



REPUBLIC OF THE PHILIPPINES

**Intellectual Property Office
of the Philippines**

GUIDELINES ON THE EXAMINATION OF BIOTECHNOLOGICAL APPLICATIONS

(Biotech Guidelines)

October 2022

FOREWORD

The first Examination Guidelines for Biotechnology was completed and published last 2018. Since then, there have been a lot of advancements in the field of biotechnology, so it is time to update this Biotechnology Examination Guidelines with more current information. This year, a Technical Working Group (TWG) was formed to work on the revision/update of the guidelines, based on the patent examination issues observed and reported by the BOP's Quality Management Unit and other patent practitioners.

The Biotechnology Examination Guidelines was created in line with IPOPHIL's strategic goals of delivering quality and timely patents, and of developing and maintaining a highly-motivated, competent, and cohesive workforce committed to serving with professionalism, transparency, and integrity. The guidelines are intended to be flexible and adaptable to new technologies, new scientific knowledge, and new trends in patent examination in the field of Biotechnology.

In the past 4 years, many advancements in biotechnology have led to new interpretations and approaches in examining patent applications in this field. These advances have also led to changes in strategy and understanding and interpretation of biotechnology applications.

This updated version has been collaboratively written by a group of Patent Examiners from the Medical Science & Biopharmaceutical Examining Division (MSBED) and Agricultural & Biotechnology Examining Division (ABED).

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TABLE OF CONTENTS

I. INTRODUCTION	4
II. BACKGROUND	6
III. DEFINITION OF TERMS	9
IV. INVENTIONS INVOLVING BIOLOGICAL MATERIALS	19
1. MICROORGANISMS	25
1.1 Eligibility	25
1.2 Novelty	25
1.3 Inventive Step	26
1.4 Enablement	27
1.5 Amendment of Accession Number of the Deposit	32
1.6 Illustrative Examples of Claims Involving Microorganisms	33
2. NUCLEIC ACIDS AND POLYPEPTIDES	36
2.1 Eligibility	36
2.2 Novelty	40
2.3 Inventive Step	42
2.4 Clarity/Enablement/Support	47
3. ANTIBODIES	53
3.1 Eligibility	53
3.2. Novelty	53
3.3 Inventive Step	58
3.4 Clarity/Enablement/Full Support	62
4. STEM CELLS	66
4.1 Eligibility	66
4.2 Public Order and Morality	72
4.3 Enablement	73
4.4 Novelty	74
4.5 Inventive Step	75
5. PLANTS AND ANIMALS	79
5.1 Eligibility	79
5.2 Novelty	86
5.3 Inventive Step	86
5.4 Enablement/Full Support	89
V. SUPPLEMENTAL DISCUSSIONS	92
Unity of Inventions Issues	92
A Priori Determination of Unity of Invention	93
A Posteriori Determination of Unity of Invention	94
Sequence Claims	99

ANNEX “A”	102
Claim Construction	102
ANNEX “B”	105
The Budapest Treaty	105
Where to Make a Deposit?	105
New and Substitute Deposits	105
ANNEX “C”	107
Suggested Readings	107
A. Patentability of Plants	107
B. Patentability of Animals	108
C. FUNK BROTHERS SEED V KALO INOCULANT	111
D. DIAMOND V CHAKRABARTY	111
E. AMP V MYRIAD	111
REFERENCES	112

REVISION HISTORY

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	00	January 2018	Initial Issue
	01	October 2022	Update

I. INTRODUCTION

Biotechnology as defined in Article 2 of Nagoya Protocol, means “any technological application that uses biological systems, living organisms, or derivatives thereof, to make or modify products or processes for specific use.”

Biotechnology is the focus of industries and specialists in today's innovation world, and it is making such astounding progress. Advances in biotechnology are so rapid that a lot of things are now possible, which, a decade ago would have seemed unimaginable. In the late 1970s, the development of gene-splicing technology (genetic engineering) marked the beginning of contemporary biotechnology. It is a type of genetic engineering in medical and veterinary research resulting in modified production and improved organisms. It is the use of microorganisms, plant and animal cells and their products for industrial, agricultural and medical purposes. More of the recent breakthroughs include cancer detection test using saliva as sample, absorbable heart stents, nanogels comprising peptides that can heal wounds faster than conventional dressing, and so on, which have been made utilizing genetic engineering along with many other inventions that improve the quality of human life.

Since the advent of biotechnology, it has been bringing to forth “unanticipated inventions”. It was not initially thought that biotechnology could manipulate either the plant or animal being, and therefore no one has ever thought of the need for evolving a comprehensive patent law on biotechnology for regulation was unforeseen. Rapid technological development in biotechnology has led to huge challenges for scientists and innovators, particularly in patenting biotechnological inventions. More specifically, inventions involving genes elicited public debates due to discomfiture with patenting natural products and the practical concerns with its consequences - balancing the need for commercial incentives to develop treatments and screening tests with the virtues of open science. Simply put, the controversies are amplified when the patent is on a building block of life.

In more recent years, discussions regarding innovations, including in the area of biotechnology, and genetic resources based on traditional knowledge gleaned from indigenous peoples and local communities have arisen and been conducted. The enactment of different laws and regulations concerning biodiversity, bioprospecting, prior informed consent, traditional medicine, and the conservation of wildlife resources is the result of an awareness of its significance for future generations. The Philippines has a huge potential for using TK to produce food and medicine because it is one of the world's largest

repositories of various biological resources in terms of plant and animal species.

In December of 2006, IPOPHL and Filipino health representatives met with joint delegations from the European Patent Office (EPO) and the State Intellectual Property Office (SIPO) of the People's Republic of China for potential information gathering and the creation of TK databases in the Association of Southeast Asian Nations' IP offices (ASEAN).¹

Several concerns connected to the patentability of biotechnological inventions, such as patent eligibility, novelty, inventive step, industrial applicability, enabling disclosure, and clarity of claims, are of great interest to users of the Patent System. The objective of this guideline is to assist Patent Examiners in conducting quality examinations and to enhance the appropriateness of practice in substantive examination in the field of Biotechnology. Certain principles in national laws based on international patents and conventions have caused doubt about the protection of biotechnological inventions, and thus, harmonization is required to clear up the confusion.

This 2022 edition of the Guidelines is an update of the Guidelines published in January 2018.

¹ Agillon, A.B., 2007

II. BACKGROUND

Biotechnology inventions, like all other technologies, are typically deemed patentable under the law, and all inventions are subject to the same general patent examination criteria and processes.

Article 27.1 of the TRIPS Agreement provides that "patents shall be available for any inventions, whether products or processes, in all fields of technology, provided that they are new, involve an inventive step, and are capable of industrial application." These requirements are uniform for all patent offices worldwide. However, biotechnology-related inventions require more than just meeting these "traditional" requisites; advances in biotechnology are bound up in ethical, religious, political and legal issues, and therefore might be prosecuted in the way more conventional inventions are prosecuted.

The distinction between a non-patentable "product of nature" and a patentable "non-naturally occurring composition of matter" was settled for the first time by US SC decision in *Diamond vs. Chakrabarty*, wherein patent was granted for laboratory-engineered bacteria that had the capacity to degrade crude oil. Subsequently, in 1998, the Trilateral Offices (EPO, JPO and the USPTO) issued a joint statement asserting that "purified natural products are not regarded as products of nature or discoveries because they do not in fact exist in nature in an isolated form. Rather, they are regarded (for patent purposes) as biologically active substances or chemical compounds and eligible for patenting on the same basis as other chemical compounds". This seemed to be the general principle adopted by national offices, including the IPOPHL, when formulating their respective guidelines in the examination of biotech inventions.

With regard to inventions on genes, the approach of some of the big IP offices, notably EPO and the JPO, is to grant patents only for isolated and purified gene sequences with a demonstrated utility. In other words, these offices look at the usefulness and industrial applicability of the isolated gene. The USPTO, on the other hand, treats isolated and purified gene sequences as products of nature and are, therefore, not eligible for patent. The USPTO does not look at the utility of isolated and purified gene sequence, but only that it was a product of nature versus an article of manufacture.

Patent Offices face continuing challenges, both in the international and domestic level, when examining patent applications for biotech inventions. Oftentimes, different national offices interpret the same provisions differently - some offices can be more liberal; the others follow the more stringent approach. The *Oncomouse* case highlights how different jurisdictions have

dealt with the same subject matter, and how they weighed the ethical dimension of a particular technology. Oncomouse (US 4736866 and two more subsequent patents), a transgenic mouse inserted with genes that are susceptible to developing tumors, provided valuable means for furthering cancer research. USPTO granted the patent for Oncomouse at a broad spectrum (non-human mammal). On the other hand, EPO initially refused the application; only after a lengthy series of rejections and appeals, and evaluations using the utilitarian cost/benefit approach, was the patent granted but limited only to the mice instead of the broader term "non-human mammals". The same utilitarian approach to the morality issue was applied by EPO in the case of a transgenic mouse for the treatment of hair loss, this time by Upjohn Company (EP 89 913 146.0), but with a different outcome. These are only a few among a slew of cases that illustrate how the benchmarks used by examiners in assessing the patentability of biotech are constantly changing, as the technology itself advances at a considerable pace.

Rationale

The Bureau of Patents has already received hundreds of applications that pertain to various areas of biotechnology. Examination of these applications is made in accordance with the IP Code and the Amended Implementing Rules and Regulations (IRR) on Patents, Utility Models and Industrial Designs. However, subject matters in the field of biotechnology are rapidly evolving, and by nature, elicit technical and ethical issues. Provisions in the IP Code and the IRR are becoming too general to address these highly specific topics; as a result, prosecution of biotech applications has become lengthy and subjective.

Currently, the substantive examination is guided by the IRR and the Manual of Substantive Examination Practice (MSEP). The IRR leads the examiners in making intentional decisions, whereas MSEP provides general instructions intended for standard applications. Examiners of biotech applications also use as reference the examination decisions of other patent offices. While the IRR and the MSEP have provided invaluable guidance, there is a need for a set of guidelines specific to biotech applications due to the advent of unanticipated inventions and issues that are beyond the realms of the MSEP.

The Guidelines for Examination of Patent Applications in the Field of Biotechnology put together the best practices in resolving the issues that clearly entail biotech inventions, and guide the examiners to the most relevant approach to most cases. These guidelines will not only help address the current technical and ethical issues in biotech applications but will also anticipate future ones. If these guidelines contradict the terms of Republic

Act 8293 and the Revised Implementing Rules and Regulations on Inventions, the provisions of the Act and Rules will take precedence over these guidelines.

The Guidelines provide definitions of biotechnology-related terms in the context of patent laws, and specific examples of eligible and non-eligible subject matters which are provided only in general terms in the IP Code and the IRR. For example, the guidelines establish a streamlined approach for determining the eligibility of inventions that are commonly mistaken as "discoveries" or "products of nature". It also endeavors to distinguish transgenes from varieties by providing criteria that separate the two. Stem cells, one of the highly polarizing subject matters due to the nature they are harvested and their practical uses, are discussed extensively and boundaries are set between what are eligible stem cells from those that are not.

III. DEFINITION OF TERMS

For the purpose of the Guidelines, these terms will be used within the context of the following definitions:

Allele

One of two (or more) variants of a gene, appearing at a particular location on a chromosome. Alleles contribute to the organism's phenotype, the organism's outward appearance. The DNA sequences controlling the traits are usually found in two copies in a eukaryotic genome wherein each copy or allele is inherited from one parent. The gene's two alleles are located in the same region in two homologous chromosomes, one inherited from each parent. The alleles may be dominant or recessive which therefore determines the expression of certain traits.

Antibody

It is a protein component of the immune system that circulates in the blood, recognizes foreign substances like bacteria and viruses, and neutralizes them. After exposure to a foreign substance, called an **Antigen**, antibodies continue to circulate in the blood, providing protection against future exposures to that antigen.²

Asexual propagation in Plants

It involves taking a part of one parent plant and causing it to regenerate itself into a new plant. The resulting new plant is genetically identical to its parent. Asexual propagation involves the vegetative parts of a plant: stems, roots, or leaves.³

American Type Culture Collection (ATCC)

It is a private, nonprofit organization committed to the acquisition, preservation, authentication, and distribution of diverse biological materials.⁴

Biotechnological Inventions

Inventions concerning biological materials, or the process of their production, modification, or utilization.

² National Human Genome Research Institute, October 2022

³ Sorensen & Garland, n.d.

⁴ Berns et al., 1996

Refer to techniques that use living organisms, or parts of them, in order to make or modify products, or to improve or modify certain or all the characteristics of plants, or animals, in order to develop micro-organisms, and organisms intended for specific uses.⁵

Biological Material

Any material containing genetic information, which can replicate directly (on its own), or indirectly, in a given biological system. Biological materials capable of direct replication include plants and animals (and their derivatives), microorganisms, cells and hybridomas. Biological materials that replicate indirectly include viruses, nucleic acids (genes, vectors), polypeptides (proteins, amino acids) and antibodies.

Basic Local Alignment Search Tool (BLAST)

An online search tool which allows the identification of regions of similarity between biological sequences (nucleotide or protein).

Breed

A group of animals of a certain species that through generations of selective breeding has become uniform in performance, appearance, and selection history.⁶

Callus

Unorganized and undifferentiated mass of plant cells.

cDNA

It is a copy of a messenger RNA (mRNA) which is produced by reverse transcription. The difference between a DNA and a cDNA is that DNA comprises both the coding (exons) and non-coding (introns) sequences, whereas cDNAs are usually used for cloning eukaryotic genes in prokaryotes and do not contain non-coding (introns) sequences. cDNA does not exist in nature.

Complementary Determining Region (CDR)

A polypeptide sequence of a variable domain of an immunoglobulin that is particularly responsible for its recognition by lymphocytes. These short

⁵ GLP, 2002

⁶ Oldenbroek et al., 2014

sequences interrupt and loop out from the framework regions (FRs), which are relatively invariant and form the basic structural β -sheet scaffolding of the domains.⁷

Destructive use of human embryo

The use of a human embryo may constitute the process of killing, aborting and other processes that would destroy the human embryo and disrupt the differentiation resulting in a fully developed organism.

Dedifferentiation in Plants

The process by which mature cells reverse their differentiated state and acquire pluripotency.⁸ The phenomenon where mature cells revert to a meristematic state to produce callus.

Diagnostic Method

The determination of the nature of a medical condition of a human or animal, usually by investigating its history, etiology, and symptoms and by applying tests.

Epitope

Also known as “antigenic determinant”, is a group of amino acids or other chemical groups exposed on the surface of a molecule, frequently a protein, which can generate an antigenic response and bind antibodies.⁹

Essentially Biological Process for the Production of Plants and Animals

A process which is based on the sexual crossing of whole genomes and on the subsequent selection of plants or animals, even if such process involves human intervention- including the provision of technical means, serving to enable or assist the performance of the process. This applies even if other technical steps relating to the preparation of the plant or animal or its further treatment are present in the claim before or after the crossing and selection steps.

EU Numbering system or EU Index

It is a numbering scheme based on the sequential numbering of the first human IgG1 sequence. It is usually used erroneously as synonymous with

⁷ GenScript, 2002-2022

⁸ Differentiation, Dedifferentiation and Redifferentiation in Plant Tissue Culture, n.d.

⁹ Science Direct, 1996

the Kabat sequence manual or Kabat Numbering. However, the EU index does not provide insertions and deletions which therefore results to clarity issues on the comparisons of IgG positions across IgG subclass and species.¹⁰

E-value

(Expectation value) is a number that describes how many times you would expect a match by chance in a database of that size. The lower the E value is, the more significant the match.¹¹

1. **E-value = 1e-50**: BLAST hits with an E value smaller than 1e-50 include database matches of very high quality.
2. **E-value = 0.01**: BLAST hits with E-value smaller than 0.01 can still be considered a good hit for homology matches, but this is not considered a 'good' e value.
3. **E-value = 10**: many hits, partly of low quality. E-value smaller than ten will include hits that cannot be considered as significant as a low e value, but if it is a divergent virus, the e value may be high.

