeds came from different breeding herds of Switzerland. Other swine were randomly obtained from farms in the U.S. Midwest. (EP1310570A1).

See for example granted family members AU737862B2 and EP0985052B1.

USA: Chester White, Berkshire and Hampshire

WO2006053061A2, entitled *Porcine Reproductive and Respiratory Syndrome Virus Receptor Components and Uses Thereof*, by Kansas State University Research Foundation, relates to diagnosis and prevention of PRRSV in pigs.

> Vimentin Polymorphisms and Swine Breeding Chromosomal DNA is extracted from ear notch biopsies of Yorkshire, Duroc, and Poland China pigs. Virnentin genomic DNA is amplified by PCR and single nucleotide polymorphisms or RFLPs are identified. Statistical analysis is performed to identify any correlations between pig breed and susceptibility to PRRSV. The experiment is repeated using Chester White, Berkshire and Hampshire pigs. Pigs that demonstrate vimentin polymorphism(s) that correlate with PRRS resistance are selected for further breeding. (WO2006053061A2)

No patent grants were identified in this patent family

Canada: Yorkshire/Landrace, Duroc and unspecified breeds

WO2008052335A1 from the University of Guelph developed a method for assessing disease risk in various breeds of pigs.

> Porcine MBL-A (Lillie et al. 2006) and porcine MBL-C (Agah et al. 2001) are expressed predominantly in the liver, so mRNA from liver was collected from a range of clinically healthy pigs, and diseased pigs submitted for necropsy examination. Liver (RNA) and testis (DNA) samples were collected from pigs from multiple commercial breeders in Ontario (Lin et al. 2005). Liver (RNA), lung (DNA) and spleen (DNA) samples were also collected from pigs submitted for necropsy to the Animal Health Laboratory, University of Guelph, Guelph, ON, Canada. DNA from 183 pigs of unspecified breeds submitted to diagnostic necropsy from various farms, and a group of 53 pigs culled with pneumonia and wound infections from a single herd of Yorkshire/Landrace cross-bred sows bred to Duroc sires were used for genotyping a miscoding mutation in MBLl. Tissues for RNA isolation were either snap-frozen in liquid nitrogen then stored at -7O0C, or collected into RNA later (10:1 RNA later to tissue ratio by volume) then incubated at 40C for 24 h, -20 0C for 24 h, and stored at -7O0C.

Tissues for DNA isolation were stored at -70 0C. (WO2008052335A1)

No patent grants were identified in this patent family.

USA: Various breeds

WO1996033288A1. Dekalb Swine Breeders Inc. and Northern Illinois University have developed a *Gene Marker Associated with Swine Proliferacy* involving a "random amplification method for determining swine genetic markers associated with small and large litter sizes… This marker can be used to inform breeding programs designed to increase the litter size of certain swine breeds."

> As a first step in determining the existence of genetic markers that are linked to litter size, it is necessary to set up reference families involving genetically disparate parents. The Chinese breed of pigs are known for reaching puberty at an early age and, also, for their large litter size. For purposes of this application, a large litter is greater than twelve. In contrast, American breeds are known for their greater growth rates and leanness but tend to produce smaller litters. Combining the characteristics of these two breeds would be of great economic importance to pork producers. The offspring of a particular Chinese x American cross should allow genetic loci involved with litter size to identified…
>
> Preferred breeds are Meishan, Fengjing, Minzhu, Duroc, Hampshire, Landrace, Large White, Yorkshire, Spotted Poland China, Berkshire, Poland China and Chester White." (WO1996033288A1)

No patent grants were observed in this patent family.

USA: Various breeds

WO1992018651A1 Iowa State University Research Foundation identified "genetic markers for pig litter size, methods for identifying such markers, and methods of screening pigs to determine those more likely to produce larger litters. The markers are based upon the presence or absence of polymorphisms in the pig oestrogen receptor gene."

> The polymorphisms are associated with the number of offspring. At least 20 and-preferably at least 40 female pigs are used in making these determinations. The number of times each female produces a litter (i.e., the parity) is at least 1 time. Preferably, the cycle of breeding and giving birth is repeated at least 2 times and most preferably 3 times. The preferred breeds of pigs are Meishan, Fengjing, Minzhu, Duroc, Hampshire, Landrace, Large White, Yorkshire, Spotted Poland China, Berkshire, Poland China, and Chester White. The most preferred breeds are Duroc, Hampshire, Landrace, Large White, Yorkshire, and Chester White. When this analysis is conducted for the Meishan breed and the

> polymorphism is determined by RFLP analysis using the restriction endonuclease Pvu II, a 4.3 kilobase fragment is associated with increased litter size. (WO1992018651A1)

Patent grants in this family include US5374526A, US5550024A and JP03404534B2.

USA: Various breeds

EP1561816A1 from the National Institute of Agrobiological Sciences filed in 2002 and published in 2005 focuses on "methods for determining genetic resistance of pigs to diseases caused by RNA viruses" (influenza). In connection with breeds the applicant states that:

> Pig farming is still popular in the Northwest region of the United States including the Iowa State. There is no detailed information on pig farming at the time of the outbreak [Spanish Influenza], but if the Landrace breed or its crossbreeds were being raised on a large scale, pig populations having a high percentage of pigs susceptible to influenza viruses may have been acting as a breeding ground for the new virus and resulting in the pandemic.(EP1561816A1)

> The level of genetic resistance to diseases caused by RNA viruses, including influenza viruses and the causative virus of PRRS, can be studied according to the present invention. Healthy animals which are more favourable for pig production can be selected based on the information. Furthermore, the incidence of respiratory diseases in piglets can be reduced, leading to increases in the survival and growth rates. (EP1561816A1)

> By selecting pigs with a high ability to suppress influenza virus propagation according to the present invention, the propagation of an influenza virus can be suppressed in pig populations, thereby reducing the chance of the emergence of new influenza virus strains, and raising the possibility of eliminating one threat against humans. (EP1561816A1).

See for example granted patent family member AU2003275705B2.

Food: Improved meat for human consumption

USA: Meishan x Large White

WO1999018192A1 entitled *Methods for the Identification and Production of Swine with Reduced Boar Taint*, by Penn State Research Foundation is focused upon synthesizing DELTA 16 steroids in pigs testes to improve meat without affecting other traits.

> One genetic screening protocol, marker assisted selection based on a chromosome 7 association (Bidanel, et al., 1997, Chromosome 7 mapping of a quantitative trait locus for fat androstenone level in Meishan x Large White F2 entire male pigs. Proc. EAAP working group "Production and Utilisation of Meat from Entire Male Pigs", pp. 115-118, M. Bonneau, K. Lundstrom, B. Malmfors, eds. Wageningen Pers, Stockholm, Sweden) appears to identify a marker associated with male reproductive development and is not specific to androstenone production. (WO1999018192A1)

No patent grants were identified in this patent family

Japan: Duroc and Landrace

EP1595447A1 from the University of Kinki filed in 2003 and published in 2005 focuses on a *Transgenic animal having Fatty acid desaturase and method of producing the same*. This patent application claims "to provide meat that is beneficial to human health, for the purpose to produce transgenic animals in which the content of unsaturated fatty acids increase is increased, transgenic animals characterized by increased content of unsaturated fatty acids that are beneficial to human health is provided by the present invention. Furthermore, the present invention also provides a method to enhance levels of unsaturated fatty acid in animals."

> The fusion gene was microinjected into pronuclei of pig early embryos. Handling of those animals was performed in accordance with the "Guidance for Experiment on Animals" (Japan's Society for Animal Experimentation (ed.), and Soft Science Publication, 1991). Collection of pig embryos, gene injection, and embryo transfer were carried out as follows. Pigs for food of about 13 months old (cross-breeds between Duroc (male) and F1 (female) Landrace x Large White, weighing about 100 kg) received the intramuscular injection of 1000 IU of eCG which was followed by the administration of 500 IU of hCG 72 hours later. Twenty four hours after the administration of hCG, the pigs indicating estrous were mated with male pigs. Twenty-six to thirty hours after the administration of hCG, Stresnil (Azaperon medicine) was administered for tranquilizing followed by inhaled anaesthesia. The oviduct was rinsed by upward current through a midventral incision, and embryos were recovered. Immediately thereafter, the fusion gene was microinjected into the pronuclei of the embryos at a concentration of 4 μg/ml. (EP1595447A1)

No patent grant was identified in this patent family.

Netherlands: Meishan

WO1997035878A2 by Dalland BV, claims a novel sequence of the pig H-FABP gene, as well as methods of using the gene and its products and also breeding methods for the pig.

> The 31 untranslated region was isolated using the 5'/3' RACE-PCR kit (Boehringer Mannheim, Mannheim, Germany) with porcine (Meishan) muscle cDNA as the template and porcine HFABP exon 1 or 3 specific primers in combination with the provided poly-A primer. (WO1997035878A2)

No patent grant was identified in this patent family.

Medical

USA: Various breeds

WO1990001066A1. Bio-Research Laboratories Inc. developed "porcine antibodies useful in therapeutic methods for treating antigen mediated diseases."

> A strain or breed of pig capable of producing immunoglobins having less of an immunogenic effect than murine immunoglobins when administered to a human can be used in this invention. The preferred pig being the mixed Yorkshire breed pigs. Examples of other breeds of pigs which-can be used include, the Duroc, Hampshire, Spotted Swine, Poland China, Chester White, Berkshire, O.I.C., Hereford, Tamworth, or mini pig breeds. (WO1990001066A1)

No patent grant was identified in this patent family.

Cattle

Table 5.2: Documents Referencing Breeds of Cattle

Number and Year	Title	Applicant	Family Members	Citations
US20050181373A1 2005	Single nucleotide polymorphism markers in the bovine CAPN1 gene to identify meat tenderness	Timothy Smith et al	1	3
US20110091878A1 2011	Dairy cattle breeding for improved milk production traits in cattle	The Wisconsin Alumni Research Foundation	7	0
US5614364A 1997	Genetic marker for improved milk production traits in cattle	Iowa State University Research Foundation	1	20

Table 5.2: Documents Referencing Breeds of Cattle (Continued)

Number and Year	Title	Applicant	Family Members	Citations
US20070275390A1 2007	Polymorphisms in fatty acid binding protein 4 ("FABP4") gene and their associations with carcass traits	Brent Woodward	1	0
US7919241B2 2007	Polymorphisms in fatty acid binding protein 4 ("FABP4") gene and their associations with measures of marbling and subcutaneous fat depth in beef cattle	Washington State University	13	4
US7972790B2 2008	Stat6 effects on livestock animal growth	University of California	1	1
WO2008100145A2 2008	Method for selection of non-human mammal producing milk with improved fatty acid composition	University of Wageningen and Holland Genetics BV	2	5
EP1219178A1 2002	Use of quillaja powder	Nor Feed APS	3	0
WO1997000017A1 1997	Nutritional supplement	Two Individuals	8	2
WO2012061899A1 2012	Animal fat product	York Foods PTY	1	0
WO2007002735A2 2007	Bovine ABCG2 gene missense mutations and uses thereof	University of Illinois and the Agricultural Research Organisation of Israel	9	0
WO2006128116A2 2006	Polymorphisms in fatty acid binding protein 4(FABP4) gene and their associations with measures of marbling and subcutaneous fat depth in beef cattle	The University of Washington	13	2
WO2006076563A2 2006	DNA markers for increased milk production in cattle	University of Missouri	9	1
US20070238110A1 2007	Genetic test for the identification of dwarfism in cattle	Iowa State University	1	0
WO2007051248A1 2007	Single nucleotide polymorphisms (SNP) and their association with tick resistance in bovine animals	Commonwealth Scientific and Industrial Research Organisation	6	0
WO2009097862A1 2009	Genetic markers for fertility	Aarhus University	2	1
WO2007112490A1 2007	Chromosomal blocks as markers for traits	Innovative Dairy Products Pty	6	6

Table 5.2: Documents Referencing Breeds of Cattle (Continued)

Number and Year	Title	Applicant	Family Members	Citations
EP1226176B1 2002	Production of mammary secretion antibodies in farm animals	Mucovax BV	17	0
EP1946766A1 2008	Reproductive Disorder Remedy	Hayashibara Biochem Laboratories	3	0
EP2040566B1 2009	Milk Fever	Nutreco Nederland BV	9	0
US7277744B2 2004	Early detection of inflammation and infection using infrared thermography	Four Individuals	6	7
WO2003020038A1 2003	A bioinoculant composition comprising bacterial strains of B. subtilis or B. lentimorbus from cows milk	Council of Scientific and Industrial Research	12	2
US6602676B1 2003	Testing method	Milk Development Council (UK)	1	1
WO2011116466A1 2011	DNA Polymorphisms as Molecular Markers in Cattle	University of Alberta	4	0
WO2011093728A1 2011	Marker assisted selection of a mammalian subject for Desired Phenotype	VialactiaBiosciences NZ Ltd	3	0
WO2010087725A2 2010	Selection of Animals for Desired Milk and/or Tissue Profile	Fronterra Cooperative Group	11	0

Improved food and milk

USA: Hereford and Angus

US20050181373A1 from the US Secretary Of Agriculture entitled *Single Nucleotide Polymorphism Markers In The Bovine CAPN1 Gene To Identify Meat Tenderness* claims a method for determining gene alleles in the gene encoding micromolar calcium activated neutral protease.

> Primers for The SNPs at position 18 of exon 9 of Seq. ID No. 3, position 17 of exon 14 of Seq. ID No. 4, and position 185 on intron 19 of Seq. ID No. 4, of the bovine CAPN1 gene were evaluated for their association with shear force in the U.S. MARC GPE Cycle VII cattle population. Shear force data was collected from meat obtained from a total of 564 steers at 3 and 14 days of carcass aging. This data is additional to that found in the two populations described in Example 1. Shear force phenotypes of longissimus muscle from GPE Cycle VII steers were collected by the modified Warner-Bratzler shear force method as

described (Shackelford S. D. et al. 1999. Evaluation of slice shear force as an objective method of assessing beef longissimus tenderness; Journal of Animal Science, Vol. 77, pp 2693-2699). Sires for this population included twenty of the top sires (by number of registered offspring) in each of seven breeds, which represent the top seven breeds by numbers of registered cattle in the United States. Semen from these sires was used on a constant background of Hereford, Angus, and MARCIII dams to provide consistent genetic background for comparison. Genotypes were collected using a Sequenom® MassArray® MALDI-TOF mass genotyping the three polymorphisms are given below: (US20050181373A1)

No patent grant was identified in this patent family.

Netherlands: Holstein Friesian

WO2010120178A1 *Methods Of Measuring Natural Immunity In Milk* by CRV Holding BV relates to breeding of cattle and predicting immunity in milk and resistance to mastitis, and using the methods to build up a population of animals.

For the present study, milk samples from 1958 heifers were available, originating from 398 farms, which are in the database of the Milk Genomics Project (MG). A lot of information is available on these samples, including the somatic cell count (SCC), determined at the Milk Control Station (Zutphen, the Netherlands), and the SCS, a derivative of the SCC. Moreover, a lot of data are available on the cows including mastitis incidence which was determined using a written enquiry. The MG project has its focus on the genetics of milk composition. In the MG, approximately 2000 cows were included, which are descendants of a number of selected bulls. Daughters of five proven bulls (200 each) and daughters of 50 test bulls (20 each) were included. All cows were at least 87.5% Holstein Friesian. The choice of farms included in the MG was based on the pedigree; farms that were registered in the database of the Dutch Dairy cattle Syndicate (NRS, Arnhem, the Netherlands) and had at least one proven bull heifer and one test bull heifer were invited to take part in the study. Selection of farms took place until 2000 animals were included in the study. Between February and March 2005 a milk sample was collected from each of the selected cows. At least three cows per herd were sampled. Milking of the cows occurred twice a day. However, only the morning milk was sampled for the MG to ensure the quality of the milk samples. Within three hours after sampling, milk was brought to a temperature of 4 0C. Sodium azide (0.03% wt/wt) was added to the sample bottles as a preservative. After refrigerated transportation, samples were aliquoted and stored at -4O0C. One day before the testing period the milk samples were transferred to -20 0C. The day before testing the samples were transferred to 4 0C. At the day of testing the samples

were aliquoted in a 96-well system (containing 1 mL tubes) that facilitated transfer of the samples to the ELISA plates. (WO2010120178A1)

No patent grant was identified in this patent family.