Explant

Any excised piece of differentiated tissue or organ taken from a plant or an animal that will be used to initiate a culture. It can be a portion of the shoot, or of the leaves, or even just some cells.

Fc Region

It is a region of immunoglobulin that allows interaction of the immune complex with other phagocytic cells and complement and also takes part in various biological functions that are determined by amino acid sequences of each domain of constant region.¹²

Kabat Numbering

It is a widely adopted and accepted standard for numbering the residues in an antibody in a consistent manner. CDRs when not defined by their specific sequence can be defined according to a Kabat numbering scheme.¹³

¹⁰ An, Z. (Ed.) (2009). Therapeutic Monoclonal Antibodies: From Bench to Clinic. p. 350

¹¹ Chan Zuckerberg Initiative, 2022.

¹² Gaurab Karki, 2018

¹³ UCL, n.d., *The Kabat Numbering Scheme*

Genetic Engineering

A technique of artificially manipulating genes by gene recombination, cell fusion or the like.

Heterologous Gene Expression

The introduction of either complementary DNA (cDNA) or complementary RNA (cRNA) encoding for a protein of interest from one species into the cell of another species, such that the hosts' cellular machinery expresses the foreign protein.

Embryo

An early stage of development of a multicellular diploid eukaryotic organism. In general, in organisms that reproduce sexually, an embryo develops from a zygote, the single cell resulting from the fertilization of the female egg cell by the male sperm cell. The zygote possesses half the DNA of each of its two parents. The zygote will begin to divide by mitosis to produce a multicellular organism. The result of this process is an embryo.

In humans, a pregnancy is generally considered to be in the embryonic stage of development between the fifth and the eleventh weeks after fertilization and is expressed as a fetus from the twelfth week.

In plants, a young, developing plant, such as the rudimentary plant inside the seed of higher plants or that inside the archegonium of mosses and ferns.

Immunoglobulins (Ig) or antibodies

These are glycoproteins produced by plasma cells having two light chains and two heavy chains in a light-heavy-heavy-light structure arrangement.¹⁴

Induced Pluripotent Stem Cells

Induced Pluripotent Stem Cells are Pluripotent Stem Cells derived from skin or blood cells that have been reprogrammed back into an embryonic-like pluripotent state that enables the development of an unlimited source of any type of human cell needed for therapeutic purposes¹⁵

¹⁴ Justiz Vaillant & Ramphul, 2020

¹⁵ <https://stemcell.ucla.edu/induced-pluripotent-stem-cells>

***In vitro* Fertilization**

In vitro fertilization (IVF) is a complex series of procedures used to help with fertility or prevent genetic problems and assist with the conception of a child. During IVF, mature eggs are collected (retrieved) from ovaries and fertilized by sperm in a lab. Then the fertilized egg (embryo) or eggs (embryos) are transferred to a uterus. One full cycle of IVF takes about three weeks.¹⁶

Microorganisms

Organisms that are invisible to the naked eye, including bacteria and other generally unicellular organisms with dimensions beneath the limits of vision which can be propagated and manipulated in a laboratory, including plasmids and viruses and unicellular fungi (including yeasts), algae, protozoa and, moreover, human, animal and plant cells.

Isolated plant or animal cells or *in vitro* plant or animal cell cultures are treated as microorganisms, since cells are comparable to unicellular organisms.

Microbiological process

Any process that makes use, or results in, a microbiological material, comprising steps that may be microbiological or non-microbiological in nature.

Monoclonal Antibody

Represents antibodies from a single antibody producing B cell and only binds with one unique epitope.¹⁷

Mutant Plants

Are a random event and require a large population for screening the best desired mutants. It is usually considered as naturally-occurring and can be unpredictable. Plant mutations, known as sports, breaks, or chimeras, are naturally occurring genetic mutations that can change the appearance of the foliage, flowers, fruit or stems of any plant.

Mutation

It is sometimes called a variant. Germline mutations which occur in eggs and sperm can be passed onto offspring, while somatic mutations which occur in body cells are not passed on.

¹⁶ <https://www.mayoclinic.org/tests-procedures/in-vitro-fertilization/about/pac-20384716>

¹⁷ Mills, et al., 2020

Nucleic acids

Long chainlike molecules composed of a series of nearly identical building blocks called nucleotides, that serve as the primary information-carrying molecules in cells as well as in viruses. Each nucleic acid contains four of five possible nitrogen-containing bases: adenine (A), guanine (G), cytosine (C), thymine (T), and uracil (U). The two main classes of nucleic acids are deoxyribonucleic acid (DNA) and ribonucleic acid (RNA).

Percent Identity

A number that describes how similar or related the query sequence is to the target sequence (how many characters in each sequence are identical). The higher the percent identity is, the more significant the match. A query sequence can have a low % identity, but still be a real hit. It is essential to take the e value into account and look for homology between conserved regions- this will be evident at the protein level.¹⁸

Plant

Any member of the kingdom Plantae, which includes both terrestrial and aquatic flora.

Plant Embryo

A young, developing plant, such as the rudimentary plant inside the seed of higher plants or that inside the archegonium of mosses and ferns.¹⁹

Plant variety

Any plant grouping within a single botanical taxon of the lowest known rank that, without regard to whether the conditions for plant variety protection as fully met, can be defined by the expression of the characteristics that result from a given genotype or combination of genotypes, distinguished from any other plant groupings by the expression of at least one (1) characteristic, and considered as a unit with regard to the suitability for being propagated unchanged. A variety may be represented by seed, transplants, plants, tubers, tissue culture plantlets, and other forms.²⁰

¹⁸ Chan Zuckerberg Initiative, 2022

¹⁹ Embryo - Plants, 2019

²⁰ Plant Variety Act of the Philippines 2002, RA 9168

Polyclonal Antibody

A mixture of antibodies that are secreted by different B cell lineages; heterogeneous mix of many antibodies that recognize the same protein.²¹

Primers

Short nucleic acid sequences which provide the starting point for a DNA synthesis.

Probes

Single-stranded DNA or RNA which are used to search for a complementary sequence in a sample genome. It is placed into contact with a sample under certain conditions which will then undergo hybridization with its complementary sequence wherein it is usually labeled with radioactive or chemical tags for visualization.

Proteins

Macromolecular polypeptides composed of amino acids linked by peptide bonds.

Query Cover

A number that describes how much of the query sequence is covered by the target sequence. If the target sequence in the database spans the whole query sequence, then the query cover is 100%. This tells us how long the sequences are, relative to each other. One must also note that a high percent identity with low query cover may be possible but is not considered a significant match since this means that the sequence is not within the same taxon.²²

Re-differentiation in Plants

The process by which dedifferentiated cells lose their ability to divide and become specialized to perform a role by converting into a part of the permanent tissue.²³ The ability of the callus cells to differentiate into a plant organ or a whole plant.

²¹ *Pacific Immunology, 2002*

²² *Chan Zuckerberg Initiative, 2022*

²³ *Differentiation, Dedifferentiation and Redifferentiation in Plant Tissue Culture, n.d.*

Sequence Alignment

It is when a sequence is identified as having a certain percent identity to a reference sequence. It should be properly disclosed whether the percent identity is relative to the full length of the reference sequence or is a partial alignment. Preferably, alignment of the sequence over the full length of the reference sequence should be used for comparison for the sake of clarity.²⁴

Sequence Identity

Refers to the occurrence of exactly the same nucleotide or amino acid in the same position in aligned sequences.²⁵

Surgery

A form of treatment of the human or animal body, by means of operation or manipulation.

Taxon

Any group or rank in a biological classification, such as phylum, order, family, genus or species, into which related organisms are classified.

Therapy

A form of treatment of the human or animal body designed to cure, alleviate, remove or lessen the symptoms of, or prevent or reduce the possibility of contracting any disorder or malfunction.

Totipotency

The ability of an individual cell to differentiate and develop into a whole organism.

Totipotent stem cells

Cells that have the capacity to self-renew by dividing and to develop into the three primary germ cell layers of the early embryo and into extra-embryonic tissues such as the placenta. A fertilized egg is a totipotent stem cell and as such can develop into any specialized cell found in the organism.²⁶

²⁴ Chan Zuckerberg Initiative, 2022

²⁵ Pertsemidis, A., Fondon, J.W. (2001). <https://doi.org/10.1186/gb-2001-2-10-reviews2002>

²⁶ Totipotent stem cells-Latest research and news/Nature, n.d.

Transformant

A cell that has received additional genetic material, either experimentally or via an infection; can be used to refer to a cell that has become malignant.²⁷

Transgene

A segment of DNA from the genome of one organism introduced into the genome of another organism by artificial techniques.

Transgenic

An organism or cell whose genome has been altered by the introduction of one or more foreign DNA sequences from another species by artificial means.²⁸

Transgenic Plants

Use tools of molecular biology to isolate clones and incorporate genes into plants. It is a more precise technique than mutation.

Vector

A vector, as related to molecular biology, is a DNA molecule (often plasmid or virus) that is used as a vehicle to carry a particular DNA segment into a host cell as part of a cloning or recombinant DNA technique. The vector typically assists in replicating and/or expressing the inserted DNA sequence inside the host cell.²⁹

²⁷ Transformant/Learn Science at Scitable, n.d.

²⁸ National Human Genome Research Institute, 2022

²⁹ National Human Genome Research Institute, 2019

IV. INVENTIONS INVOLVING BIOLOGICAL MATERIALS

ELIGIBILITY

To determine if a biological material is eligible for patent protection, the following provisions from Republic Act 8293 vis-a-vis the requirements set forth in the Revised Implementing Rules and Regulations on Inventions must be considered:

RA 8293

Sec. 21. Patentable Inventions. - Any technical solution of a problem in any field of human activity which is new, involves an inventive step and is industrially applicable shall be patentable. It may be, or may relate to, a product, or process, or an improvement of any of the foregoing. (Sec. 7, R. A. No. 165a)

Sec. 22. Non-Patentable Inventions. - The following shall be excluded from patent protection:

22.1. Discoveries, scientific theories and mathematical methods;

22.2. Schemes, rules and methods of performing mental acts, playing games or doing business, and programs for computers;

22.3 Methods for treatment of the human or animal body by surgery or therapy and diagnostic methods practiced on the human or animal body. This provision shall not apply to products and composition for use in any of these methods;

22.4. Plant varieties or animal breeds or essentially biological processes for the production of plants or animals. This provision shall not apply to microorganisms and non-biological and microbiological processes.

Provisions under this subsection shall not preclude Congress to consider the enactment of a law providing sui generis protection of plant varieties and animal breeds and a system of community intellectual rights protection:

22.5. Aesthetic creations; and

22.6. Anything which is contrary to public order or morality. (Sec. 8, R. A. No. 165a)

REVISED IRR of 2022

Rule 202. Non-patentable Inventions. – The following shall be excluded from patent protection:

- (a) Discoveries, scientific theories, and mathematical methods, a law of nature, a scientific truth, or knowledge as such;³⁰*
- (b) Abstract ideas or theories, fundamental concepts apart from the means or processes for carrying the concept to produce a technical effect;*
- (c) Schemes, rules, and methods of performing mental acts and playing games;*
- (d) Method of doing business, such as a method or system for transacting business without the technical means for carrying out the method or system;*
- (e) Programs for computers;*
- (f) Methods for treatment of the human or animal body by surgery or therapy and diagnostic methods practiced on the human or animal body. This provision shall not apply to products and compositions for use in any of these methods;*
- (g) Plant varieties or animal breeds or essentially biological process for the production of plants and animals. This provision shall not apply to microorganisms and non-biological and microbiological processes;*
- (h) Aesthetic creations; and*
- (i) Anything which is contrary to public order, health, welfare, or morality, or process for cloning or modifying the germ line genetic identity of humans or animals or uses of the human embryo.*

NOVELTY

A patent application involving a biological material is novel if it does not form part of a prior art³¹ (Section 23 of RA 8293 as amended/Rule 203 of the Revised IRR of 2022).

³⁰ In the case of drugs and medicines involving known substances, please refer to the Implementing Rules and Regulations of Republic Act 9502, otherwise known as the “Universally Accessible Cheaper and Quality Medicines Act of 2008”.

³¹ **Prior Art** - Everything which has been made available to the public anywhere in the world, before the filing date or the priority date of the application claiming the invention.

INVENTIVE STEP

A patent application involving a biological material is inventive if, having regard to prior art, it is not obvious to a person skilled in the art at the time of the filing date or priority date of the application claiming the invention (*Section 26 of RA 8293 as amended/ Rule 206 of the Revised IRR of 2022*).

INDUSTRIAL APPLICABILITY

An application involving a biological material satisfies the requirement on industrial applicability if it can be produced and used in any industry (*Sec. 27 of RA 8293 as amended/ Rule 208 of the Revised IRR of 2022*).

If the use of an invention relating to biological material cannot be inferred from the description, the claims, or drawings, it is considered that the invention is industrially inapplicable.

ENABLING DISCLOSURE

The enabling disclosure shall contain a clear and detailed description of at least one way of performing the invention using working examples. It shall contain a sufficient and clear disclosure of the technical features of the invention including the manner or process of making, performing, and using the same, leaving nothing to conjecture. Said disclosure shall be based on the description, claims and drawings and also in light of the common general knowledge at the time of filing.

The general test of Enabling disclosure is to a person skilled in the art, possessing ordinary skills, and ordinary/common knowledge in the art, is able to perform the invention:

- a) without an undue burden;
- b) without any inventive effort or
- c) without undue experimentation

In case of chemical substance and pharmaceutical subject matter, the disclosure must include one or more representative embodiments or working examples, a description of the result of the pharmacological test in the case of pharmaceutical subject matter, and all compounds must include their claimed activity (*Rule 406.1 of the Revised IRR (2022)*).

Things to consider in determining if the biological inventions meet the enablement requirements based on the following types of Invention³²:

(1) Invention of a product

It is necessary to clearly identify and understand the invention in the claims and statement in the description so as to enable a person skilled in the art to make or create and use the product. The product should be described by its specific feature (function, characteristics, etc.) or structure.

(2) Invention of a process

It is necessary to clearly identify and understand the invention in the claims and statement in the description so as to enable a person skilled in the art to use the process. The said process may take the form of method of producing a product, method of using a product, a method of measuring or method of controlling.

(3) Invention of a process for manufacturing a product

It is necessary to clearly identify and understand the invention in the claims and statement in the description so as to enable a person skilled in the art to manufacture the product by using the process. The process should contain a starting material, the process steps and the final product.

Applications involving biological materials shall adhere to the general requirement for enabling disclosure (*Rule 406.1 of the Revised IRR, 2022*). Specific illustrations are provided in the succeeding sections of the Guidelines.

When the application refers to a nucleotide or amino acid sequence, the sequence listing forms part of the description, and therefore shall be included in the submission. It may be inserted at any point within the description whenever suitable; however, particularly for nucleotide or amino acid sequence listing that exceeds a page long, it is standard for the sequence listing to be placed at the end of the description, and the pages numbered separately from the description and claims.

Sequence listings may be submitted as a paper document and/or in portable document format (PDF) in accordance with IPOPHL Memorandum Circular No. 15-001. The Sequence Listing must be submitted in Portable Document

³² JPO Examination Guideline Part II Chapter I Section 3.1.

Format (PDF) with Optical Character Recognition (OCR). If the Sequence Listing was submitted in an electronic format other than PDF OCR, the applicant shall be invited to submit the same in PDF OCR within two (2) months from the date of mailing of the invitation. If the applicant fails to comply with the invitation, the Sequence Listing shall be treated as if it was submitted on paper for the purposes of computing the fee for each sheet in excess of thirty (30). If the applicant files the Sequence Listing in both electronic format and paper, the paper copy will be disregarded in the further procedure (*Office Order No. 14-196 Series of 2014*).