New Zealand: Holstein Friesian and Jersey

WO2011028134A9 is entitled *Biological Markers And Uses Thereof* by the Livestock Improvement Corp Ltd and describes methods for inferring the size potential of an animal and/or its offspring, particularly but not exclusively, methods for identifying and selecting animals on the basis of their live weight and/or growth rate potential.

Figure 5: Effect on live weight (in Kgs; X-axis) and frequency (number of observations in the studied population; Y-axis) for the 20 hidden haplotype states modelled with Dualphase (Druet and Georges, 2009) in the New Zealand outbred dairy cattle population. Shades of grey distinguish the breed origin of the corresponding animals: Holstein-Friesian (black), Jersey (grey), crossbred (white). The number of haplotype states in each class is given above the corresponding bars. Figure 6: Upper track (labelled "Genes"): A. Organization of the eight genes mapping to the 750Kb critical region LYN, RPS20, MOS, PLAG1, CHCHD7, RDHE2, SDR16C6 and PENK). Middle track (labelled "SNP"): Positions of the 14 candidate Quantitative Trait Nucleotides (QTN), plus splice site variant detected in CHCHD7 (half height). Brown track (labelled "Phastcons conserved elements, 5-way Vertebrate Multiz Alignment"): Location of "Phastcons" multispecies conserved elements. (B) Orthologous locus in zebrafish (D. rerio) (WO2011028134A9)

No patent grant was identified in this patent family.

USA: Jersey, Angus and Limousin

US20050181373A1. Timothy Smith et al developed “a method for determining one or more alleles of the gene encoding micromolar calcium activated neutral protease effecting meat tenderness in a bovine animal, comprising assaying a sample of nucleic acids.”

Haplotypes inherited from the sires were established based on a selection of 10 SNPs representing genetic variation within the Piedmontese Angus sire. Two SNPs representing predicted amino acid changes, two SNPs representing silent substitutions within the coding region, and six SNPs representing intron variation were selected out of 38 total SNPs heterozygous in the Piedmontese Angus sire. Six of the SNPs selected reside on the half of the gene 5' to the approximately 100 kb intron 10, while the remaining four are located in the half 3' to intron 10. The haplotypes inherited by the sire from the Piedmontese

> grandsire and Angus grandam were identified by inferring the haplotypes based on offspring that were homozygous for all of the SNPs tested and comparing these genotype patterns with markers used in the QTL analysis. (US20050181373A1)

See patent grant US7238479B2 in this patent family.

Australia: Angus and Brahman

WO2008134818A1. *Genetic Origin Of Mitochondrial Genome And Traits Associated Therewith* by Adelaide Research & Innovation Pty Ltd relates to methods for determining the genetic origin of the mitochondrial genome of a cell, and to methods for identifying an organism with a mitochondrial genome of different genetic origin to the nuclear genome.

> Example 1 Material and Methods Blood samples from 212 Angus (Bos taurus) and 179 Brahman (Bos indicus) heifers were obtained from at least three properties/herds each in Australia. DNA was extracted by standard procedures and used in PCR reactions to amplify the mitochondrial DNA (mtDNA) control region as described (Hiendleder et al. (2003) Biol. Reprod. 68(1) 159- 166). Diagnostic restriction enzymes (e.g. BstNl, Ddel, Sspl, and their isochizomeres) that distinguish between the two major cattle mtDNA haplotypes, i.e. Bos taurus and Bos indicus, were identified by virtual digestion of Bos taurus and Bos indicus CR nucleotide sequences (Hiendleder et al. (2003) Biol. Reprod. 68(1) 159-166) and visual inspection of restriction sites in an alignment of more than 100 mtDNA control region sequences o(iota) Bos taurus and Bos indicus type from the NCBI database. (WO2008134818A1)

No patent grant was identified in this patent family.

USA: Wagyu x Limousin

WO2007139546A2. *Polymorphisms In Fatty Acid Binding Protein 4("Fabp4") Gene And Their Associations With Carcass Traits* by Brent Woodward, relates to the identification of single nucleotide polymorphisms (SNPs) within the bovine genes encoding fatty acid binding proteins and their associations with economically relevant traits in beef production.

> Direct sequencing of PCR products from two DNA pools was performed on ABI 3730 sequencer in the Laboratory for Biotechnology and Bioanalysis (Washington State University) using a standard protocol. However, DNA sequencing did not confirm the existence of a G/A substitution in exon 3 or a variation in the number of CA repeats in the 3' untranscribed region of the bovine FABP4gene between HMS and LMS pools. Instead, two single nucleotide polymorphisms (SNPs) were detected in the products amplified with

the second primer pair, including a G/C substitution located at position 7516 (FIG. 2A) and a G/C substitution at 7713 bp within the CA repeat region (FIG. 2B). Restriction map analysis indicated that the G/C substitution at 7516 bp could be genotyped by PCR-RFLP using restriction enzyme MspAll. This G/C SNP in the bovine FABP4 gene was then individually genotyped in DNA from Wagyu X Limousin F animals with recorded marbling scores and SFD measurements. After PCR amplification, the amplicons were digested at 37 Ã‚Â°C for three hours with 2U of MspAll (New England Biolabs, Beverly, MA) followed by analysis on 1.5% agarose gels. The 452 bp amplicon with the C/G substitution at 7516 bp contains a single polymorphic site for the restriction enzyme MspAll. Therefore, GG homozygous animals have one MspAll site and reveal after complete digestion two bands: 100 bp and 352 bp. In comparison, homozygous animals with C allele have lost the MspAll recognition site at this position and show only the 452 bp band. Heterozygous animals are identified by the presence of three bands after MspAll digestion (FIG. 3). Of the 232 animals genotyped, 139 were homozygotes with allele C, 2 1 were homozygotes with allele G, and the remaining 72 were heterozygotes with both alleles C and G (Table 1). The genotype distribution was in Hardy-Weinberg equilibrium. (WO2007139546A2)

No patent grant was identified in this patent family.

USA and Israel: Holstein

WO2007002735A2. *Bovine ABCG2 Gene Missense Mutations And Uses Thereof* from the University Of Illinois and the Agricultural Research Organisation Of Israel claims an isolated polynucleotide comprising a coding region of the ABCG2 gene which can be used in cattle breeding and selection.

ABSTRACT A quantitative trait locus (QTL) affecting milk fat and protein concentration was localized to a 4cM confidence interval on chromosome 6 centred on the microsatellite BM143. The genes and sequence variation in this region were characterized, and common haplotypes spanning five polymorphic sites in the genes IBSP, SPP1, PKD2, and ABCG2 for two sires heterozygous for this QTL were localized. Expression ofSPP1 and ABCG2 in the bovine mammary gland increased from parturition through lactation. SPP1 was sequenced, and all the coding exons of ABCG2 and PKD2 were sequenced for these two sires. The single nucleotide change capable of encoding a substitution of tyrosine-581 to serine (Y581S) in the ABCG2 transporter was the only polymorphism corresponding to the segregation status of all three heterozygous and 15 homozygous sires for the QTL in the Israeli and US Holstein populations. (WO2007002735A2)

See patent grants AU2006261660, EP1896616 and US7803919.

USA: Holstein

US20110091878A1 and US20080307535A1. The Wisconsin Alumni Research Foundation developed a method for "identifying a SNP site at position 1296 of bovine uterine milk protein (UTMP) coding sequence (which) indicates a desirable productive life in a dairy cattle."

> Dairy cows are significant investments for dairy farmers, and enormous efforts, such as systematic animal breeding programs and artificial insemination, have been and continue to be invested in ensuring that the animals have high and sustained productivity, and that the milk produced is of high quality or has desired composition. A successful breeding family is the Holstein line derived from Carlin-M Ivenhoe Bell. More than 25% of the highest total performance index Holstein bulls in the United States are progenies of this individual. (US20110091878A1)

See patent grants US7897749B2 and US7807361B2 in this patent family.

USA: Holstein

US5614364A. Iowa State University Research Foundation applied for "Genetic markers in the bovine PIT-1 gene which are associated with increased milk production and increased protein and fat content in cattle."

> To confirm the association of the markers of the invention with increased dairy performance, presence or absence of the marker was correlated with overall milk production as well as fat and protein content of milk. Dairy cows in the study were from a group maintained at Iowa State University which is scientifically designed to genetically mimic the United States Holstein population. (US5614364A)

Patent grant US5614364A is the only member of this family.

USA: Limousin

US20070275390A1 by Brent Woodward and US7919241B2 & US20070020658A1 by Washington State University applied for protection in relation to: "the identification of single nucleotide polymorphisms (SNPs) within the bovine genes encoding fatty acid binding proteins and their associations with economically relevant traits in beef production."

> …direct sequencing of PCR products from two DNA pools was performed on ABI 3730 sequencer in the Laboratory for Biotechnology and Bioanalysis (Washington State University) using a standard protocol. However, DNA sequencing did not confirm the existence of a G/A substitution in exon 3 or a variation in the number of CA repeats in the untranscribed region of the bovine

> FABP4 gene between HMS and LMS pools … This G/C SNP in the bovine FABP4 gene was then individually genotyped in DNA from Wagyu Limousin F2 animals with recorded marbling scores and SFD measurements. After PCR amplification, the amplicons were digested at 37° C for three hours with 2U of MspA1I (New England Biolabs, Beverly, Mass.) followed by analysis on 1.5% agarose gels … Of the 232 animals genotyped, 139 were homozygotes with allele C, 21 were homozygotes with allele G, and the remaining 72 were heterozygotes with both alleles C and G. (US7919241B2)

Patent grants in this family include AU2006249318B2, AU2006249319B2 and US7662564B2.

USA: Various breeds

US7972790B2. The University of California developed a method for the "selection of livestock animals, including bovines, whose genotypes based in the STAT6 gene are correlated with phenotypes reflecting desirable carcass and feedlot traits."

> The cattle breed DNA resource consists of approximately 6 animals of each of 12 cattle breeds (5 Black Angus, 6 Red Angus, 3 Horned Hereford, 3 Polled Hereford, 4 Charolais, 5 Simmental, 4 Limousin, Chianina, 6 Brahman, Santa Gertrudis, 3 Wagyu). The animals of each breed were selected to be unrelated at least 3 generations back. An effort was made to have the presence of diverse lines or types within each breed. At least 5 straws of semen were obtained from each animal. The semen came from 3 sources: purchased by Merial from semen AI companies, from Charles Farber (University of California at Davis) and from Milton Thomas (New Mexico State). Tables 1 and 2 show the details of the individual samples, source and number of semen straws. High quality DNA was extracted from one semen straw from each animal and four straws kept frozen for future use. DNA was extracted using PureGene DNA extraction kit, quantified on a UV spectrophotometer and tested for integrity on an agarose gel. The DNA panel was used as a SNP discovery resource by re-sequencing of the STAT6 gene as described below. (US7972790B2)

One patent grant, US7972790B2, is observed in this patent family.

Netherlands: Holstein-Friesian

WO2008100145A2 by University of Wageningen and Holland Genetics BV is for a "Method for selection of non-human mammal producing milk with improved fatty acid composition."

> Animals. This study is part of the Milk Genomics Initiative, which focuses on the genetic background of detailed milk composition. As part of this study,

> morning milk samples and blood samples were collected from 1918 first lactation cows on 398 commercial herds in The Netherlands. At least three cows per herd were sampled; cows were milked twice a day. Cows descended from one of fifty young bulls (843 cows), from one of five proven bulls (888 cows), or from other proven bulls (187 cows). The NRS (Arnhem, the Netherlands) provided the pedigree of the cows. Each cow was over 87.5 percent Holstein-Friesian, and was in lactation between Day 63 and Day 263. (WO2008100145A2)

No patent grant was identified in this patent family.

Switzerland: Red Holstein

EP1219178A1 from Nor Feed APS filed in 2000 and published in 2002 focuses on "an Oral composition, an animal feed or a feed additive containing an active amount of quillaja powder, as well as the use thereof for a daily consumption of milk-producing farm animals. Good health conditions are obtained for the farm animals and the produced milk."

> The present experiment was performed in Switzerland, where a herd of milk cows of the race Red Holstein was divided into a test group and a control group. The cows were fed before and during the test with conventional animal feed with a composition varying in response to the season. At any time the control group and the test group were fed with the same animal feed apart from the fact that during the test period from 1 September to 6 September the daily animal feed of the test group had been admixed 5 g of quillaja powder per cow and during the following period 7.5 g of quillaja powder per cow. (EP1219178A1).

Patent grants in this family include DK174176B1 and EP1219178B1.

Argentina: Holstein Friesian

WO1997000017A1 from two US individuals focuses on a nutritional supplement to improve milk and meat.

> EXAMPLE 1: An experiment was conducted with cattle to determine whether the metabolic corrector provided a marked improvement in the general metabolism (specifically in the ruminal metabolism) of cattle through the use of human medical techniques, thereby improving the production of beef and milk. The specific objective of the experiment was to determine the correction of the digestive media through the use of diagnosed metabolic correctors in a milking herd in Argentina. The breed of cattle was Holstein Friesian cows. (WO1997000017A1).

No patent grant was observed in this family.

Japan: Wagyu Cattle

WO2012061899A1 from York Foods PTY published in 2012 involves "a commercially packaged, edible fat product derived from the fatty tissue of wagyu beef cattle; method of manufacturing same; and food products incorporating same."

> Herein, reference to the term 'wagyu' will be understood by those skilled in the art to refer to those breeds of cattle, originating in Japan but now farmed in other regions, that are predisposed to intense marbling of fat in muscle meat, and which have a distinct profile of fatty acids and fat compounds in said fat. In particular, it includes those cattle that are full-bloods, half-bloods and quarter-bloods. (WO2012061899A1).

No patent grant is observed in this family.

USA: Holstein

WO2007002735A2 & EP1896616B1 by University of Illinois and the Agricultural Research Organisation of Israel localised a quantitative trait locus (QTL) affecting milk fat and protein concentration.

> A quantitative trait locus (QTL) affecting milk fat and protein concentration was localized to a 4cM confidence interval on chromosome 6 centred on the microsatellite BM143. The genes and sequence variation in this region were characterized, and common haplotypes spanning five polymorphic sites in the genes IBSP, SPP1, PKD2, and ABCG2 for two sires heterozygous for this QTL were localized. Expression of SPP1 and ABCG2 in the bovine mammary gland increased from parturition through lactation. SPP1 was sequenced, and all the coding exons of ABCG2 and PKD2 were sequenced for these two sires. The single nucleotide change capable of encoding a substitution of tyrosine-581 to serine (Y581S) in the ABCG2 transporter was the only polymorphism corresponding to the segregation status of all three heterozygous and 15 homozygous sires for the QTL in the Israeli and US Holstein populations. (WO2007002735A2)

A second member of this patent family specifies that:

> Segregating quantitative trait loci (QTL) for milk production traits on chromosome BTA6 were reported in U.S. Holsteins, British black and white cattle, Norwegian cattle, and Finish Ayrshires. Three QTLs affecting milk, fat, and protein production, as well as fat and protein concentration are segregating on BTA6 in the Israeli Holstein population. The QTL with the greatest significance was located near the middle of the chromosome, with a confidence interval of 4 cM for protein percentage centred on microsatellite BM143. Two

> unrelated Israeli sires were found to be heterozygous for this QTL, whereas seven other sires were homozygous for the QTL. (EP1896616B1)

Patent grants in this family include AU2006261660B2, EP1896616B1 and US7803919B2.

USA: Limousin

WO2006128116A2. The University of Washington worked on the "identification of single nucleotide polymorphisms (SNPs) within the bovine genes encoding fatty acid binding proteins and their associations with economically relevant traits in beef production."

> Evidence has shown that the fatty acid binding protein 4 (FABP4), expressed in adipose tissue interacts with perioxisome proliferator-activated receptors and binds to hormone-sensitive lipase, thus playing an important role in lipid metabolism and homeostasis in adipocytes. The objective of this study was, therefore, to investigate associations of the bovine FABP4 gene with fat deposition in Waygu x Limousin F2 crosses. Both cDNA (625 bp) and genomic DNA (803 lbp) sequences of the bovine FABP4 gene were retrieved from the public databases and aligned to determine its genomic organization. Two pairs of primers were designed, which target two regions of the gene, one from bases 5433 to 6106 and one from bases 7417-7868 (AAFCO1 136716). Direct sequencing of PCR products on two DNA pools from high/low marbling animals revealed two G/C substitutions at positions 7516 and 7713, respectively. The former G/C substitution can be revealed by PCR-RFLP using restriction enzyme MspAlI and was genotyped on 246 F2 animals in the reference population. (WO2006128116A2)

Patent grants in this family include AU2006249318B2, AU2006249319B2, US7662564B2 and US7919241B2.