However, Sequence Listings filed online may be contained in separate files or in one file, depending on the requirements of the online filing system requirements. Similarly, the type of file format shall depend on the online filing system requirements. Application documents must comply with such online filing requirements (*Rule 419 (i) of the Revised IRR (2022)*).

Provisions in the Revised IRR relating to biological materials:

Rule 408. *Requirements of Application relating to Biological Materials and Microorganisms.* –

Where the application concerns a microbiological process, or the product thereof, involving the use of a microorganism which cannot be sufficiently disclosed in the application in such a way as to enable the invention to be carried out by a person having ordinary skills in the art and such material is not available to the public, the invention shall only be regarded as disclosed if:

- (a) A culture of the microorganism has been deposited in a depositary institution before filing the application (refer to Annex B for the list of IDA);*
- (b) The depositary institution and the file number of the culture deposit are stated in the application. If this information is not yet available at the time of filing the application, the said information shall be submitted within two (2) months from the request of the Examiner. Publication of the application under Section 44 of the IP Code shall be held pending until submission of the information;*
- (c) The application as filed gives relevant information as is available to the applicant on the characteristics of the microorganism.*

Rule 409 *of the Revised IRR (2022) Requirements of Application relating to Biological Materials and Microorganisms before Allowance.*

An application which concerns a microbiological process, or the product thereof, involving the use of any novel strain of microorganism shall be allowed only when the following conditions are met:

- (a) A deposit was made in:*

 - (i) a recognized international depositary authority or a recognized depositary authority located in the Philippines; or*
 - (ii) a Philippine depositary authorized for the deposit, which guarantees the availability and protection of the viability of the strain at least during the period of the patent;*

- (b) Proof of such deposit together with the proper identification or deposit number assigned by the depositary; and*
- (c) That the depositary should be under the contractual obligation to place the culture in permanent collection and to provide access to persons who shall have interest therein with regard to matters relating to the patent application as published.*

The provisions in the IP Code and the IRR provide that a biological material is eligible for patent protection if it does not fall under the classes of non-patentable inventions. An additional requirement for microorganisms is that a culture of such must have been deposited in a depositary institution before filing the application.

Wherein the patentability of a biological material cannot be ascertained, i. e. whether or not the biological material falls within the meaning of "discovery" provided by Chapter IV (page 52) of the MSEP, nor of a product of "essentially biological processes" (page 55, MSEP), it is crucial that not only there is a human intervention involved, but the intervention was an indispensable aspect of the invention and not merely as an aid to the isolation of the biological material or to the performance of an otherwise essentially biological process. Specific illustrations of patentable biological materials are provided in the succeeding sections of the Guidelines.

1. MICROORGANISMS

The Philippines is a signatory of the Budapest Treaty, thus patent applications involving microorganisms must satisfy the provisions under Budapest Treaty.

Inventions relating to microorganisms are not limited to the novel microorganisms per se and to their use, but also to the use (or method of use) of known microorganisms for various applications.

1.1 Eligibility

Finding a microorganism occurring freely in nature is a mere discovery and is therefore unpatentable as such. However, a microorganism which is isolated from its natural environment or produced by means of a technical process, e.g., using a microbiological process, may be the subject of an invention, even if such microorganism occurred in nature. If the microorganism is isolated from its natural environment, the specification shall provide the characterizing technical features of said microorganism.

Illustrative Example 1

Claim: A bacterium X isolated from a water reservoir.

Analysis

Said bacterium may be patent eligible if the specification provides the characterizing technical features of the isolated microorganisms.

Illustrative Example 2

Claim: A bacterium X wherein ABC1 gene is inserted, purpose of which is to enable said bacterium to absorb heavy metal content in a given environment.

Analysis

Said bacterium X is patentable subject matter on the ground that such bacterium is a product of a microbiological process via human intervention, that is, the insertion of ABC1 gene onto its genome which gives it the surprising characteristic (i.e., ability to absorb heavy metal) not found in the wild species.

1.2 Novelty

For inventions involving microorganisms or microbiological processes to be novel, it is required that no prior art disclosing the claimed microorganism or microbiological processes must be found.

In patent terms, ‘novel’ means not previously ‘made available to the public’. So, the first person to find and isolate a new bacterium from a soil sample, for example, might have made a potentially patentable invention. If the bacterium is claimed in the patent application in a technically-isolated form, that form will be novel over the previously-known mixture of that bacterium with numerous other microorganisms in the soil.

1.3 Inventive Step

The inventive step of a claim pertaining to microorganism must be assessed based on the taxonomic characteristics of the microorganism and on the advantageous effects that result from the use of the microorganism.

Illustrative Example 1

Claim: A biologically pure culture of *Lactobacillus casei* with ATCC No. XXX.

Analysis

If the claimed microorganism possesses taxonomic characteristics substantially different from those of known species, and these characteristics give the microorganism advantageous effects, then inventive step may be satisfied.

Lactobacillus casei is a Gram-positive, nonmotile, nonspore-forming, and catalase-negative bacterium. The taxonomy of the *L. casei* group has been debated for a long time, mainly because of the failure of differentiation, even by molecular techniques, between most of *L. casei* and *Lactobacillus paracasei* strains. The currently accepted nomenclature and taxonomic division of the *L. casei* group is as follows: (1) *L. casei* (type strain: ATCC 393TM); (2) *L. paracasei* subsp. *paracasei* (type strain: ATCC 25302TM) and *L. paracasei* subsp. *tolerans* (type strain: ATCC 25599TM); and (3) *Lactobacillus rhamnosus* (type strain: ATCC 25599TM). The combination of the group-specific PCR with SNaPshot minisequencing is successfully used for species identification within the *L. casei* group. In detail, the use of primers designed on the basis of the *rpoA* gene sequences of the *L. casei* group and phylogenetically related reference species, allows us to differentiate strains

belonging to the *L. casei* group from other strains belonging to the genus *Lactobacillus*.³³

Alteration of the genetic makeup of a microorganism for it to exhibit a desired phenotype must be assessed if it involves inventive step. Such alteration must not be obvious to a person skilled in the art.

Illustrative Example 2

Claim: A variant of *Bacillus amyloliquefaciens* transplanted with ABC1 gene, said variant exhibits enhanced expression of antibiotic protein barnase.

Prior art 1: A biologically stable strain of *Bacillus amyloliquefaciens*.

Prior art 2: An antibiotic Polymixin B with improved potency, said antibiotic was produced by *Bacillus polymyxa*.

Analysis

The claim is inventive, the skilled person would not predict that the addition of gene ABC1 could result in improved characteristic (i.e. enhanced expression of barnase).

However, if there is a prior art that discloses insertion of ABC1 gene into the bacterial genome to enhance or induce barnase production, then the inventive step of this claim may be disputed.

1.4 Enablement

1.4.1 If the microorganism in question is a mutant of a known microorganism, and the mutation process is reproducible, then the mutant can adequately be described in the patent application. If it is a newly discovered microorganism that has never been known before, or if the specification does not enable the skilled person to produce the microorganism (such in the case of a mutant of an existing species), a sample of the microorganism must be deposited with one International Depositary Authority (IDA) or a recognized depositary authority located in the Philippines; or a Philippine depositary authorized for the deposit for the enablement requirement to be deemed satisfied in all the contracting states of the Budapest Treaty.

³³ Gobbeti, Marco. (1999). *LACTOBACILLUS: Lactobacillus casei*. ScienceDirect. <https://www.sciencedirect.com/topics/agricultural-and-biological-sciences/lactobacillus-casei>

1.4.2 The enablement requirement for inventions relating to microorganisms must be carried out pursuant to *Section 35 of the IP Code*, and *Rule 406.1 of the Revised IRR*.

1.4.2.1 Applications relating to microorganisms shall disclose clearly the known features of the product invention.

The microorganism must be

- (a) Identified by its species name (if the invention pertains to a new species) or strain name following the species name (if the invention pertains to a new strain) in accordance with standard nomenclature for microorganisms. Further, the microbiological characteristics must be described, e. g. taxonomic characteristics, morphological and metabolic characteristics, or genetic characterization relevant to the inventive concept of the microorganism;
- (b) Described by the method by which the microorganism was produced, in a way that a skilled person may be able to replicate such method; and
- (c) Described in a manner that the skilled person may be able to use the microorganism for purposes stated in the application.

Illustrative Example 1

Claim: A biologically pure culture of mutants of *Aspergillus niger* with ATCC No. xxx.

Analysis

The present invention satisfies the enablement requirement since a deposit of a newly discovered microorganism has been made.

Illustrative Example 2

Claim: A *Marinobacter spp.* isolatable from oil-polluted soil, characterized by its ability to decompose n-alkane and trichloroethylene in an aerobic environment, and having all the identifying characteristics of *Marinobacter spp.* ATCC No. nnn.

Analysis

The present invention satisfies the enablement requirement since a deposit of a newly discovered microorganism has been made.

Illustrative Example 3

Claim: A recombinant bacterium comprising a bacterium which was transformed by a vector carrying the ABC gene.

Analysis

The present invention will satisfy the enablement requirement if the claimed recombinant bacterium is described in the specification such that a skilled person can reproduce it.

Illustrative Example 4

Claim: *Bacillus subtilis* T-169 strain, having dioxin decomposing ability.

Analysis

The present invention will not satisfy the enablement requirement if a deposit of *Bacillus subtilis* T-169 strain is not made. It is necessary to deposit the *Bacillus subtilis* T-169 strain since it is a microorganism that is not easily available for a person skilled in the art.

Illustrative Example 5

Claim: The use of a substantially pure culture of a new strain of *Candida albicans* as an antagonist for fungal pathogens responsible for the rapid decay of post-harvest fruits.

Analysis

In this example, *Candida albicans* must have been characterized, or the accession number provided, in a preceding claim, for it to be considered as enabled.

Illustrative Example 6

Claim: A process for the decomposition of organic halogenated compounds in soil sample, comprising adding a culture of a bacterium to the soil sample, for it to be considered as enabled.

Analysis

Again, in this example, the bacterium must have been characterized, or the accession number has been provided, in a preceding claim for it to be considered as enabled.

Illustrative Example 7

Claim: Process for the production of γ -decalactone from ricinoleic acid by β -oxidation using *L. saturnus*.

Analysis

Again, in this example, *L. saturnus* must have been characterized, or the accession number has been provided, in a preceding claim, for it to be considered as enabled.

1.4.3 For inventions involving known microorganisms, a proof of deposit is not necessary for microorganisms easily available for a person skilled in the art, which includes the following:

1. Commercially available microorganisms, such as baker's yeast, koji (*Aspergillus oryzae*), *Bacillus natto*, etc.
2. Microorganisms in a case where it has been evident, prior to filing, that the microorganisms have been stored at a reliable culture collection and are freely furnished from a catalog or the like issued by the culture collection. The storage number of the microorganism should be stated in the originally attached description;
3. Microorganisms which can be produced by a person skilled in the art on the basis of the description.

Illustrative Example 1

Overview of the Description:

While it is desired to obtain β -galactosidase having a sufficient enzymatic activity at the acidic region since raw materials of neutral to acidic pH such as milk, cheese whey, lactose solution is assumed as subject to be processed by β -galactosidase, microorganisms producing β -galactosidase having the sufficient enzymatic activity in the acidic region were not known at the time of the filing of the present application.

The β -galactosidase according to claim 1 isolated from *Streptomyces lividans* xyz-1 strain by a specific approach. In addition, the *Streptomyces lividans*

xyz-1 strain was listed as storage number ATCC ***** in the catalog published from ATCC, and could be freely furnished prior to filing the present application.

Claim 1: A β -galactosidase which is derived from *Streptomyces lividans* xyz-1 strain (ATCC *****), having the following physicochemical properties:

- a) action and substrate specificity: hydrolyzing a substrate having β -D-galactosidase bond to release a D-galactose group.
- b) Optimal pH: 4.5
- c) Stable pH: 3.0 to 5.5
- d) Optimal temperature: 55 °C
- e) Stable temperature: 50 °C
- f) Molecular weight: 200 kD as measured by gel permeation method.

Analysis

In this case, the *Streptomyces lividans* xyz-1 strain is a microorganism which was stored in ATCC, reliable storage culture collection, and which was obvious prior to filing the present application that can be freely furnished by the catalog published from ATCC. In addition, the description states the storage number of the *Streptomyces lividans* xyz-1 strain.³⁴

Accordingly, the *Streptomyces lividans* xyz-1 strain is a microorganism which is easily available for the person skilled in the art and thus a person skilled in the art can isolate the β -galactosidase according to claim 1 by using specific approach stated in the description.

Therefore, it is not necessary to deposit the *Streptomyces lividans* xyz-1 strain in an International Depositary Authority.

Illustrative Example 2

Overview of the Description:

The taxonomical property of the *Coryneform* bacterium strain K-336 producing L-arginine which was isolated from the soil based on chemical tolerance was analyzed in detail to examine any variation with native similar species. In the result, it was revealed that the coryneform bacterium strain K-336 is a new species.

It was publicly known prior to filing the present application that the group of genes including ArgA gene and ArgH gene is responsible for L-arginine biosynthesis pathway in the *Coryneform* bacterium. The inventors first isolated and purified ArgG gene containing the nucleotide sequence

³⁴ JPO Biological Inventions Guidelines Annex B Chapter II

represented by SEQ ID NO: 1 from the *Coryneform* bacterium strain K-336, and expressed ArgG gene by well-known gene engineering approaches and they have confirmed that a protein encoded by ArgG gene is argininosuccinic acid synthase. The nucleotide sequence of the DNA encoding ArgG gene is included in the description.

Claim 1: An isolated DNA encoding argininosuccinic acid synthase derived from *Coryneform* bacterium strain K-336 and containing a nucleotide sequence represented by SEQ ID NO: 1.

Analysis

In this case, the invention according to claim 1 relates to DNA, not the *Coryneform* bacterium strain K-336. In addition, the nucleotide sequence of the DNA is specifically represented in the description. Accordingly, a person skilled in the art can obtain the DNA through artificial synthesizing method, etc. based on this nucleotide sequence. In addition, a person skilled in the art can incorporate the DNA into an appropriate expression vector, and can manufacture a transformant bearing the expression vector.

Therefore, it is not necessary to deposit the *Coryneform* bacterium strain K-336 in an International Depositary Authority (IDA).

1.5 Amendment of Accession Number of the Deposit

- a) An amendment to convert or add an accession number is acceptable because it does not introduce any new technical matter, as long as microbiological or cytobiological characteristics of the biological material are described in the originally attached description, claims or drawings, to the extent that the biological material can be specified, and the deposit of the biological material can be specified based on the name of the depositary institution, etc. In such cases, particular care must be taken to ensure that there is no new matter being introduced. However, if there is doubt about the identity of the biological material in changing the accession number, notice may be given of the reason for refusal.
- b) An amendment converting a storage number of a biological material to an accession number based on the deposit of the biological material with a depositary institution for the purpose of patent procedure, is acceptable because it does not introduce any new technical matter, as long as the biological material used is stored at a reliable culture collection, the storage number of the biological material is explicitly stated in the originally attached description, etc., and it is clear that

the identity of the biological material is not lost. In such a case, the applicant should make an amendment of the accession number without delay. A proof showing the conversion of the storage number of a biological material to an accession number must be submitted.