USA: Holstein

WO2006076563A2 and WO2006076419A1 by the University of Missouri identify DNA markers for improved milk production or meat production to aid in breeding regimes.

> The genetic basis of bovine milk production is of immense significance to the dairy industry. An ability to modulate milk volumes and content has the potential to alter fanning practices and to produce products which are tailored to meet a range of requirements. In particular, a method of genetically evaluating bovine to select those which express desirable traits, such as increased milk production and improved milk composition, would be desirable. (WO2006076563A2)

The techniques of the present invention may potentially be used with any bovine, including Bos taurus and Bos indicus cattle. In particular embodiments of the invention, the techniques described herein are specifically applied for selection of beef cattle, as the genetic assays described herein will find utility in maximizing production of animal products, such as meat. As used herein, the term "beef cattle" refers to cattle grown or bred for production of meat or other non-dairy animal products. Therefore, a "head of beef cattle" refers to at least a first bovine animal grown or bred for production of meat or other non-dairy animal products. Examples of breeds of cattle that may be used with the invention include, but are not limited to, Africander, Albères, Alentej ana, American, American White Park, Amerifax, Arnrit Mahal, Anatolian Black, Andalusian Black, Andalusian Grey, Angein, Angus, Ankole, Ankole-Watusi, Argentine Criollo, Asturian Mountain, Asturian Valley, Australian Braford, Australian Lowline, Ba-Bg, Bachaur, Baladi, Barka, Barzona, Bazadais, Beefalo, Beefmaker, Beefrnaster, Belarus, Red, Belgian Blue, Belgian Red, Belmont Adaptaur, Belmont Red, Belted Galloway, Bengali, Berrendas, Bh-Bz Bhagnari, Blanco Orejinegro, Blonde d'Aquitaine, Bonsmara, Boran, Braford, Brahrnan, Brahmousin, Brangus, Braunvieh, British White, Busa, Cachena, Canary Island, Canchim, Carinthian Blond, Caucasian, Channi, Charbray, Charolais, Chianina, Cholistani, Corriente, Costeflo con Cuernos, Dajal, Damietta, Dangi, Deoni, Devon, Dexter, Dhanni, Dølafe, Droughtmaster, Dulong, East Anatolian Red, Enderby Island, English Longhorn, Evolène, Fighting Bull, Florida Cracker/Pineywoods, Galician Blond, Galloway, Gaolao, Gascon, Gelbray, Gelbvieh, German Angus, German Red Pied, Gir, Glan, Greek Shorthorn, Guzerat, Hallikar, Hariana, Hays Converter, Hereford, Herens, Highland, Hinterwald, Holando-Argentino, Horro, Hungarian Grey, Indo-Brazilian, Irish Moiled, Israeli Red, Jamaica Black, Jamaica Red, Jaulan, Kangayam, Kankrej, Kazakh, Kenwariya, Kerry, Kherigarh, Khillari, Krishna Valley, Kurdi, Kuri, Limousin, Lincoln Red, Lohani, Luing, Maine Anjou, Malvi, Mandalong, Marchigiana, Masai, Mashona, Mewati, Mirandesa, Mongolian, Morucha, Murboden, Murray Grey, Nagori, N'dama, Nelore, Nguni, Nimari, Ongole, Orma Boran, Oropa, Parthenais, Philippine Native, Polish Red, Polled Hereford, Ponwar, Piedmontese, Pinzgauer, Qinchuan, Rätien Gray, Rath, Rathi, Red Angus, Red Brangus, Red Poll, Retinta, Rojhan, Romagnola, Romosinuano, RX3, Sa-Sg, Sahiwal, Salers, Salorn, Sanhe, Santa Cruz, Santa Gertrudis, San Martinero, Sarabi, Senepol, Sh-Sz, Sharabi, Shorthorn, Simbrah, Sinimental, Sin, Slovenian Cika, South Devon, Sussex, Swedish Red Polled, Tarentaise, Telernark, Texas Longhorn, Texon, Tharparkar, Tswana, Tuli, Ukrainian Beef, Ukrainian Grey, Ukrainian Whitehead, Umblachery, Ural Black Pied, Vestland Red Polled, Vosges, Wagyu, Welsh Black, White Cáceres, White Park, Xinjiang Brown and Yanbian

cattle breeds, as well as animals bred therefrom and related thereto. (WO2006076419A1)

No patent grants were observed in the families for WO2006076563A2 and WO2006076419A1.

Cattle Health

Belgium and Denmark: Holstein-Friesian

WO2010012690A1 *A Genetic Marker Test for Brachyspina and Fertility in Cattle* by a number of individuals provides a method for determining whether a bovine is affected by Brachyspina by analysing its genomic DNA or its RNA and a means of selecting cattle for breeding.

To position the gene causing BS, we collected tissue samples from six affected individuals in the Holstein-Friesian dairy cattle population. Samples originated from the Netherlands, Denmark and Italy. DNA was extracted from the tissue samples and genotyped using a previously described panel of 60.000 bovine SNPs (HG 6OK panel)(3), alongside control samples from healthy control individuals from the same breed. The ensuing genotypes were examined visually as well as with the previously described ASSHOM and ASSIST (3) programs. A chromosomal region spanning 2.46 Mb shared homozygous by descent by the six affected individuals was readily identified. The haplotype sharing was shown to be highly significant. The critical region, bounded by the nearest recombinational events, encompassed 56 annotated genes (Figure 3). (WO2010012690A1)

See grants AU2009275988 and EP2310528.

Australia: Various breeds

WO2007051248A1 entitled *Single Nucleotide Polymorphisms (SNP) And Their Association With Tick Resistance In Bovine Animals* from the Commonwealth Scientific And Industrial Research Organisation and others, relates to a method for assaying for the occurrence of a single nucleotide polymorphism which can lead to an increase in resistance.

9. A method as claimed in claim 8 wherein the cow is a pure breed selected from the group consisting of Ayrshire, Brown Swiss, Australian commercial dairy cow, Dairy shorthorn, Holstein, Guernsey, Sahiwal, Illawarra, Jersey, Meuse-Rhine-Issel, Red Poll, Sirnmental, Australian Red breed, Australian Friesian Sahiwal and Australian milking zebu, or crosses thereof. (WO2007051248A1)

No patent grants were observed in the family.

USA: Dexter and Angus

US20070238110A1. Iowa State University developed a genetic test for dwarfism in cattle.

> Next, we evaluated mutations know to cause dwarfism in Dexter cattle. For this study, DNA was sent to Australia for genotyping and CRC for Innovative Dairy Products, The University of Sydney, Camden, NSW, Australia. These mutations were not present in our American Angus samples. In addition, we completed a microsatellite analysis of this region to test for loss of heterozygosity. Again, the results were negative. Thus, the gene responsible for dwarfism in Dexter Cattle is different than that in American Angus cattle. Results of this genotyping are not included in this report, because the mutations and microsatellites tested were coded such that we cannot say what or where they are. This was done to maintain confidentiality, because there is a patent currently in review for these mutations. (US20070238110A1)

One patent grant US7700291B2 was observed in this family.

Australia: Various breeds

WO2007051248A1 by Commonwealth Scientific and Industrial Research Organisation et al developed a method for assessing tick resistance in cattle by "assaying for the occurrence of a single nucleotide polymorphism (SNP) identified in any one of SEQ ID Nos: 1 to 210, wherein the identification of said nucleotide occurrence is associated with increased tick resistance in the animal."

> A method … wherein the cow is a pure breed selected from the group consisting of Ayrshire, Brown Swiss, Australian commercial dairy cow, Dairy shorthorn, Holstein, Guernsey, Sahiwal, Illawarra, Jersey, Meuse-Rhine-Issel, Red Poll, Sirnmental, Australian Red breed, Australian Friesian Sahiwal and Australian milking zebu, or crosses thereof. (WO2007051248A1)

No patent grant was observed in this family.

Denmark & Sweden: Holstein

WO2009097862A1 by Aarhus University provides "genetic markers…for the determination of fertility in a bovine subject (and) its off-spring."

> Materials and methods: Population Danish and Swedish Holstein grandsire families were analysed in a granddaughter design. Twenty nine Danish and seven Swedish families were included. Five of the seven Swedish grandsire families also have sons in Denmark. The number of sons per grandsire ranged from 16 to 160 with an average of 6 1 sons per grandsire family. In total 2,182 sons were genotyped. (WO2009097862A1)

No patent grant was observed in this family.

Australia: Multiple breeds

WO2007112490A1 by Innovative Dairy Products Pty developed a method for predicting a phenotype in cattle by analysing a nucleic acid sample for the presence of genetic markers.

> Methods and Materials 1.1 DNA samples and selection of bulls. A panel of 1,546 Holstein Friesian bulls born between 1955 and 2001 was selected for genotyping. Most of these bulls were born in Australia (1,435) with smaller numbers being born in USA (53), Canada (35), New Zealand (8), Netherlands (8), Great Britain (3), France (3) and 20 Germany (1). There were more bulls from the recent cohorts than from older cohorts. This panel of bulls represents near-to-normal distributions for Australian Breeding Values (ABVs) for the most common production traits recorded through the Australian Dairy Herd Improvement Scheme. (WO2007112490A1)

No patent grant was observed in this family.

Netherlands: Holstein-Friesian

EP1226176B1. This patent grant to Mucovax Holding concerns the production of mammary secretion antibodies by administering compositions of antigens to mammary glands and lymph nodes for unspecified scientific and medical uses.

> Gestating Holstein-Friesian and MRY dairy cows were maintained according to generally accepted dairy management practices in the Netherlands. In experiments described in this communication, mostly Holstein-Frisian cows were employed. Additionally, pregnant goats were selected and maintained in a separate farm, also according to generally accepted management practices. (EP1226176B1)

Other patent grants in this family include AU779776B2, US6974573B2,

US7074454B1 and US7332165B2.

Japan: Holstein

EP1946766A1. This patent document from Hayashibara Biochem Laboratories states that, "the present invention has objects to provide a reproductive disorder remedy for warm-blooded animals."

> It is known that bovine easily gets a reproductive disorder accompanying decreased appetite and deteriorated health by stress from hot weather and delivery. […] Twenty-nine Holstein cows, all of them were three to seven years old, about 600 kg of body weight, and expected to deliver at August to September, were randomly divided into following three groups, a group for once administration (eight), that for three-times administration (nine), and that for no administration (12, as controls). For the group for once administration, one gram of the agent was administrated once per individual at seven days before expected date of delivery. For the group for three-times administration, one gram of agent was administrated once per day per individual through oral route for three days from seven days before expected date of delivery. The health conditions of cows before and after delivery were monitored and the results are in Table 1. (EP1946766A1)

One patent grant EP1946766B1 was observed in this family.

Netherlands: Holstein

EP2040566B1. This patent grant to Nutreco Nederland B.V. "relates to a ruminant feed supplement for the treatment of milk fever."

> Feeding rumen protected rice bran can change calcium balance and stimulate calcium homeostasis. In one trial, the product described in Table 1 was fed to nine pregnant non lactating Holstein cows at the Nutreco Ruminant Research Centre (Boxmeer, The Netherlands). The cows received 2000 g of product for a week, after having been monitored for one week. Thereafter they were observed for another week after the end of supplementation. The treatment produced a significant decrease in urinary calcium showing that calcium homeostatic mechanisms were triggered by the supplementation. The withdrawal of the treatment produced an increase in calcium excretion beyond the initial levels suggesting that calcium absorption had been up-regulated by the treatment. (EP2040566B1)

Other patent grants in this family include AU2007259468B2 and US8252349B2

Canada: Holstein

US7277744B2. This is a patent grant awarded to 4 Canadian inventors for "early detection of inflammation and infection using infrared thermography."

> Twenty mature lactating Holstein cows at 120 days post-partum were housed at the Agriculture and Agri-Food Canada Dairy Research Unit at Lennoxville, Quebec, and were managed in a manner consistent with and representative of the dairy industry in North America, and in compliance with the Canadian Council of Animal Care Guidelines. (US7277744B2)

Other patent grants in this family include AU766215B2.

India: Sahiwal Cattle

WO2003020038A1 is a PCT application from the Council of Scientific and Industrial Research in India. According to the application, "the present invention relates to a synergistic composition useful as bioinoculant, said composition comprising bacterial strains of accession Nos. NRRL B-30486, NRRL B-30487, and NRRL-B 30488, individually or in all possible combinations, and optionally carrier, with each of the strains showing plant promoter activity, phytopathogenic fungi controlling activity, abiotic stress conditions tolerating capability, phosphate solubilisation capability under abiotic stress conditions; further, a method of producing said composition thereof, and in addition, a method of isolating said bacterial strains from milk of the cow 'Sahiwal'."

> India is one of the few countries in world, which has contributed richly to the International livestock gene pool and improvement of animal population in world. Cattle and buffalo contribute nearly 15% of the gross national income. The country possesses 23% of world 25 bovine population … By far Sahiwal is the best breed of the subcontinent. (WO2003020038A1)

Patent grants in this family include AU2002345299B2, EP1423011B1 and US7097830B2.

UK: Friesian and Holstein

US6602676B1 from the Milk Development Council (UK) published in 2003 states that "This invention relates to a method of predicting pregnancy, particularly, in a cow." In connection with breeds it specifies that:

> Milk samples for P 4 assay and reproductive data were collected from British Friesian and Holstein Friesian cows in seven commercial herds. The cows were housed in a free-stall system and fed rations to meet their production and maintenance requirements. (US6602676B1).

The US patent grant is the only member of this patent family.

Predicting animal behaviour

Brazil: Nellore Cattle

WO2011116466A1 from the University of Alberta in Canada and Genoa Biotecnologia in Brazil published in 2011 addresses "a method for predicting cattle temperament and behaviour through the analysis of one or more single nucleotide polymorphisms (SNPs) mapped at specific regions of the bovine genome."

> Initially, a small group study of 1,189 cattle from the farm Jacarezinho (Aracatuba, SP - Brazil) were evaluated. All these animals were pure contemporary Nellore breed, having similar ages and were submitted to similar nutritional programs. The parameters measured in these animals behaviour after release from the crush (animals held for 5-10 minutes, blood samples taken, and then released) accounting were flight speed (FS) and plasma Cortisol levels. The term "flight speed" or "FS" as used herein is defined as the time to run 1.7 meters detected with sensors and measured in milliseconds. Cortisol levels in 1,189 cattle were analysed […]. Based on the asymmetrical distribution of Cortisol levels, two groups of animals, referred to as "inferior" and "superior" were selected for genotyping experiments. The "inferior" group of animals comprises animals with Cortisol values equal or lesser than the value of the 10th percentile (0.4 mcg/dL). The "superior" group comprises animals with Cortisol values equal or greater than 90th percentile (4.0 mcg/dL). The inferior group comprised 124 animals whereas the superior group had 19 animals available. A sample of 75 animals on each side is representative of polar behaviour. "Polar behaviour" as used herein means grouping of extreme calm or aggressive individuals." (WO2011116466A1).

No patent grant is presently reported in this patent family.

New Zealand: Holstein and Friesian

WO2011093728A1 from Vialactia Biosciences NZ Ltd "provides methods of genotyping mammalian subjects for desired lactoferrin phenotypes by determining the lactoferrin genotype of the subject."

> A Holstein Friesian x Jersey crossbred trial was conducted using an F2 trial design with a half-sibling family structure. Reciprocal crosses of Holstein Friesian and Jersey animals were carried out to produce six Fl bulls of high genetic status. 850 F2 female progeny forming the basis of the trial herd were then produced through mating of high genetic status Fl cows with these Fl bulls. The herd was formed over two seasons; animals in cohort one were born in

spring 2000, and entered their first lactation in spring 2002, while animals in cohort two were born in spring 2001 and entered their first lactation in spring 2003. A total of 724 F2 cows entered their second lactations and colostrum samples collected from over 600 of these. The animals were farmed under standard New Zealand dairy farming practices using a pasture based management system. All animal work was conducted in accordance with the Ruakura Animal Ethics committee. (WO2011093728A1)

No patent grant is presently reported in this patent family.