- c) An amendment converting a reference number of biological material to a corresponding accession number is obviously acceptable, as long as the reference number issued by the depositary institution is described in the originally attached description. A proof showing the conversion of the reference number of a biological material to an accession number must be submitted.
- d) An amendment adding microbiological characteristics of biological material such as fungus or bacterium is not acceptable because it typically introduces new technical matter, unless those characteristics are inherently presented in the originally attached description etc. Even if the accession number of the biological material stated in the originally attached description etc., is not changed and the microbiological characteristics of the biological material are described in the originally attached description etc. to the extent that the taxonomic species of the biological material such as fungi and bacteria can be specified.³⁵

1.6 Illustrative Examples of Claims Involving Microorganisms

Illustrative Example 1

Claim 1: A modified microorganism of the genus *Corynebacterium* producing putrescine or ornithine, wherein an activity of transcriptional regulator of sugar metabolism (SugR) is weakened compared to its endogenous activity and an activity of citrate synthase (GltA) is enhanced compared to its endogenous activity.

Claim 2: The microorganism according to claim 1, wherein the transcriptional regulator of sugar metabolism consists of an amino acid sequence of SEQ ID NO: 1 or SEQ ID NO: 3.

Analysis

Eligibility: The specification provides a modified microorganism of *Corynebacterium glutamicum* strains that are modified to produce putrescine or ornithine. The subject matter of said claims are considered an eligible subject matter.

³⁵ JPO Biological Inventions Guidelines Annex B Chapter II

Enablement: Claims 1 and 2 lack enablement for being directed to a wide variety of the species within the genus *Corynebacterium*. The specification only provides examples of a specific strain which is the *Corynebacterium glutamicum* strains modified to produce putrescine or ornithine.

It is also noted that independent claim 1 is defined in terms of results to be achieved- the activity of transcriptional regulator of sugar metabolism (SugR) is weakened compared to its endogenous activity and an activity of citrate synthase (GltA) is enhanced compared to its endogenous activity.

Prior Art 1: Discloses a *Coryneform* bacterium modified to produce L-ornithine and inhibited by nicotinamide adenine dinucleotide hydrogen (NADH) bacteria to increase the activity of citrate synthase.

Prior Art 2: Discloses microorganism of the genus *Corynebacterium*, specifically wild type strain *Corynebacterium glutamicum* ATCC 13032 or glutamate overproduction strain KCCM-10785p which deleted cg2115 (sugR) that regulates the expression factor of glucose metabolism.

Prior Art 3 : The prior art discloses SEQ ID NO: 1 of the present invention.³⁶

Novelty

Claims 1 and 2 are novel. Prior art documents 1/2/3, taken independently, failed to disclose the attenuation of the activity of the transcriptional regulator of sugar metabolism (SugR) compared to its endogenous activity.

Inventive Step

Claim 1 is not inventive when the teachings of D1 and D2 are combined. Considering that D1 and D2 shares the same technique in manipulating a gene in a *Coryneform* strain, it is obvious to a person skilled in the art to use the well-known techniques from D1 and D2 to modify a gene from the genus *Corynebacterium* producing putrescine or ornithine to weaken the activity of transcriptional regulator of sugar metabolism (SugR) as required by independent claim 1.

Claim 2 lacks inventive step when the teachings of D1, D2 and D3 are combined.

Illustrative Example 2

Claim 1. A process for the preparation of a modified strain of the yeast *Schizosaccharomyces pombe*; said process comprising the following steps:

- a. inoculating yeast culture of *Schizosaccharomyces pombe* (Accession No. 3360) in a solution selected from the group

³⁶ Derived from PCT Application PCT/KR2016/003198

consisting of saline solution and Ringer Salt solution to obtain a primary culture and subjecting the same to serial dilutions to obtain serially diluted cultures comprising yeast strain;

Analysis

Eligibility: A process involving modification of a known strain is patentable subject matter.

Enablement: The Accession Number of the specific strain used is indicated and is fully disclosed in the description, hence satisfies the enablement requirement.

Illustrative Example 3

Claim 8. A modified strain of *Schizosaccharomyces pombe* yeast; that remains stable at 12 to 14% dissolved solid and which withstands the temperature of about 32 to about 34 degrees Celsius.

Analysis

Eligibility: A product claim directed to a modified strain is a patentable subject matter.

Enablement: There is no indication in the description that the strain is deposited, hence enablement requirement is not met.³⁷

³⁷ Derived from PH/1/2011/000177

2. NUCLEIC ACIDS AND POLYPEPTIDES

2.1 Eligibility

2.1.1 Patent Eligible Biological Materials

Patent eligible subject matters relating to biological materials include:

- a) Genotypically or phenotypically modified organisms such as genetically modified bacteria, plants, and non-human organisms; and
- b) Isolated biological materials involving human intervention, purification and/or manipulation, wherein the isolated biological materials have industrial applicability and demonstrate technical effect.

Specific examples:

- i. synthetic DNA or nucleic acid sequences only where the genetic information does not exist in the DNA blueprint or genome of any human or other organism
- ii. an isolated protein expressed by a gene
- iii. vectors (such as plasmids or bacteriophage vectors or viruses) containing a transgene
- iv. methods of transformation using a gene
- v. host cells carrying a transgene
- vi. higher plants or animals carrying a transgene
- vii. organisms for expression of a protein from a transgene
- viii. general recombinant DNA methods such as PCR and expression systems

2.1.1.1 Isolated from Natural Environment

Biological materials such as nucleic acids and genes or polypeptides and proteins (collectively, they will be referred to as "molecules" in this section) found in the cells, whether a DNA or an RNA, that have been removed or isolated from their biological environment where they naturally exist, are eligible for patent.

Isolated molecules, although containing the same compositions and structures as those found in their natural existence, are eligible for patent on the basis that such do not usually occur in an isolated form in nature and that human intervention is necessary for the isolation and preparation of said molecule.

A complementary DNA (cDNA) which comprises naturally occurring exons of the DNA but lacks naturally occurring introns is considered as patent

eligible. It is considered as patent eligible because it is still distinct from the naturally occurring DNA from which it was derived. Moreover, a cDNA is usually produced using a reverse transcriptase on a mRNA which therefore makes it generally known in the state of art as a synthetic DNA that is manipulated in the laboratory and produced for ease of use in research. Hence, a cDNA is not deemed as a product of nature and is, therefore, patent eligible.³⁸

Illustrative Example 1

Overview of the Description:

The specification describes a naturally occurring herbal plant that grows wild in the Sierra Madre Mountain ranges which when damaged or crushed, the leaves produce protein W, which activates chemical defenses against herbivores and is naturally encoded by Gene W, which is part of chromosome 3 of the said herbal plant and has the nucleic acid sequence disclosed as SEQ ID NO: 1.

The specification also discloses substitution modifications of Gene W, *e.g.*, nucleic acids having one or more nucleotide bases that are substituted with different bases relative to SEQ ID NO: 1. One of the modifications changes a naturally occurring adenine to a guanine, *e.g.*, the first nine nucleotides are “TAC GGG AAA” in naturally occurring Gene W and “TAC GGG AAG” in the modified nucleic acid.

No substitution modifications of Gene W are known to occur in nature. The modified nucleic acids have 90% or greater identity to SEQ ID NO: 1. Labelling of the nucleic acids, *e.g.*, with a fluorescent or radioactive label, is also disclosed.

The specification further discloses vectors comprising SEQ ID NO: 1 and a heterologous nucleic acid. The specification defines “heterologous” nucleic acid sequences as nucleic acid sequences that do not naturally occur in the herbal plants, but from the following natural origins, *e.g.*, sequences from other plants, bacteria, viruses, or other organisms. Disclosed heterologous nucleic acids include plant viral vectors such as tobacco mosaic virus, and other viral promoters.

Claim 1: An isolated nucleic acid comprising SEQ ID NO: 1.

³⁸ Association for Molecular Pathology v. Myriad Genetics, 2013 WL 2631062 (June 13, 2013)

Claim 2: An isolated nucleic acid comprising a sequence that has at least 90% identity to SEQ ID NO: 1 and contains at least one substitution modification relative to SEQ ID NO: 1.

Claim 3: The isolated nucleic acid of claim 1, further comprising a fluorescent label attached to the nucleic acid.

Claim 4: A vector comprising the nucleic acid of claim 1 and a heterologous nucleic acid sequence.

Analysis

Claims 1-4 are patent eligible. The eligibility of the claims is assessed in their broadest reasonable interpretation.

Claim 1 - although the claimed nucleic acid has the same nucleotide sequence as that occurs in nature, it has different structural characteristics than naturally occurring Gene W since the chemical bonds at each end were severed in order to isolate it from the chromosome on which it occurs in nature.

Claim 2 - the claim is limited to nucleic acids in which the nucleotide sequence has been changed to contain at least one non-naturally occurring substitution modification relative to SEQ ID NO 1. The claimed nucleic acids have different structural characteristics than the naturally occurring nucleic acid, e.g., one or more nucleotides have been changed relative to the natural sequence.

Claim 3 - The claim is limited to a molecule that includes nucleic acid and a fluorescent label, which combination does not occur in nature as a single molecule. Claim 3, therefore, is patent eligible.

Claim 4 - The claim is limited to vectors comprising a non-natural combination of Gene W (SEQ ID NO: 1) with a sequence from another organism, and thus does not read on the naturally occurring chromosome in the herbal plant. This non-natural combination results in the vectors having a different genetic structure and sequence than the naturally occurring nucleic acids, i.e., different structural characteristics.

2.1.1.2 Discoveries and Scientific Theories

New property of a known material or article that has no technical effect is considered a mere discovery and patent ineligible. If, however, that property

is in fact industrially applicable and demonstrates a technical effect, then this constitutes an invention which may be patentable.

Discovering a naturally-occurring substance previously unknown is also mere discovery and therefore unpatentable, *Sec. 22.1 of the Intellectual Property Code* and *Rule 202 (a) of the Revised Implementing Rules and Regulations for Patents*. However, if isolation of a naturally-occurring substance involves human intervention, demonstrates a technical effect and industrial applicability, it may be patentable.

Illustrative Example 1

Overview of the Description:

Said isolated DNA molecule can be used in gene therapy with enhanced efficacy.

Claim: An isolated DNA molecule comprising a nucleic acid sequence encoding the amino acid as defined in SEQ ID NO: 1.

Analysis

Said DNA molecule is considered patent eligible because the description reveals that the DNA molecule was isolated involving human manipulation. Practical use of the isolated DNA molecule in gene therapy is also evident in the description. The disclosure demonstrates the enhanced efficacy of using the isolated DNA molecule over the control in gene therapy, therefore, proving the surprising technical effect of the claimed invention.

Illustrative Example 2

Overview of the Description:

The description merely describes the isolation of *Bacillus* sp. AR012 from soil.

Claim: An isolated polynucleotide sequence represented as SEQ ID NO: Y (Accession No. XXXXXX) from *Bacillus* sp. AR012.

Analysis

Said isolated *Bacillus* sp. is considered patent ineligible because the filed disclosure does not mention any functional features nor the technical effect of isolating said isolated *Bacillus* sp. from soil which is considered as a mere discovery and falls under *Section 22.1 of RA 8293*, as amended.

2.1.2 Patent Ineligible DNA or gene sequences

Gene sequences, DNA, RNA, or nucleic acid sequences *per se* that replicate the genetic information in the DNA blueprint or genome of any human or other organism are patent ineligible. Thus, human beings and related biological processes for their generation are not patentable.³⁹

Furthermore, mere isolation and identification of any other gene or DNA molecule in its naturally-occurring form is also considered patent ineligible.

However, any gene or DNA molecule that was isolated involving human intervention and has industrial applicability and technical effect may be patentable.

Illustrative Example 1

Overview of the Description:

The description discloses an isolated polynucleotide sequence of breast cancer gene 1 (BRCA1) and of breast cancer gene 2 (BRCA2) as defined in SEQ ID NO: X and SEQ ID NO: Y, respectively. Both BRCA1 and BRCA2 genes are inherited from each human parent, wherein normal BRCA1 and BRCA2 genes produce proteins that help repair damaged DNA.

Claim 1: An isolated polynucleotide sequence of BRCA1 as represented by SEQ ID NO: X.

Claim 2: An isolated polynucleotide sequence of BRCA2 as represented by SEQ ID NO: Y.

Analysis

Claims 1 and 2 are not considered patent eligible since the claimed polynucleotide sequences which involve BRCA1 gene (SEQ ID NO: X) or BRCA2 gene (SEQ ID NO: Y) are related to hereditary breast and ovarian cancer gene. Hence, the claimed polynucleotide sequences are considered a product of nature, i.e. genetic information from a human, which can be vital information for patients in obtaining genetic screening in order to make informed medical decisions.

2.2 Novelty

³⁹ Association for Molecular Pathology v. Myriad Genetics, 2013 WL 2631062 (June 13, 2013)

Generally, any invention is considered novel if it has not been made available to the public by means of written or oral description, by use, or disclosed anywhere in the world prior to the effective filing date of a patent application.

These biological molecules should not have been previously described nor have been found to exist in nature in their free or isolated form, nor known to be a part of any previously described domain.

Illustrative Example 1: Isolated gene

Claim: An isolated human H2-relaxin gene.

Analysis

Assuming that no prior art has been found that describes or indicates that the gene exists in nature in its isolated form, the isolated human H2-relaxin gene is considered novel.

Illustrative Example 2: Polynucleotides or gene sequences

Claim: A transgenic rice plant comprising a polynucleotide molecule comprising a nucleotide sequence as defined in SEQ ID NO: 1, wherein said rice plant is resistant to glyphosate herbicide treatment.

Prior Art: A transgenic rice plant comprising a polynucleotide molecule comprising a nucleotide sequence having at least 80% identity with SEQ ID NO: 1.

Analysis

Isolated biological molecules that are not previously disclosed or found to exist in nature anywhere in the world prior to the effective filing date of a patent application is considered novel. Since the transgenic rice plant in the prior art does not completely disclose the nucleotide sequence in SEQ ID NO: 1 and only has at least 80% identity with SEQ ID NO: 1, the claimed transgenic rice plant is considered novel.



Figure 2. Comparison of the % Sequence Identity (Claim vs Prior Art)

2.2.1 Vector

A claim to a vector comprising a novel gene and that the promoter/regulatory region/or other vector component, such as origin of replication or restriction enzyme site, is new or never been described in any prior art, the vector satisfies *Section 23 of the IP Code/Rule 203 of the Revised Implementing Rules and Regulations for Patents for Novelty*.

2.3 Inventive Step

In general, the problem solution approach (PSA) in the inventive step determination applies to all types of invention. An inventive step cannot be acknowledged when methods of isolation of biological materials were routine and the isolated biological materials did not have any unexpected technical effect or features. Presence of a surprising technical effect may render an invention inventive. However, this surprising technical effect must be substantiated, for example, by experimental data submitted as part of the description. Furthermore, an inventive step could be acknowledged if a claimed sequence imparts an unexpected property to the nucleic acid molecule.

2.3.1. Gene and Polypeptide

A claim directed to a polypeptide wherein said polypeptide is novel and has inventive step, an invention directed to a gene encoding that polypeptide involves inventive step as well.

However, if a claim is directed to a polypeptide that is publicly known but the gene encoding of said polypeptide is not, then an inventive step cannot be acknowledged for a gene encoding that polypeptide since the polypeptide itself is known. A person skilled in the art could expectedly determine the amino acid sequence of polypeptide A at the time of filing.

Note if a claim directed to a gene is defined by a specific nucleotide sequence and has advantageous effects in comparison with the other genes encoding a protein and but has different nucleotide sequences that cannot be predicted by a person skilled in the art, the invention of said gene involves inventive step.

Meanwhile, when an amino acid sequence of a protein is publicly known, a biotechnological application directed to a gene encoding said protein does not involve inventive steps. However, if the gene is described by a specific nucleotide sequence and has advantageous effects that a person skilled in the art cannot expect in comparison with other genes having a different

nucleotide sequence encoding said protein, the invention directed to said gene involves inventive steps.

Illustrative Example 1

Overview of the Description:

The description discloses recombinant DNA molecules displaying a growth-enhancing biological activity of swine growth hormone which are effective in improving the rate of growth of and meat production and quality in swine.

Further, the process used for selecting the DNA sequences of the present invention consists of selecting an SGH-related cDNA sequence chosen by hybridization to a probe from bovine growth hormone. Second, a probe constructed by digestion of the SGH-related cDNA is used.

Claim: A recombinant DNA molecule encoding swine growth hormone X.

Prior Art: The prior art teaches the partial amino acid sequence of swine growth hormone X polypeptide, the high degree of sequence relatedness between swine, bovine and human growth hormone polypeptides, as well as the isolated DNA molecules, encoding human and bovine growth hormone.

Analysis

Based on the prior art, it would have been obvious to a person skilled in the art to isolate a DNA molecule encoding swine growth hormone using probes based on the partial amino acid sequence and identify its sequence since the DNA sequences of human and bovine homologs are already known and has similar characteristics and functions as human and bovine homologs.

Illustrative Example 2

Overview of the Description:

The description demonstrates that the Cry2Ab protein expressed in transgenic plants such as corn, sorghum, and sugarcane have 98%, 92% and 96% efficacy, respectively, in controlling *Chilo sacchariphagus*, in contrast to the commercially available pesticide having only 50% efficacy.

Claim: A method of controlling *Chilo sacchariphagus* in plants, wherein the method involves contacting *Chilo sacchariphagus* with Cry2Ab protein, wherein Cry2Ab protein comprises an amino acid sequence as defined in SEQ ID NO:1, wherein Cry2Ab protein is expressed in transgenic plants such as corn, sorghum, and sugarcane.

Prior Art 1: Document 1 (D1) discloses a method of controlling pest damage lepidopteran pests in plants, wherein the method involves contacting *Helicoverpa armigera* and *Chilo suppressali*, *Propylea japonica* with Cry2Ab protein, wherein Cry2Ab protein comprises an amino acid sequence having 95% identity to SEQ ID NO:1, wherein said Cry2Ab protein is expressed in a transgenic rice. The efficacy of said protein in controlling *Helicoverpa armigera* and *Chilo suppressali* was reported to be 30% and 40% higher than the commercially available pesticide used as control.

Prior Art 2: Document 2 (D2) discloses a method of controlling *Chilo sacchariphagus* infestation in plants, the steps involve the application of synthetic nucleotide sequence encoding an insecticidal Cry1A.105 protein as in SEQ ID NO: 2.

Analysis

A person skilled in the art knowledgeable with the teachings of D1 regarding the use of Cry2Ab protein in controlling *Helicoverpa armigera* and *Chilo suppressali* would not be motivated to modify the disclosed method and apply Cry2Ab protein to *Chilo sacchariphagus* in view of D2 since D2 teaches application of a different insecticidal protein, Cry1A.105 which is considered to teach away from the present invention. Hence, the claimed method is not obvious over D1 in view of D2.

Illustrative Example 3

Overview of the Description: The description discloses an isolated cDNA encoding brain beta-amyloid polypeptide, wherein the polypeptide may be used in the diagnosis and treatment of Alzheimer's disease.

Claim: An isolated cDNA encoding brain beta-amyloid polypeptide associated with Alzheimer's disease.

Prior art: Polypeptides isolated from cerebrovascular amyloid deposits of Alzheimer's patients and provided guidelines for synthesis of degenerate oligonucleotide probes. It also taught methods for constructing and screening cDNA libraries.

Analysis

It would have been obvious based on the prior art to isolate a cDNA encoding brain beta-amyloid polypeptide from an adult brain cDNA library since the prior art already disclosed isolated polypeptides from cerebrovascular amyloid deposits of Alzheimer's patients wherein construction and screening of cDNA based on these polypeptides. The prior art teachings lead to the isolation of the claimed DNA.

Illustrative Example 4

Overview of the Description:

The description demonstrates that the antiviral activity of interferon $\alpha 2$ polypeptide is 30 times more potent than an interferon $\alpha 1$ polypeptide.

Claim: A recombinant DNA sequence of SEQ ID NO: X encoding human interferon $\alpha 2$ polypeptide.

Prior Art: A nucleic acid sequence of SEQ ID NO: X1 encoding human interferon $\alpha 1$ polypeptide wherein it has 90% sequence identity with the instant claim's interferon $\alpha 2$ polypeptide.

Analysis

The claimed human interferon $\alpha 2$ is structurally close to the prior art's human interferon $\alpha 1$. However, the claimed invention is considered not obvious since as exemplified in the description, the claimed human interferon is thirty times more potent in its antiviral activity than its prior art analogue.

Illustrative Example 5

Overview of the Description:

The present application discloses new stable crystals of the protein P and its step-by-step method of preparation. The experimental data shows that the new structure and form of the crystal of protein P (having unit lattice constants of $a=4.0$ nm, $b=7.8$ nm and $c=11.0$ nm) confers storage stability. The description further presents that the routine prior art used for the crystallization of a protein cannot be applied to obtain protein P, and that there had been technical difficulties in manufacturing the claimed crystal of the protein P.

Claim 1: Crystal of a protein P, having unit lattice constants of $a=4.0$ nm, $b=7.8$ nm and $c=11.0$ nm.

Claim 2: A method of crystallizing protein P which comprises the steps of: a) contacting a protein crystallizing agent with a protein-containing solution; and b) precipitating and crystallizing the resulting protein mixture to produce crystal of protein P, wherein the protein crystallizing agent comprises at least one compound selected from the group consisting of compound A, an amide derivative of an amino acid, a salt thereof and a solvate thereof; and wherein if the mixture contains compound A or a salt thereof or a solvate thereof.

Prior Art 1: Crystal of protein Q having needle- or rod-like crystals with a length of 2-25 μm and its method of production.

Prior Art 2: A method of crystallizing a protein which involves the steps of purifying thawed protein feed solution using desalting column, followed by concentrating the purified protein; adding deionized water to the concentrated protein to grow crystals; incubating and mixing the solution gently for 12 hours at 34 degrees C.

Analysis

No prior art documents published before or at the time of filing discloses the manufacture of protein P. Prior art 1, the closest prior art, discloses crystals of protein Q, but said crystals differ in shape and structure from crystals of protein P. Furthermore, applying the disclosed method of producing crystals of protein Q in prior art 1 would not result to the claimed crystals of protein P.

Prior art 2 teaches a conventional method of crystallizing any protein.

As shown in the description, the distinct characteristics of the newly manufactured crystals of protein P confer storage stability.

In light of the foregoing, the person skilled in the art, who is knowledgeable with the teachings of prior art 1 regarding crystals of protein Q, would not be sufficiently guided to expectedly arrive at the claimed invention by applying the publicly known method used for crystallizing a protein as taught in prior art 2. Therefore, the subject matter of claims 1 and 2 involves an inventive step.

2.3.2. Vector

An invention directed to a vector with new genetic insert may be regarded as inventive if at least one of the following elements is **NOT** taught in the prior art:

- (a) the antibiotic resistance markers in the vector,
- (b) the origin of replication for the vector,
- (c) the restriction site(s) for insertion of the gene of interest, and

- (d) the regulatory region (promoter and terminator for the coding sequence to be inserted).

The inventive step of the claimed vector may further be supported by providing unexpected results, such as unexpectedly high replication rates, better maintenance of the genetic insert in culture overtime, much smaller vector size allowing for easier insertion of genetic material into the recipient cell, increased/reduced copy number of the genetic insert into the recipient cell, or improved ability to insert multiple genes of interest at a single restriction site, etc.

2.3.3. Probes

Probes which are defined by its nucleotide sequence and have advantageous effects that are beyond the expectations of a person skilled in the art may be considered inventive. It must also be taken into account that the DNA sequence to which it shall be used as a probe must have proper disclosure of function and biological activity.

Some technical features of a probe that may be considered inventive can be but are not limited to the following :

- (a) the gene the probe detects is inventive
- (b) elicits a more accurate detection
- (c) results to a more precise diagnosis

However, if gene X to which a probe is used for detection is considered not inventive a claim to the probe itself is consequently considered as not having inventive step.^[40]

2.4 Clarity/Enablement/Support

2.4.1 Enablement and Support

To satisfy sufficiency of disclosure and enablement requirements, the following may be presented or described in the description:

- i. method or process as to how these biological materials are produced;
- ii. the origin or source, conditions of treatment;
- iii. the collection, isolation, purification, characterization and identification processes involved; and
- iv. uses and/or functions; among others.

⁴⁰ JPO Trilateral Project 24.1-Biotechnology

In the event these biological materials cannot be sufficiently disclosed in the application in such a way as to enable the invention to be carried out by a person having ordinary skills in the art and such material is not available to the public, the invention shall be disclosed according to *Rules 408 or 409 of the Revised IRR of 2022*.

As mentioned, genes which when technically isolated or produced, are patentable as long as these have specific and credible functions.

Illustrative Example 1

Overview of the Description:

The specification provides an example on the use of a specific viral vector.

Claim: A method of delivering cloned DNA to a host cell, using a viral vector.

Analysis

Objection on enablement and support in the claim may be raised. The claim encompasses any and all viral vectors in the art while the specification only exemplifies a particular or specific viral vector and does not enable any and all viral vectors.

As known in the art of vectors, viruses behave differently when infecting cells; some viruses require cells to be actively dividing, so that the viral DNA can be inserted in the DNA of the host cell while other viruses do not require actively dividing cells for infection. Likewise, the claim may be objected to as not enabled to “any and all cells”, as a particular viral vector may only be able to infect certain cell types. The objection is made to limit the claims to narrow the scope as to what the invention fully supports and disclosed.

On the other hand, one way to establish support to a broader claim is to provide sufficient working examples in the description that a claim to a genus (or broad class) can be asserted.

When the invention is directed to an unpredictable art such as biological materials, examples showing use of one species within a broad class will usually not suffice to provide support for a broad claim, unless a relationship between the specific species shown and others (for which examples are not shown or not available) within the broad category is established. The disclosure should provide experimental data or other evidence to support broader, generic claims since it may not be possible to claim a broad genus not fully supported in the description.

2.4.1.1 Analogues or variants of Polynucleotides or Polypeptides

Analogues or variants of polynucleotides or polypeptide sequences, in the form of additions, substitutions or deletions, could extend to an almost infinite number of variants. Thus, any claim seeking to protect variants thereof does not lack support as long as the claim is restricted to variants sharing a common and/or specific activity (e.g., a nature-identical material).^[41]

2.4.1.2 Probes

When a probe is specified by an amino acid sequence, an infinite number of corresponding DNA sequences are expected. This can be further elucidated through the genetic code table which summarizes the relationship between amino acids and codons wherein for some amino acids there can be more than one corresponding codon that is DNA or RNA sequence of three nucleotides. It is highly unlikely that all such DNA sequences would be useful as probes. In such a case, undue experimentation would be required to carry out the claimed invention. Generally, such a claim would not be allowed because the enablement requirement is not satisfied.

Furthermore, enablement requirement is generally considered not to be satisfied also in cases where DNA probes for analysis are specified by homological, hybridization and addition/deletion/substitution sequences since this may encompass features wherein probes are specific for a region of the disclosed sequence that is varied.⁴²

2.4.2 Clarity Requirements

2.4.2.1 Nucleic Acids and Nucleotides

The following inventions relating to nucleic acids/ genes are considered clear but are not limited thereto:

- a. A gene is defined by specifying its nucleotide sequence as represented by a SEQ ID NO.
- b. A structural gene is defined by specifying an amino acid sequence of the protein encoded by said gene as represented by a SEQ ID NO.
- c. The modification in the gene is defined (e.g., deletion, substitution, addition and the like)
- d. A gene is defined with its function/s
- e. A vector is defined by specifying the complete or partial nucleotide sequence as represented by a SEQ ID NO. with their functions and/or by specifying its elements and functions in the application.

⁴¹ *Kirin-Amgen Inc. and others v. Transkaryotic Therapies Inc. and others [2003] RPC3 (Court of Appeal)*

⁴² *JPO Trilateral Project 24.1-Biotechnology*

For non-coding nucleic acids such as DNA fragments or probes, the general requirements for drafting a claim are as follows:

- a. Specifying the nucleotide sequence, wherein further a non-coding nucleotide is described by specifying the target gene;
- b. One must have a precise definition of the DNA fragment or probe length;
- c. Said probe should strictly hybridize with the specific polynucleotide to be detected; and/or
- d. It does not hybridize with polynucleotides with similar polypeptides.

For clarity requirements, isolations of these genes shall be clear and unambiguously disclosed in the application and that genes shall be defined by their technical features such as the sequences are defined by:

- (a) reference to the corresponding nucleotide sequence ID number, as illustrated below;

SEQ ID NO: 1

AGGCTAAGTGGTCCTCCACCTCAATCTCCTGGAAAGCT
AAGACTACAG

or

- (b) specifying an amino acid sequence of the protein encoded by said gene exemplified below;

Ser Gly Ser Thr Gly Gln Trp His Ser Glu Ser Gly Ser Phe Arg

or

- (c) a combination of the terms such as substitution, deletion or addition as well as the term hybridize with the generic terms of the gene's functions demonstrated herein below.

Illustrative Example 1 - Polynucleotides

Claim: A polynucleotide selected from the group comprising of:

- i. a polynucleotide consisting of DNA sequence represented by SEQ ID NO: 1 AGGCTAAGT GGTCTCCCA CCTCAATCTC...
- ii. a polynucleotide which hybridizes under specific conditions to the polynucleotide whose DNA sequence is complementary to that of the

DNA sequence as defined in (i) and encodes a protein having the activity of enzyme A.

Illustrative Example 2 - Gene Modifications

Claim: A polynucleotide encoding a protein of (i) or (ii) as follows:

- i. a protein whose amino acid sequence is represented by Met-Asp-...
Lys-Glu
- ii. is a protein derived from the protein of (i) by deletion, substitution or addition of one or more amino acids in the amino acid sequence defined in (i) and having the activity of enzyme A.

Illustrative Example 3 - Gene Modifications

Claim: An isolated nucleic acid encoding a bispecific antibody that binds to CDX and CDY, wherein the bispecific antibody comprises an anti-CDX arm comprising a first binding domain comprising :

- (a) a VH domain comprising the amino acid sequence of SEQ ID NO: 1 and
- (b) a VL domain comprising the amino acid sequence of SEQ ID NO: 2,

and the anti-CDX arm comprises T366S, L368A, Y407V, and N297G substitution mutations and (b) the anti-CDY arm comprises T366W and N297G substitution mutations (EU Numbering).^{[3]43}

Illustrative Example 4 - Non-coding nucleic acid/ nucleotide

Claim 1: A probe whose nucleotide sequence is represented by SEQ ID No. X.

Claim 2: An siRNA targeting XX gene whose nucleotide sequence is represented by SEQ ID No. X.

2.4.2.2 Proteins and Polypeptides

When it comes to proteins, clarity may be exemplified in the description by the isolation or purification of the protein, also by specifying its amino acid sequence, its function, physicochemical properties, or how it is produced.

The following inventions relating to proteins are considered clear but are not limited thereto:

⁴³ US 10865251 B2 Anti-CD3 antibodies and methods of use (*modified*)

- a. A recombinant protein is described by specifying an amino acid sequence or a nucleotide sequence of a structural gene encoding said amino acid sequence.
- b. A recombinant protein is described by combining terms such as "deletion, substitution or addition" and "X% or more of sequence identity", with functions of the recombinant protein, and if necessary, with origin or source of gene encoding the recombinant protein, in a generic form.
- c. A protein obtained by isolating from or purifying natural products is defined by specifying the function, physicochemical properties, an amino acid sequence, a production process, etc.