New Zealand: Friesian and Jersey

WO2010087725A2 from the Fronterra Cooperative Group of New Zealand undertook work to mutate the DGAT1 gene in cattle to produce altered milk.

Genomic DNA was isolated from whole blood or semen from 185 sires frequently used for artificial insemination in the New Zealand dairy population, and from 80 sires and 1595 cows representing the BoviQuest Friesian-Jersey crossbreed herd (Spelman RJ, et al., 2001, Proc. Assoc. Advmt. Anim. Breed. Genet. 14:393-396). The samples were genotyped for the A8078C mutation in a custom-designed Gold assay (SEQUENOM, San Diego, CA, USA) using the PCR primers given in SEQ ID NO:5 and SEQ ID NO:6, and the extension primer given in SEQ ID NO:7. DNA from eight animals from the Cow 363 pedigree heterozygous for the mutation was used as positive controls. (WO2010087725A2)

No patent grant is presently reported in this patent family.

Sheep and Goats

Table 5.3: Documents Referencing Breeds of Sheep

Number and Year	Title	Applicant	Family Members	Citations
WO2009065204A1 2009	Method of identifying prolificacy in Mammals	Brasil Pesquisa Agropec	7	0
US20020004051A1 2002	Materials and methods for preventing, or reducing the severity of heart water disease in animals	University of Florida	2	0
WO2010114398A1 2010	Cell culture system	Agres Ltd	1	0
EP1423141B1 2004	Vaccine	Massey University and New Zealand Meat Board	7	0
WO1999054443A1 1999	Human bile slat-stimulated lipase (BSSL) obtainable from transgenic sheep	Astra AB and PPL Therapeutics	10	4

Table 5.4: Documents Referencing Breeds of Goats

Number and Year	Title	Applicant	Family Members	Citations
EP0241272A2 1987	Method of stimulating cashmere growth on cashmere producing goats using melatonin	New Zealand Scientific and Industrial Research	3	1
WO1997019589A 1997	Method for development of transgenic goats	Nexia Biotech Inc	8	7

Sheep Breeding

New Zealand: Booroola

WO2001048204A1. *Mutilated BMP1B Receptor As Regulator Of Ovulation Rate* by Agres Ltd, relates to a sequence, which differs from wild type polypeptides that can be used in a test to identify heterozygous or homozygous female and male sheep.

> The Booroola Merino rates among the top breeds of sheep in the world in terms of ovulation rate. Sheep derived from the Booroola Merino strain carry a major autosomal mutation that increases ovulation and litter size (Davis et al 1982), and the mutation has been named FecB (fecundity). The effect of FecB is additive for ovulation rate (ovulation rate increasing by about 1.5 for each copy) and on average, one copy of FecB increases litter size by about one extra lamb and two copies increase litter size by about 1.5 lambs. Homozygotes FecelFece

(1313), heterozygotes FecelFeck-(B+) and noncarriers Feeff'-Yeeff'-(++) of the Booroola gene can be segregated on the basis of ovulation-rate recordings. The physiological effects of the FecB gene have been extensively characterised (McNatty et al 1986, 1987, Hudson et al 1999). There is evidence that the high ovulation rate of the FecB B FecBB ewes may be related to an alteration in intraovarian regulation (Fry et al 1988, McNatty et al 1993) 1 Application of the Booroola gene in the sheep industry A Booroola ram is currently of added value if the carrier status of the ram is known. Rams carrying the Booroola gene have been exported to many countries, including France, Britain, South Africa, Poland, Chile, Israel, Netherlands and the USA, with the intention of introgressing the high lambing found in the Booroola into their own flocks. (WO2001048204A1)

See the 2004 grant AU772907 associated with this patent family.

Sheep health

Brazil: Santa Ines Sheep

WO2009065204A1 by Brasil Pesquisa Agropec developed a method of predicting prolificacy in mammals, by means of analysing a specific molecular marker for a novel mutation correlated to the increase of the ovulation rate.

Example 1: Sequencing of exon 2 in the GDF-9 gene in the naturalized Brazilian strain Santa Ines. The objective of this task was to sequence the exon 2 in the GDF-9 gene, which includes the coding region of the mature peptide, in ewes of the naturalized Brazilian strain Santa Ines. The ewes analysed were descendants of multiple births, being candidates for presenting alterations in the GDF -9 gene. (WO2009065204A1)

No patent grant is presently reported in this patent family.

Zimbabwe: Merino sheep

US20020004051A1 This patent application from the University of Florida "pertains to materials and methods for preventing, or reducing the severity of, heart water disease in animals" and makes specific reference to sheep from Zimbabwe.

Merino or Merino-Dorper-cross sheep (6 months old) were used in vaccine trials. These sheep were obtained from heart water-free farms in Ruwa and Mazowe in the regions of the highveld of Zimbabwe, where both Amblyomma tick vectors and heart water have not been recorded since the start of veterinary surveillance around the turn of the century. Although they were free of heart water, some sheep were serologically positive (false positives) on C.

ruminantium antigen immunoblots due to cross-reactions with agents such as Ehrlichia species. It has previously been shown that such sheep are fully susceptible to heart water challenge. To avoid any bias, such false positive sheep were distributed equally into vaccinated and control groups. The vaccinated groups were inoculated with the inactivated organisms with adjuvant and the control groups with adjuvant mixed with phosphate buffered saline (PBS; NaH2PO42H 2O, 0.0028 M; Na2HPO 4; 0.0072M; NaCl, 0.15 M; pH 7. 3), except in the adjuvant selection trial described below. All inoculations were performed by the subcutaneous route, and any reaction at the injection site was recorded. In addition, any clinical reaction following vaccination was also recorded. Following challenge with a lethal dose of C. ruminantium (intravenous or via ticks), the rectal temperature of each sheep was recorded daily, and protection was determined by comparing differences in rickettsemia, time to death, and mortality rates between the vaccinated and control sheep. However, the ultimate indicator of protection was the level of mortality in the vaccinated compared to control groups. Clinical signs, though recorded, were not used as a parameter of protection since they are not specific for heart water and can vary widely from per acute to mild forms of the disease. (US20020004051A1).

One patent grant US6342230B1 is recorded in this patent family.

New Zealand: Romney, Dorset and composite breeds

WO2010114398A1 by Agres Ltd is for a "method of preparing a dermal papilla cell culture which assists the aggregative behaviour of the cells" using cells collected from sheep.

Experiments also varied in the degree to which the aggregation was completed. In some cases, the process stopped at the fourth or even the third stage described above. There was also variation between cell strains isolated from different animals. A few strains never aggregated well enough to allow robust measurement of aggregate size. Of a total of 19 cell strains isolated to date from 12 sheep of New Zealand strongwool breeds (Romney, Romney x Dorset, and composite breed), 11 aggregated well and have been used in quantitative assays, five have initially aggregated but have not been tested in a standard assay, and three did not aggregate during the derivation process. In the useful cell strains, the aggregative behaviour was stable for at least five passages. (WO2010114398A1)

No patent grant is presently reported in this patent family.

New Zealand: Romney lambs

EP1423141B1 from Massey University was published in 2012 and claims a vaccine for vaccination against Johne's disease.

> Studies were performed with three-month old male neutered Romney lambs obtained from Massey Agricultural Services, Palmerston North, New Zealand. The animals were kept on farming blocks with open grazing and water ad libitum. The sheep used in this study were selected on the basis of negative reactivity with Johnin PPD mycobacterial antigen. (EP1423141B1).

Examples of patent grants in this family include US7387773B2, US7758875B2 and AU2002326240B2.

Transgenic sheep

UK: Poll Dorset

WO1999054443A1 from Astra AB and PPL Therapeutics is directed to: "transgenic sheep whose germ cells and somatic cells contain a recombinant nucleotide molecule comprising a nucleotide sequence encoding for human BSSL. The invention also relates to methods for producing said transgenic animals, as well as to methods for producing human BSSL derived from transgenic animals."

> Production of Transgenic Sheep 2.1 Source and organization of the animals. The study used only adult ewes and adult rams of the Poll Dorset breed which had been resident at PPL Therapeutics, East Mains, Ormiston, since their importation from New Zealand or which were born at East Mains. All ewes were more than 12 months old at the start of the study. All rams had proven fertility during 1994. (WO1999054443A1)

Patent grants in this family include AU758725B2 and US6525241B1.