Illustrative Example 1: Recombinant Protein

Claim: A recombinant protein of (i) or (ii) as follows:

- (i) a protein whose amino acid sequence is represented by Met-Tyr-...Cys-Leu
- (ii) a protein whose amino acid sequence has X% or more of sequence identity of the amino acid sequence of (i) and which has the activity of enzyme A.

3. ANTIBODIES

3.1 Eligibility

Antibodies that have been removed or isolated by technical means from their biological environment where they naturally exist are eligible for patent, because although they contain the same compositions and structures as those found in their natural environment, they are eligible for patent on the basis that such do not usually occur in an isolated form in nature and that human intervention is necessary for the isolation and preparation of said antibodies.

3.2. Novelty

As discussed above, it has become an accepted practice to describe antibodies in terms of the antigen to which they bind. A written description of the antibody can be provided by a written description of the antigen. In general, if the antigen is novel, then an antibody against said antigen is considered to be novel, provided the antigen is well-defined in the application.

However, where the prior art discloses and enables antibodies that bind with a close structural relative of the new antigen, then a claim to an antibody reactive with such new antigen (e. g. an antibody “capable of binding” or “that specifically binds” to antigen) will be anticipated if the claim is construed to encompass cross-reacting antibodies of the prior art.

In general, antibodies can be defined by (but are not limited to) the following:

- (a) their own structure (amino acid sequences);
- (b) nucleic acid sequences encoding the antibody;
- (c) reference to the target antigen;
- (d) target antigen and further functional features;
- (e) functional and structural features;
- (f) the production process;
- (g) the epitope; and
- (h) the hybridoma producing the antibody.⁴⁴

⁴⁴ EPO Guidelines for Examination (Antibodies): General Remarks (5.6.1)

3.2.1 Polyclonal Antibody

Illustrative Example 1

Overview of the Description:

The specification discloses a novel protein X isolated from a bacterial pathogen. This novel protein X may be used as a diagnostic target for detecting disease caused by the bacterium. Also disclosed are the amino acid sequence of the novel protein X (SEQ. ID No: 1), methods of purifying novel protein X using recombinant techniques, and methods of preparing antibodies to the novel protein X by immunizing a suitable mammalian host. The gene encoding the protein X was cloned by immunoscreening a phage library with an antibody reactive with a close homologue **H** of the novel protein, said homologue **H** is defined by Sequence ID No. 22.

Claim: An antibody capable of binding to the protein X defined by SEQ ID No: 1.

Prior Art: An antibody capable of binding to the protein **H** defined by Sequence ID No. 22.

Analysis

The claimed antibody is not new. Despite the fact that the protein defined by SEQ ID No: 1 itself is novel, the claimed antibody is anticipated since an old and known antibody has already been used and shown the requisite binding capability (i. e. the antibody used for immunoscreening) to a close homologue of the novel protein.

Illustrative Example 2

Overview of the Description:

The specification discloses the development of a polyclonal antibody to localize and quantify xanthine oxidase in tissues and biological fluids and uses thereof.

Claim: A polyclonal antibody that specifically binds to human xanthine dehydrogenase and human xanthine oxidase, wherein said antibody is linked to a detectable label.⁴⁵

⁴⁵ WO/1996/038483 *Monoclonal and Polyclonal Antibodies against Recombinant Human Xanthine Oxidase, Method of Their Use and a Kit Containing Same (modified)*

Prior Art: A method of preparing monoclonal antibodies to xanthine oxidase and other proteins of bovine milk-fat-globule membrane.⁴⁶

Analysis

The claimed antibody is new. Despite the fact that the prior art disclosed the antibodies to xanthine oxidase, the present claim is not anticipated since it relates to monoclonal antibodies.

3.2.2 Monoclonal Antibody

For a new antibody to a known antigen to overcome novelty rejections, it should be defined by other specific structural or functional features conferring a particular technical effect that is advantageous compared to the prior art. These special structural or functional features may be:

Structural	Functional
<ul style="list-style-type: none">• Specific amino acid sequences• One or more CDR sequences• Variable region sequences• Structurally modified F_c region• Specific glycoforms• Specific isotypes• Fragments• % Threshold Difference	<ul style="list-style-type: none">• Binding affinity• Binding specificity• Binding a defined epitope (Amino acid sequence)• Blocking the binding of a specific antibody to the epitope• New biological function

Illustrative Example 1

Overview of the Description:

The present invention discloses a monoclonal antibody with six (6) structural characterization of CDRs (SEQ ID Nos 1-6), the binding of the antibody to protein A, and preparation of said antibody for use in method M for the utilization of its neutralizing activity.

Claim: A monoclonal antibody which binds with protein A, said antibody is prepared by method M and is useful for its neutralizing activity, wherein the six CDRs comprising said antibody are described by SEQ ID NO. 1-6.

⁴⁶ Benboubetra, et. al. *Human Monoclonal Antibodies to Xanthine Oxidase*. *Biochem Soc Trans*, 1990, Vol. 18, pages 1008-1009 (modified)

Prior Art: A monoclonal antibody which binds with protein A, said antibody is prepared by method M and is useful for its neutralizing activity, wherein said antibody is characterized by the amino acid sequence of the six CDRs given by SEQ ID NO. 10-15.

Analysis

The claimed antibody is novel over the prior art despite the affinity to a known protein A and having a known mode of action. Novelty is established due to structural characterization of the six CDRs. This case may happen in large proteins with multiple epitopes.

Illustrative Example 2

Overview of the Description:

This invention relates to TCRs (T-cell receptors), individual TCR subunits (alone or in 15 combination), and subdomains thereof, soluble TCRs (sTCRs), for example, soluble alpha/beta dimeric TCRs having at least one disulfide inter-chain bond between constant domain residues that are not present in native TCRs, and cloned TCRs, said TCRs engineered into autologous or allogeneic T-cells or T-cell progenitor cells, and methods of making same, as well as other cells bearing said TCR.

Claim: An antigen recognizing construct comprising at least one complementary determining region (CDR) 3 having at least 80% sequence identity to an amino acid sequence selected from SEQ ID NOs 44, 52, 60, 68, 76, and 84.⁴⁷

Prior Art: A variable region of T cell receptors (TCR) or B cell receptors (BCR) quantitatively analyzed using non-biased gene sequence analysis comprising: The CDR3 sequence according to SEQ ID NO: W is identical over 13 of 15 amino acids to SEQ ID No: A of the application; The CDR3 sequence according to SEQ ID NO: X is 81.2% identical over the full-length to SEQ ID No: B of the application; The CDR3 sequence according to SEQ ID NO: Y is 91.7% identical over the full-length to SEQ ID NO: C of the application; and the CDR3 sequence according to SEQ ID NO: Z is identical over nine of 15 amino acids to SEQ ID NO: E of the application.⁴⁸

⁴⁷ WO/2017/158103 - Transfected T-Cells and T-Cell Receptors for Use in Immunotherapy Against Cancers

⁴⁸ HAQUE, T., et. al. "Treatment of Epstein-Barr-virus-positive post-transplantation...", *The Lancet Publishing Group*, GB, vol. 360, no. 9331, pages 436-442, 10 August 2002 (10.08.2002)

Analysis

The claim is directed to an "antigen recognizing construct" comprising a sequence having at least 80% identity to any one of the sequences shown in SEQ ID NOs: A, B, C, D, E and F. The subject matter lacks novelty over the prior art since the sequences according to SEQ ID Nos: A, B and C are **more than 80% identical to CDR3 sequences** according to SEQ ID NO: W, X and Y.

Sequence similarity searching, typically with BLAST, is the most widely used, and most reliable, strategy for characterizing newly determined sequences. Sequence similarity searches can identify "homologous" proteins or genes by detecting excess similarity – statistically significant similarity that reflects common ancestry.⁴⁹

*If the relevant prior art discloses a sequence having a percent sequence identity **equal or greater than** the sequence of the claimed invention, then said claim is not novel.*

Illustrative Example 3

Overview of the Description:

The specification discloses monoclonal antibodies that bind to the complement factor 5 (CS) protein, and methods of use thereof, wherein said antibodies are fully human antibodies that bind to CS protein which is useful for inhibiting or neutralizing CS activity, thus providing a means of treating or preventing a CS-related disease or disorder in humans.

Claim: An antibody or antigen-binding fragment thereof that binds specifically to complement factor 5 (C5) protein, wherein the antibody or antigen-binding fragment thereof interacts with one or more amino acids.

Prior Art: An antibody targeting complement protein C5, composition, and methods of use thereof in treating diseases.

Analysis

The claim is not novel. Considering the claim construction, any C5 specific antibody can destroy its novelty. Although it is clear to which part of the

⁴⁹ Pearson, WR. *Curr Protoc Bioinformatics*. 2013 June; Chapter 3: Unit 3.1.
doi: 10.1002/0471250953.bi0301s42.

sequence the antibody binds, those antibodies can be reliably produced, for example, by immunization with the epitope.

3.2.3 The following are examples of claims that are considered to overcome novelty rejections over antibodies of known antigens (but are not limited thereto):

1. An isolated antibody or functional fragment thereof comprising an antigen-binding region that is specific for target protein c-Met, wherein said antibody or functional fragment thereof binds to human c-Met with a KD at or below 4.6 pM (*Binding affinity*).
2. An antibody reactive with the pyridinoline in peptide-linked pyridinoline but not with free pyridinoline which is useful in an assay to indicate bone resorption (*Binding specificity*).
3. A monoclonal antibody that specifically binds to antigenic epitope of human IL-22RA polypeptide, wherein said antigenic epitope is selected from (a) epitope consisting of SEQ ID NO. 1, (b) an epitope consisting of SEQ ID NO. 43, and (c) an epitope consisting of SEQ ID NO. 93, wherein the antibody reduces or neutralizes the activity of a human IL-22 polypeptide (*Binding an epitope*).
4. A monoclonal antibody capable of recognizing and binding the high-affinity tyrosine kinase receptor of Nerve Growth factor (NGF), named TrkA, and acts as an antagonist for the binding of NGF to TrkA (*New biological function*).
5. A monoclonal antibody, or an antigen-binding fragment thereof, which: a. binds to human CD47, b. blocks SIRPa binding to human CD47, c. increases phagocytosis of human tumor cells; and d. induces death of human tumor cells (Structural-Fragments).⁵⁰

3.3 Inventive Step

A claim to a novel antibody of known antigen can be considered inventive if

- the antigen which it binds has a surprising technical effect;
- it has an additional inventive feature supported by working examples; and
- it is properly described and enabled by the description.

On the other hand, even if a claim relating to a method of generating or producing antibodies against an antigen is non-obvious, it will be considered a mere routine experimentation if the antibody produced from the method

⁵⁰ WO/2017/049251 - Therapeutic CD47 Antibodies

thereof did not result to any unexpected impact (i.e. the antibody has the same composition and activity as the prior art). Hence, no inventive step can be acknowledged.

However, if the claim is directed to the method for producing antibody, and the method itself has an unexpected impact, for example, on the properties of the antibody, such method may be determined as being inventive.

Unless a surprise technical effect is demonstrated by the application or unless there was no reasonable expectation of success in generating antibodies with the required qualities, antibody binding to a known antigen does not entail an inventive step.

Further, when compared to known and enabled antibodies, some unexpected technical outcomes include increased affinity, improved therapeutic effectiveness, decreased immunogenicity or toxicity, unanticipated species cross-reactivity, or a novel antibody format with demonstrated binding activity.⁵¹

3.3.1 Polyclonal Antibody

Illustrative Example 1

Overview of the Description:

The specification discloses the development of a polyclonal antibody to localize and quantify xanthine oxidase in tissues and biological fluids and uses thereof (same as 3.2A. Illustration 2).

Claim: A polyclonal antibody that specifically binds to human xanthine dehydrogenase and human xanthine oxidase, wherein said antibody is linked to a detectable label.⁵²

Prior Art: A method of preparing monoclonal antibodies to xanthine oxidase and other proteins of bovine milk-fat-globule membrane.⁵³

Analysis

Although the claimed antibody is deemed novel in 3.2A. Illustration 2, said prior art teaches an antibody that binds to xanthine oxidase. The technical feature provided is obvious in that the person skilled in the art (PSA) can

⁵¹ EPO Guidelines for Examination (Antibodies): Inventive Step of Antibodies (5.6.2)

⁵² WO/1996/038483 - Monoclonal and Polyclonal Antibodies against Recombinant Human Xanthine Oxidase, Method of Their Use and a Kit Containing Same

⁵³ Benboubetra, et. al. Human Monoclonal Antibodies to Xanthine Oxidase. *Biochem Soc Trans*, 1990, Vol. 18, pages 1008-1009.

easily use said prior art to modify the monoclonal antibody to polyclonal antibody.

3.3.2 Monoclonal Antibody

Illustrative Example 1

Overview of the Description:

The specification discloses an antibody which is produced by the method M, said method M involved immunization of the subject with the conjugated immunogen, screening of the serum, then isolation and purification of the antibody. Further analysis reveals the novel amino acid structure of the complementarity determining regions of the antibody. The novel antibody binds a known protein A.

Claim: A monoclonal antibody which binds with protein A, said antibody is prepared by method M and is useful for its neutralizing activity, wherein said antibody comprising the six CDRs as being those of SEQ ID NO. 1-6.

Prior Art: A monoclonal antibody which binds with protein A, said antibody is prepared by method XYZ and is useful for its neutralizing activity, wherein said antibody is characterized by the amino acid sequence of the variable domains of the light chain and heavy chain described by SEQ ID NO. 7 and 8, respectively.

Analysis

The antibody is obvious in view of the prior art. Even if the method of production of the claimed antibody is different from the prior art, said method did not give the claimed antibody any unexpected impact (i. e. the antibody has the same composition and activity as the prior art).

Illustrative Example 2

Overview of the Description:

The invention relates compounds comprising anti-DLL3 antibodies or immunoreactive fragments thereof having one or more unpaired cysteine residues conjugated to pyrrolobenzodiazepines (PBDs) and use of the same for the treatment or prophylaxis of cancer and any recurrence or metastasis thereof.

Claim: An antibody drug conjugate of the formula: Ab-[L-D]_n or a pharmaceutically acceptable salt thereof wherein a) Ab comprises a DLL3 antibody comprising one or more unpaired cysteines; b) L comprises an optional linker; c) D comprises a PBD; and d) n is an integer from about 1 to about 8.⁵⁴

Prior Art: An antibody modulator conjugates or antibody-drug conjugates that may be used for the diagnosis and/or treatment of proliferative disorders, wherein such conjugates may be represented by the formula M-[L-D]_n where M stands for a disclosed modulator or target binding moiety, L is an optional linker or linker unit, D is a compatible drug or prodrug and n is an integer from about 1 to about 20.⁵⁵

Analysis

It will be appreciated that, unless otherwise dictated by context, the terms "antibody-drug conjugate" or "ADC" or the formula M-[L-D]_n shall be held to encompass conjugates comprising both therapeutic and diagnostic moieties. In such embodiments antibody-drug conjugate compounds will typically comprise anti-CD324 as the modulator unit (M), a therapeutic or diagnostic moiety (D), and optionally a linker (L) that joins the drug and the antigen binding agent. People skilled in the art will observe that a number of different reactions are available for the attachment or association of therapeutic or diagnostic moieties and/or linkers to binding agents. It would have been obvious at the time of the invention to modify the method to include a DLL3 antibody to develop an antibody drug conjugate that can be used in treating or ameliorating proliferative disorders.

Illustrative Example 3

Overview of the Description:

The specification discloses a method of measuring antibody response against COVID-19 infection in humans. Also disclosed herein is a kit which uses a combination of SARS-COV-2 antigens and an enzyme labeled secondary antibody that specifically detects IgM and IgG response during the course of infection.

Claim: A method for detecting antibody response against COVID-19 infection comprising the steps of incubating a pre-diluted serum or plasma into individual wells each containing SARS COV-2 Spike 1, Spike 2 and Nucleoprotein antigens; binding of either IgM or IgG antibody to the viral antigen is detected by the use of a secondary antibody

⁵⁴ WO/2017/049251 - Engineered Anti-DLL3 Conjugates and Methods of Use

⁵⁵ WO/2013/119960 - Anti-CD324 Monoclonal Antibodies and Uses Thereof

labeled with an enzyme reporter; and detecting IgM and IgG against SARS-COV-2 Spike 1, Spike 2 or Nucleoprotein antigens is indicative of an antibody response to COVID-19.

Prior Art: A serum antibody testing method for the diagnosis of COVID-19 patients, wherein the levels of IgM and IgG specific to N and S protein were detected by ELISA (enzyme-linked immunosorbent assay) technique.

Analysis

The claimed method is not inventive. The claimed method for detecting antibody response against COVID-19 infection is not the same from the prior art. However, said method did not give the claimed antibody any unexpected impact (i.e. same antibody as the prior art).

3.4 Clarity/Enablement/Full Support

Antibodies are chemical compounds, thus may be described according to their chemical structure, the process by which they are made, and physical and/or chemical properties.

In practice, patent claims define the antibodies by reference to one or more of the following: (a) the antigen to which the antibody binds; (b) a novel epitope; or (c) the sequence of the antibody polypeptide.

Wherein a new antigen is discovered and its therapeutic use is disclosed, it would enable a skilled person to produce an antibody to said antigen. Therefore, claims related to the antibody will be taken into consideration, even if the actual antibody has not yet been produced. Claims of such type are broad and encompass all the next-generation antibodies against the said target antigen.

Illustrative Example 1

Overview of the Description:

The specification discloses a novel protein isolated from a bacterial pathogen. This novel protein may be used as a diagnostic target for detecting diseases caused by the bacterium. Also disclosed are the amino acid sequence of the novel protein (SEQ. ID No: 1), methods of purifying novel protein using recombinant techniques, and methods of preparing antibodies to the novel protein by immunizing a suitable mammalian host (although no working examples of the antibody are provided). The novel protein appears to be a

member of a new class of bacterial proteins, and a sequence search reveals that its closest structural relative is 20% identical, with no common domain of significance.

Claim: An antibody capable of binding to the protein defined by SEQ ID No: 1.

Analysis

The claim is enabled. Since the protein is new, it exhibits only a little structural similarity to known protein, and has utility as a diagnostic target, the antibodies prepared against it are likewise new, obvious and industrially useful. The specification is enabling both on (a) the method of preparation of the claimed antibody, and (b) the description of the antigen (i.e. the amino acid sequence). The claim, therefore, is fully supported by the specification.

Illustrative Example 2

Overview of the Description:

The specification discloses a correlation between a novel hydrophobic peptide and a disease. The amino acid sequence of the novel peptide is provided (SEQ ID No: 1), and chromatographic analysis reveals that it is a low-molecular-weight member of a class of peptides to which no known antibodies have ever been prepared despite several attempts. The specification further asserts that antibodies to the peptide may be prepared for eventual use in the immunoassay for the disease (although no working examples of the antibody reactive to the novel peptide are provided).

Claim: An antibody capable of binding to the protein defined by SEQ ID No: 1.

Analysis

The claim is objectionable because it lacks enablement. No antibodies were raised against the novel peptide (i. e. it was merely asserted) and the specification teaches that, despite several attempts, no antibodies have yet been produced against peptides of similar type. A person skilled in the art would not regard the specification as enabling with regard to the production of the claimed antibody.

Illustrative Example 3

Overview of the Description:

The specification discloses a series of antibodies with specific pairing of heavy chain variable domain (V_H) comprising CDR3 (SEQ. ID. 1) and light chain variable domain (V_L), and that said series of antibodies binds with antigen X. The V_H domains are highly homologous to each other, and share identity over a large portion of the other CDR and framework regions. The V_L sequences are highly homologous to each other in the CDR and frameworks regions. The specification further suggests that it is well-established in the art that the CDR3 region alone can determine the specificity of the antibody.

Claim: An isolated antibody that binds to human antigen X, said antibody comprises a heavy chain variable domain and a light chain variable domain, said heavy chain variable domain comprises the CDR3 in SEQ ID No: 1.

Analysis

The enablement may be established if and when data or working examples that demonstrate that CDR3 of Sequence ID No. 1 can confer antigen specificity to a randomized sequence are provided. This is so because it is widely known that CDR3 is not solely responsible for antigen binding, as a number of references describe that all six CDR regions provide important contacts with antigen.

Illustrative Example 4

Overview of the Description:

The specification discloses a method for inducing, augmenting or prolonging an immune response to an antigen in a patient, comprising administering to the patient an effective dosage of a humanized antibody that specifically binds to human CTLA4, wherein the antibody blocks binding of human CTLA4 to human B7.

Claim: An anti-CTLA4 antibody which inhibits the binding of CTLA4 to human B7.⁵⁶

⁵⁶ WO/2012/120125 - Humanised Anti CTLA-4 Antibodies

Analysis

The claim is rejected since it includes results to be achieved, and must be amended to further provide narrower interpretation of the accorded claim of how said advantageous effects/results are achieved.

Proper drafting:

*“An anti-CTLA4 antibody which inhibits the binding of CTLA4 to human B7, **wherein said antibody comprises variable regions having CDR sequences A, B, and C.**”*

4. STEM CELLS

4.1 Eligibility

In evaluating applications relating to stem cells (including their use and derived products), the primary consideration is the origin of such stem cells. More particularly, caution must be exercised when the stem cells are embryonic in nature, as this could potentially be raised on patentable subject matter, particularly with regards to Sec. 22.6 of the IPCode (on public order and morality), as explained below. It is important to look at the description in particular, the sources of the stem cells, and how they were isolated and obtained. This is to categorize whether the use of the embryo as a base material involved direct destruction or not.

Direct destruction may include the isolation of the embryo such that said embryo will no longer develop into a viable human or animal form. Likewise, the term human embryo represents an organism which is capable of developing into a human being.

The use of a human embryo may constitute the process of killing, aborting and other processes that would destroy the human embryo and disrupt the differentiation which could have led to a fully developed organism.

4.1.1 Non-Eligible Human Stem Cells

Applications relating to stem cells and products thereof, and methods of obtaining said stem cells, are non-eligible if said stem cells are isolated by means involving direct destruction of the human embryo, as these constitute an invention that is against public order or morality (*Sec. 22.6 of the IP Code*).

Human embryo, in the context of being a source of stem cells, has been broadly defined, and has not been given restrictive meaning so as to cover any organism capable of developing into a human being, to fully protect human dignity and to prevent commercialization of embryos.

In view of this, embryonic stem cells that may fall within the exclusion from patentability are those isolated from:

- a) earlier stages of the human embryo up to the fetal stem cells (approximately 8th-week post-fertilization),
- b) aborted fetal stem cells and their derivatives, and
- c) primary embryonic stem cell lines directly isolated from the human embryo.

Caution must be exercised where there is no mention, in the claims nor in the description, of the method by which the stem cell was isolated. Where an invention requires the use of cells that originate from a process which was originally established to require the destruction of a human embryo, the invention is not eligible. In such cases where it cannot be absolutely ascertained from the claims or description from where such stem cells were isolated, it may be more legally prudent to consider this as falling within Sec 22.6 of the IP Code.

Among the types of stem cells, totipotent stem cells, which are capable of developing into a functional organism, are excluded from patent protection.

Under Rule 202 (i) of the Revised IRR, Philippine Patents are not to be granted in respect of biotechnological inventions which concern:

- i. Processes for cloning human beings - defined as any process including techniques of embryo splitting, designed to create a human being with the same nuclear genetic information as another living or deceased human being.*
- ii. Processes for modifying the germ line genetic identity of human beings (A process that uses laboratory-based technologies to alter the DNA makeup of an organism (i.e. human). This may involve changing a single base pair (A-T or C-G), deleting a region of DNA or adding a new segment of DNA.)*
- iii. Uses of human embryos for industrial or commercial purposes - obtained by a method which necessarily involved the destruction of human embryos from which the said product is derived, even the said method is not part of the claim. The point in time at which such destruction takes place is irrelevant.*
- iv. Processes for modifying the genetic identity of animals which are likely to cause them suffering without any substantial medical benefit to man and animal and also animals resulting from such processes. The substantial medical benefit referred to, includes any benefit in terms of research, prevention, diagnosis or therapy.*
- v. Any biological material and method able to seriously endanger human beings, animals, or plant life, or able to cause serious damage to health or environment, including its use is likely to jeopardize public order and morality (such as terminator gene technology).*
- vi. Human stem cell cultures which at the filing date can only be obtained by destroying human embryos are not patentable, even if the destruction is not part of the claims.⁵⁷*

⁵⁷ EPO Decision G 0002/06 (Use of embryos/WARF) of 25.11.2008

4.1.2 Additional non-patentable subject matter⁵⁸

1. Human beings, fetuses, zygotes, blastocysts, embryos, fertilized ova, and equivalents;
2. Totipotent human cells;
3. Methods of *in vitro* fertilization⁵⁹;
4. Processes for cloning at the four-cell stage or by replacing nuclear DNA;
5. Processes that involve the creation of a human embryo regardless of the manner in which it was generated, including, but not limited to, fertilization of gametes and nuclear transfer.

Illustrative Example I

Overview of the Description

The isolated mammalian neural stem cells and/or neural progenitor cells for use in the present invention may be obtained from the central nervous system of a mammalian, preferably a primate such as, but not limited to, a human. Oligodendrocyte progenitors and pre-progenitors are known to exist in white matter of the central nervous system. As such, suitable sources from which to isolate cells for use in the present invention include, but are not limited to, the optic nerve, corpus callosum and spinal cord. In addition, isolated stem cells may be derived from a mammalian fetus, preferably a primate fetus, such as but not limited to a human fetus, using methods known in the art. In some embodiments, the isolated stem cells are prepared from human fetal spinal cord tissue obtained from a human fetal spinal column. In a preferred embodiment, isolated cells for use in the present invention are obtained from 8-24 weeks gestational age, preferably 12-18 weeks gestational age human fetal spinal cord.

Claims:

1. An isolated expandable human neural cell wherein the cell is a progenitor cells or stem cell, wherein the cell maintains its capability to differentiate into neurons, astrocytes, and oligodendrocytes, wherein the cell maintains its ability to differentiate into oligodendrocyte lineage cells efficiently throughout subsequent passages, and wherein the cell expresses at least cell surface antigens CD133 and CD140a.

⁵⁸ IP Australia Patent Manual of Practice and Procedure - Section 2.9.3.5 Human Beings and Biological Processes for Their Generation

⁵⁹ From the provided definition of *in vitro* fertilization (IVF), the subject matter of *in vitro* fertilization falls under Sec. 22.3 of the IPCode (Methods of treatment of the human and animal body by surgery or therapy) and therefore considered as non-patentable inventions.

2. The expandable human neural cell of claim 1, wherein the cell is derived from a human fetal neural tissue selected from the group consisting of spinal cord, cerebral cortex, hippocampus, striatum, basal forebrain, ventral mesencephalon, locus coeruleus, hypothalamus, cerebellum, corpus callosum and optic nerve.
3. The expandable human neural cell of claim 2, wherein said neural tissue is isolated from the human spinal cord at 8-24 weeks gestation.

Analysis

The present specification teaches that the biological material concerned is obtained from human fetal spinal column wherein said biological material is preferably obtained from 8-24 weeks gestational age. Under the Philippine Law, invention that is contrary to morality, in particular the use of human embryos is not allowable subject matter, thus, excluded from patent protection. Accordingly, the products obtained from such excluded uses are also non-patent eligible subject matter. In the present specification, the source of the biological material could be regarded as human embryo. At the gestational age of 8-24 weeks, isolation of such stem cells have a high likelihood of affecting the further development of the embryo.

Illustrative Example 2

Silence or vagueness of the claims and description regarding the method of isolation of stem cells.

Overview of the Description:

The description provided the use of embryonic stem cells. No destruction of the embryo was mentioned, nor was there any clear mention of how the stem cells would be isolated or acquired.

Claim 1. Use of stem cells in an adjunctive treatment of immune dysfunction in a subject, wherein the stem cells can differentiate into at least one cell type of each of at least two of the endodermal, ectodermal, and mesodermal embryonic lineages; express telomerase, are allogeneic or xenogeneic to the subject, do not provoke a deleterious immune response in the subject, and are effective to treat the immune dysfunction in the subject.

Analysis

Non-patent eligible. Caution must be exercised when there is no mention in the claims and description of the method by which the stem cell is isolated. Even though destruction of the embryo is not mentioned in the description, since the subject matter of the claimed invention relates to embryonic stem cells, the stem cells may still fall within the exclusion, i.e., a) up to 8 weeks post-fertilization, b) aborted fetal stem cells and their derivatives, and c) primary embryonic stem cell lines directly isolated from the human embryo. The applicant should specifically disclose the source of the embryonic stem cells to ascertain the identity of the stem cells used and draft the claim to include such.

Illustrative Example 3

Overview of the Description:

The description discloses that the stem cells are characterized in that they are not embryonic stem cells, embryonic germ cells, or germ cells.

Claim 1. Use of stem cells in an adjunctive treatment of immune dysfunction in a subject, wherein the stem cells can differentiate into at least one cell type of each of at least two of the endodermal, ectodermal, and mesodermal embryonic lineages; express telomerase, are allogeneic or xenogeneic to the subject, do not provoke a deleterious immune response in the subject, and are effective to treat the immune dysfunction in the subject.

Analysis

Patent eligible. The applicant specifically disclosed the source of the stem cells which are within the subject matter of eligible human stem cells because they are not sourced from embryos.

4.1.3 Eligible Human Stem Cells

Applications relating to and use of stem cells, methods of obtaining, producing, manufacturing and uses thereof are considered patentable subject matter if the sources of said stem cells do not constitute direct destruction of human embryo or disruption of the differentiation resulting into a fully developed organism. The following types of stem cells may be considered eligible as these do not fall within the definition of item (non-eligible stem cells):

- i. pluripotent stem cells;
- ii. multipotent stem cells;
- iii. in vitro fertilized embryonic stem cells;
- iv. somatic (adult) stem cells;
- v. stem cells derived from umbilical cord blood and other stem cells derived from the umbilical cord, placenta and placental membrane; and
- vi. embryonic stem cell lines that are not directly isolated from a human embryo.

4.1.3.1 Eligibility of products for human embryonic cell culture

Culture Media, supports, or apparatuses “suitable for” use with human embryonic cells, or even specifically designed for this purpose, are not *per se* excluded from patentability. Their production normally does not require the use of human embryos as base material.⁶⁰

Illustrative Example 1

Overview of the Description:

The present invention provides a medium for the proliferation of stem cells, particularly iPS cells, which characteristically contain a water-soluble polymer and albumin (hereinafter to be also referred to as the medium of the present invention). A medium for proliferation is a medium that enables replication (i.e., proliferation) of a stem cell while maintaining the replication competence, pluripotency and unipotency of the cell.

Claim 1. A medium for culturing an iPS cell, comprising: polyvinyl alcohol; and an albumin, wherein the albumin and the polyvinyl alcohol are included in the medium in a weight ratio of 1:1.1 to 100, and an amount of fatty acid binding to the albumin is not more than 2.2 mg per 1 g of the albumin.⁶¹

Analysis

The claim is eligible since the subject matter of the culture medium does not require the use of human embryos as base material.

4.1.3.2 Eligibility of Induced Pluripotent Stem Cells

Since Pluripotent Stem Cells do not involve the destruction of the embryo, Pluripotent Stem Cells reprogramming factors and the Induced Pluripotent Stem Cells themselves are patent eligible.