Fibre production: Goats

Australia and New Zealand: Cashmere goats

EP0241272A2 from New Zealand Scientific and Industrial Research from 1987 concerns a method using melatonin for stimulating cashmere growth on cashmere producing goats.

> Many more goats and goat farmers are required and the production of each goat must be increased substantially from 50 to 200 gm/animal. Currently in New Zealand, large numbers of feral animals are being screened for high cashmere production. Bucks with cashmere weights of 250-400 gm/animal have been identified. In Australia, feral bucks with weights of 600-800 gm/animal are

being used for breeding and it seems certain that similar animals will be found in New Zealand once the screening process has been running for a time. In the meantime, high producing bucks are being imported into New Zealand from Australia and semen from these animals is being distributed around New Zealand by commercial organisations. (EP0241272A2).

No patent grant is presently reported in this patent family.

Increased milk production: Goats

Canada: Nigerian Dwarf Goats

WO1997019589A from Nexia Biotech published in 1997 identifies a "method for development of transgenic goats."

> By "transgene" is meant a DNA sequence introduced into the germ line of nonhuman animal by way of human intervention such as by any of the methods described herein. By "dwarf goat" is meant a Nigerian Dwarf goat or a Pygmy goat or any other goat of small size comparable to that of a Nigerian Dwarf goat or a Pygmy goat. (WO1997019589A1)

> Recent evaluation of the milk of a Nigerian dwarf doe from our herd found average of 5.6% fat, 4.3% protein and 4.9% lactose (8 samples). This surpasses the standard goat average protein content of 3.0% for a Quebec dairy reporting lactational yields for 34 milking dairy goats (Canadian Goat Society Quarterly, Nov. 1994). (WO1997019589A1).

Patent grants in this family include AU721132B2 and EP0871357B1.

Equine

Table 5.5: Documents Referencing Breeds of Horses

Number and Year	Title	Applicant	Family Members	Citations
WO2011149419A 2011	Vaccine against streptococcal infections based on recombinant proteins	Intervacc	6	1

UK: Welsh Mountain Ponies

WO2011149419A from Intervacc is for a vaccine against Streptococcal Infections based on recombinant proteins:

> This vaccination and challenge study was performed at Animal Health Trust, Lanwades Park, Kentford, Newmarket, Suffolk, CB8 7UU, UK sponsored by Intervacc AB Sweden (study identification B009/001). Study II (study

identification B009/002) was also performed at the same location. The objective of these studies were to determine the level of protection conferred on vaccination with variants of Intervacc's new multi-component subunit vaccine following intranasal challenge with wild type S. equi strain 4047 in Welsh Mountain ponies. (WO2011149419A1)

No patent grant is presently reported in this patent family.

Avian

Table 5.6: Documents Referencing Breeds of Birds

Number and Year	Title	Applicant	Family Members	Citations
WO2008142124A1 2008	Recombinant protein production in avian EBX TM cells	Vivalis	13	13

France: White Leghorn Chickens and Peking Ducks

WO2008142124A1 by Vivalis of France "relates to the use of avian embryonic derived stem cell lines, named EBx TM, for the production of proteins and more specifically glycoproteins such as antibodies" and their uses in the treatment of cancer and inflammatory diseases.

EXAMPLE 1: chicken EByl3 cell line from SPF chicken strain VALO 1.1 - RAW MATERIAL Eggs Specific Pathogen Free (SPF) strain called VaIo. The valo strain is a white Leghorn strain produced and delivered by Lohmann from Germany. Those SPF chicken eggs, supplied with a certificate of analysis, are tested for: CAV, Avian adenoviruses (group 1, serotypes 1-12 and group 3), EDS, Avian Encephalomyelitis Virus, Avian Leukosis Viruses/RSV (including Serotype ALV-J), Avian Nephritis Virus, Avian Reoviruses, Fowlpox Virus, Infectious Bronchitis Virus, Infectious Bursitis Virus (IBDV), Infectious Laryngo Tracheitis Virus, Influenzavirus Type A, Marek's Disease Virus, Mycoplasmosis (Mg + Ms), Mycobacterium avium, Newcastle Disease Virus, Reticuloendotheliosis Virus, Salmonella pullorum, Other Salmonella Infections, Avian Rhinotracheitis Virus (ART), Hemophilus paragallinarum. VaIo chicken eggs were only submitted to a disinfection with the decontaminant to avoid any risk of contamination linked to the manipulation of eggs during the transport. (WO2008142124A1)

EXAMPLE 2: Duck EBx cell line EB66 2.1 - RAW MATERIAL Duck Eggs Duck eggs from Peking strains GL30 were obtained from GRIMAUD FRERES SELECTION (La Corbiere, Roussay France). The parent ducks were vaccinated against Escherichia CoIi (Autogenous vaccine CoIi 0 1 & 02), Pasteurella

multocida (Landavax), Duck viral hepatitis (Hepatovax), Erysipelothrix rhusiopathiae (Ruvax), Avian metapneumovirus (Nemovac), Salmonella typhimurium & Enteridis (Autogenous vaccine), Riemerella antipestifer (Autovaccine Riemerella), Avian metapneumovirus (Nobilis RTV inactive) and Erysipelothrix rhusiopathiae (Ruvax). After receipt, fertilized Peking duck eggs were submitted to a disinfection in an hypochloryde bath followed by decontamination with Fermacidal (Thermo) to avoid any risk of contamination linked to dusts attached on the shell. (WO2008142124A1)

Patent grants in this patent family include AU2008252902B2 and EA17964B1.

Annex Summary*

Annex 1 – Co-occurrence Analysis

This Annex document describes the process used to identify technology clusters in the patent landscape for animal genetic resources.

Annex 2 – Search Terms

Annex 2 contains relevant terms used in sub-searching patent documents previously identified by text-mining for FAO Animals and classification (technology) co-occurrence analysis. It consists of the following Excel worksheets:

1. *Subsearch terms*: List of breeding related terms identified from Derwent World Patent Index (DWPI) and Web of Science (WoS) scientific literature. Includes a review of the WoS terms.
2. *New Breeds of Animals Cluster Subsearch*: Term co-occurrence cluster matrix within the New Breeds of Animals technology cluster.
3. *Biotechnology Cluster Subsearch*: Term co-occurrence cluster matrix within the Biotechnology technology cluster.
4. *FAO Biotechnology Terms*: Full and edited list of Biotechnology terms obtained from the Food and Agriculture Organisation.
5. *FAO Biotechnology Terms and Species Co-occurrence in Patent Claims*: Counts for term and multi-term co-occurrence with animal names (species).
6. *FAO Biotechnology Terms, Species and Patent Publication Cross Reference*: A table of terms, animal name and patent publication number references.

Annex 3 – Patent Classification Review

Annex 3 contains a review of the IPC and CPC codes identified in patents found by text- mining animal Latin and common names. It consists of the following Excel worksheets:

1. *Identified IPC Review*: Tri-party review of IPC codes and their relevance to FAO Animal Genetic Resources (AGR) split into those obtained by Latin and common species names.
2. *Identified CPC Review*: Review of CPC codes relevant to AGR.
3. *Cumulative Classification Reduction for IPC Codes*: Investigates the impact of each IPC code on the universe of publications.

Annex 4 – Breed Review

Annex 4 contains a review of text-mined breed names in the patent universe. It consists of the following Excel worksheets:

1. *Breeds Review*: Lists of identified breed names with bibliographic information and a manual review based on context.
2. *Breeds Context*: A list of all the texts surrounding breed names matches in the patent universe.
3. *Reviewed Breeds from New Breeds of Animal Cluster*: Breed instances reviewed using MAXQDA.
4. *Reviewed Breeds from Biotechnology Cluster*: Breed instances reviewed using MAXQDA.

Annex 5 – Publication Summary

Annex 5 contains a list of patents references including harmonization information such as Family Numbers, species in titles, abstracts and claims (TAC), terms and classification clusters. It consists of the following worksheets:

1. *Universe Summary*: All publications identified by text-mining Latin and common animal names in patents from the major jurisdictions.
2. *Indicator Summary*: All publications within the Patent Indicator for Animal Genetic Resources for Food and Agriculture.

*The Annexes are available in the electronic version of the report.

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