⁶⁰ Examination in the field of biotechnology @ the EPO – Part I DNA/Protein sequences & cells

⁶¹ Derived from US 10457911 B2

Cells produced from induced Pluripotent Stem Cells (i.e. cardiac muscles, red blood cells, pancreatic cells etc.) are not exempted from patentability, however, since these cells cannot be differentiated from similar existing cells, these cells are considered to be not novel.

4.2 Public Order and Morality

Article 27 of the TRIPS Agreement states that Members may exclude from patentability inventions, the prevention within their territory of the commercial exploitation of which is necessary to protect ordre public or morality, including to protect human or plant life or health or to avoid serious prejudice to the environment provided that such exclusion is not made merely because the exploitation is prohibited by their law.

This provision in TRIPS is incorporated under Section 22.6 of the IP Code. Notably, the law does not explicitly enumerate what is immoral or against public order.

In the absence of any statute and jurisprudence defining what public order or morality in the context of intellectual property protection is, the determination of going against public order and morality can depend on the Examiner's sound judgment vis-à-vis international exclusions on patentability as defined by their respective charters. The Examiner may also be guided by case law definitions, even if these are not limited to patent considerations.

Below is a list which can serve as a guide on how to determine whether or not a certain invention is within the bounds of morality.

4.2.1 Philippine Jurisprudence

“Morality” refers to what is good or right conduct at a given circumstance.

Morality may be religious, in which case what is good depends on the moral prescriptions of a high moral authority or the beliefs of a particular religion.

Morality may also be secular; in which case it is independent of any divine moral prescriptions. What is good or right in a given circumstance does not derive its basis from any religious doctrine but from the independent moral sense shared as humans.

“Secular standards, independent of religious beliefs, must be the basis for determining immorality.”⁶²

⁶² AC 9549 Separate Concurring Opinion J. Leonen

4.2.2 Other countries' exclusions on patentable subject matter involving stem cells

Serbia: Inventions whose commercial use would be contrary to public order or morality, in particular: processes for cloning human beings, processes for modifying genetic identity of germ cells of human beings, uses of human embryos for industrial or commercial purposes, processes for modifying the genetic identity of animals which are likely to cause them suffering without any substantial medical benefit to man or animal, and also animals resulting from such processes.

Spain & Sweden: Inventions contrary to public order or morality, in particular: processes for cloning humans; modifying the germ line genetic identity of humans; uses of human embryos for industrial or commercial purposes; and processes for modifying the genetic identity of animals which are likely to cause them suffering without any substantial medical benefit, and animals resulting from such processes.

Switzerland: Processes for forming chimeras and hybrids using human gametes or human totipotent cells; parthenogenic processes using germline genetic material; processes for modifying the germ line genetic identity of human clones, hybrids, chimeras; parthenogenic offspring and germ line cells thus obtained; unmodified human stem cells and unmodified lines of stem cells.

EPO: Inventions, the commercial exploitation of which would be contrary to public order or morality, in particular in respect of biotechnological inventions which concern the following:

- a. Processes for cloning human beings
- b. Processes for modifying the germ line genetic identity of human beings
- c. Uses of human embryos for industrial or commercial purposes
- d. Processes for modifying the genetic identity of animals which are likely to cause them suffering from such processes

UAE: Inventions contrary to the laws of Islamic Sha'riah.

4.3 Enablement

Inventions relating to stem cells shall clearly and completely disclose in the specification the source of the stem cells, the media/medium culture/s where said stem cells are grown, the isolation and characterization of the stem cells including the (optimized) parameters for culturing the stem cells. Moreover, experimental data such as clinical tests shall support one or more

representative embodiments or working examples and the description of the resulting effect.

4.4 Novelty

If none of the prior art documents disclose the stem cell of the subject invention, the stem cell is novel. Likewise, if a process or method of inducing differentiation is not described in any documents then such process or method is also novel.

Illustrative Example 1

Overview of the Description:

The present invention relates, in general, to stem cells and, in particular, to a hematopoietic stem cell (HSC) growth factor produced by introducing D factor, E factor and F factor.

Claim 1. An induced hematopoietic stem cell (HSC) which is produced by introducing D factor, E factor and F factor.

Prior Art

Pluripotent stem cell which is produced by introducing A factor, B factor and C factor.

Analysis

The claim is novel over the prior art because it discloses a stem cell different from that of the prior art. HSC gives rise or differentiates into blood cells namely, red, white cells and platelets, and to initiate such differentiation, factors D, E, and F are introduced. The prior art, on the other hand, describes pluripotent stem cell which gives rise to any type of tissues, and to initiate the differentiation of the stem cells into these tissues, several factors A, B, and C are introduced.

However, if the starting cell or the process/method of inducing differentiation (i.e., introducing genes to initiate differentiation of the stem cell) is novel, and the resulting cells are not different from the already known differentiated cells, then the resulting cells are not novel.

Illustrative Example 2

Overview of the Description:

The present invention relates to methods for producing human pancreatic endocrine precursor cells from definitive endoderm cells, wherein the pancreatic endocrine precursor cells express NKX6.1 and PDX1.

Claim 1. A method for producing a population of pancreatic endocrine precursor cells expressing Pdx-1 and NKX 6.1 comprising the steps of:

- obtaining a population of definitive endoderm cells differentiating the population of definitive endoderm cells into a population of pancreatic endoderm cells;
- differentiating in a Dulbecco's Modified Eagle's Medium (DMEM) - high glucose medium the population of pancreatic endoderm cells into a population of pancreatic endocrine precursor cells expressing NKX6.1 and PDX1.

Prior Art

The prior art describes an insulin-producing cell isolated from an *in vitro* culture of bone marrow cells obtained from a human subject. The prior art further discloses a method for making a pancreatic endocrine precursor marker-expressing cells includes the steps of:

- i. obtaining human bone marrow mononuclear cells from a subject; and
- ii. culturing the obtained human bone marrow cells under the conditions that cause the cultured cells to express detectable levels of glucagon, insulin and mRNAs encoding insulin, Pdx-1, NeuroD, and NKX 6.1. [U4].

Analysis

The claimed method is novel over the prior art since the prior art does not disclose the specific methods (steps a, b and c) described by claim 1 in producing a population of pancreatic endocrine precursor cells expressing Pdx-1 and NKX6.1 markers. The resulting cells, however, are not novel despite the method of their production being novel since the prior art already discloses pancreatic endocrine precursor cells expressing Pdx-1 and NKX6.1 (among others).

4.5 Inventive Step

If a gene to initiate differentiation is introduced to a stem cell and both are well known in the art, the method of obtaining the cell by using a means

which a person skilled in the art commonly uses, then the claim directed to the stem cell does not involve an inventive step. However, if the cell obtained by a specific combination is not conceived by the person skilled in the art and further provides a surprising technical effect, then the claim directed to the stem cell involves an inventive step.

Illustrative Example 1

Overview of the Description:

The present invention relates to cells expressing markers characteristic of the pancreatic endocrine lineage that co-express NKX6.1 and insulin.

Claim 1. A population of cells expressing markers characteristic of the pancreatic endocrine lineage that co-express NKX6.1 and insulin and wherein less than 10% of the cells in the population express glucagon.

Claim 2. The population of cells in claim 1, wherein at least 30% of the cells express NKX6.1.

Claim 3. The population of cells in claim 1, wherein at least 40% of the cells express NKX6.1.

Claim 4. The population of cells in claim 1, wherein at least 50% of the cells express NKX6.1.

Claim 5. The population of cells in claim 1, wherein at least 60% of the cells express NKX6.1.

Claim 6. The population of cells in claim 1, wherein at least 5% of the cells express insulin.

Claim 7. A method to generate a population of cells expressing markers characteristic of the pancreatic endocrine lineage that co-express NKX6.1 and insulin and wherein less than 10% of the cells in the population express glucagon, the method comprising the steps of:

- a. culturing pluripotent stem cells;
- b. differentiating the pluripotent stem cells into cells expressing markers characteristic of the definitive endoderm lineage;
- c. differentiating the cells expressing markers characteristic of the definitive endoderm lineage into cells expressing markers characteristic of the pancreatic endoderm lineage; and

- d. differentiating the cells expressing markers characteristic of the pancreatic endoderm lineage into cells expressing markers characteristic of the pancreatic endocrine lineage that co-express NKX6.1 and insulin and minimal amounts of glucagon by culturing the cells expressing markers characteristic of the pancreatic endoderm lineage in a medium supplemented with a factor capable of inhibiting BMP, a TGF β receptor signaling inhibitor, and a protein kinase C activator.

Prior Art

Prior Art 1: Pancreatic endocrine lineage cells express several markers including NKX6.1, insulin and glucagon.

Prior art 2: Describes the differentiation of insulin-secreting pancreatic cells from embryonic stem cells (ESCs). These cells are NKX6.1-positive and only secrete insulin.

Prior art 3: The process of addition of noggin to the medium of differentiation of pluripotent cells into pancreatic cells increases insulin secretion

Analysis

For claims 1-6:

Although neither prior art 1 nor 2 teaches the percentages of the markers, the technical features of claims 1-6 are merely the range that a skilled person would choose in accordance with circumstances, without the exercise of inventive skill, in order to solve the problem posed. Claims 1-6 lack an inventive step.

For claim 7:

The only difference between the subject matter of claim 7 and the disclosure of prior art 3 is the inclusion of BMP-inhibitors, TGF β receptor signaling inhibitors and a protein kinase activator.

The problem being solved is the provisions of an alternative method to generate a population of cells expressing markers characteristic of the pancreatic endocrine lineage that co-express NKX6.1 and insulin.

The solution is given with a method that includes BMP-inhibitors, TGF β receptor signaling inhibitors and a protein kinase activator in the medium

after the pluripotent cells have been differentiated into cells of the pancreatic endoderm lineage.

Although prior art 1-2 teach pancreatic endocrine lineage cells, in particular insulin-secreting pancreatic cells, respectively, and prior art 3 teaches the addition of noggin in a media to initiate differentiation into pancreatic cells, there are no direct teachings regarding the supplemental factors, in particular, BMP-inhibitors, TGF β receptor signaling inhibitors and a protein kinase activator in a media to produce a population of cells expressing markers characteristic of the pancreatic endocrine lineage that co-express NKX6.1 and insulin. In view thereof, the subject matter of claim 7 involves an inventive step.

5. PLANTS AND ANIMALS

5.1 Eligibility

Plants and animals are patentable if the technical feasibility of the invention is not confined to a particular animal breed or plant variety. Inventions that concern plants and animals are patentable provided that the application of the invention is not technically confined to a single animal breed or plant variety. If the invention particularly is confined to a single animal breed or plant variety, legal protection other than the IP Code may apply.

5.1.1 Eligibility of Plants

Section 22.4 of the Intellectual Property Code of the Philippines or R.A. 8293, as amended and Rule 202 (g) of the 2022 Revised Implement Rules and Regulations for Patents provide that plant varieties per se are not patent eligible. Plant varieties can be protected under the *Philippine Plant Variety Protection, R.A. 9168*.

However, a process claim for the production of a plant variety is not a priori excluded from patentability merely because the resulting product constitutes or may constitute a plant variety.

5.1.1.1 The exception to patentability applies to plant varieties regardless of the way in which they were produced. Therefore, plant varieties containing genes introduced into an ancestral plant by recombinant gene technology are excluded from patentability. More so, products of asexual propagation are excluded from patentability more particularly, if the application of the invention is technically confined to a single plant variety.

Illustrative Example

Claim: A plant seedling comprising a scion that contains gene X joined to a rootstock by grafting.

Analysis

The claim is patent ineligible. In this case, the prevailing plant will be the scion which is confined to the variety of its parent plant.

5.1.1.2 A claim wherein specific plant varieties are not individually claimed is not excluded from patentability even though it may embrace

plant varieties. More so, claims to transgenic plants are acceptable, unless expressed in plant variety terms or the invention is confined to modifying a particular plant variety. It may be, therefore, that if all the examples in an application are directed towards modifying a single variety, there could be a presumption that the invention is specifically for a plant variety.

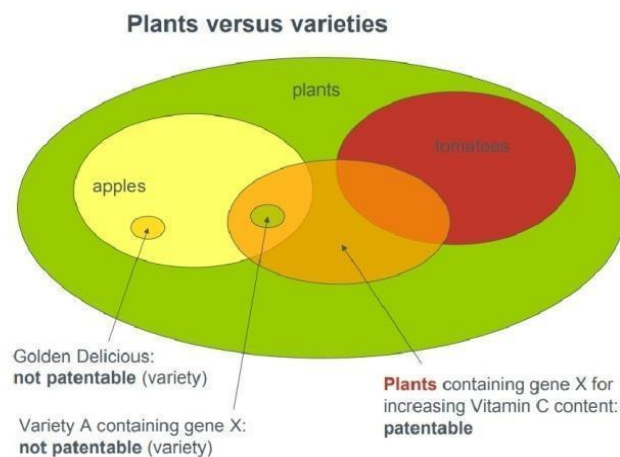


Figure 3. Yeats, S. (11 October 2011) Latest Developments in Patenting Plant Inventions in Europe.

Illustrative Example

Claim 1: A transgenic plant comprising a recombinant polynucleotide encoding a polypeptide, wherein the polynucleotide is operably linked to a promoter suitable for expression in plants.

Claim 2: A transgenic plant according to claim 1, wherein the plant is selected from the group consisting of rice, corn, soybean and wheat.

Analysis

The claims are patent eligible because they relate to a transgenic plant, which is neither expressed in variety terms nor is the invention confined to modifying a particular plant variety.

5.1.2 Eligibility of Animals

A claim covering but not identifying animal breed is not a claim to a breed. In the absence of the identification of a specific animal breed in a product claim, the subject matter of the claimed invention is neither limited nor directed to a breed or breeds within the meaning of *Sec. 22.4 of R.A. 8293*; if an invention does not deal with a single animal breed it can still be patentable provided other requirements are satisfied.

Illustrative Example

Claim 1: 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 . . .

Claim 2: The mammal of claim 1, said mammal being a rodent.

Claim 3: The mammal of claim 2, said rodent being a mouse.

Analysis

The claims are patent eligible because they relate to a transgenic animal, which is neither expressed in breed terms nor is the invention confined to modifying a particular animal breed.

5.1.2.1 Patentability consideration for Animals

- a. Medical Purpose - Animals can be genetically altered for a variety of medical uses. First, animal models can help researchers better comprehend how certain genes function. The expression of new genetic information can occur from the integration of foreign DNA, but it can also prevent the expression of existing genetic information. By preventing gene expression and analyzing the modifications that occur, the function of the gene can be determined. Second, studying the expression and mechanics of genetically determined inherited human diseases using genetically engineered animals helps scientists. Third, based on the genetic manipulation of animals, researchers may be able to create gene therapies for humans. Fourth, animals that have undergone genetic modification may produce crucial therapeutic proteins.
- b. Veterinary Purpose - biotechnological alterations can also serve the interests of modified animals. Additionally, agricultural animals like cows, pigs, and chickens can have their agriculturally relevant output increased by genetic manipulation.
- c. Socio-Economic Purpose - Animals used for agriculture may be genetically altered to allow for their exploitation in previously unsuitable environments. For example, sleeping sickness leads to inefficient milk and meat production. By developing resistance in genetically modified animals, animal biotechnology research may be able to eradicate sleeping sickness, which can, in turn, increase milk and meat production. These advancements may raise the life

expectancy in underdeveloped nations and improve their socioeconomic situation.

- d. Environmental Purpose - Environmental efforts on ecosystem recovery, biodiversity conservation, the preservation of the natural and cultural environment, human health, sufficient material cycles free from dangerous substances, sustainable resource use, effective energy usage, and consumption habits, may focus on utilizing biotechnology developments.

5.1.3 Essentially biological processes for the production of plants and animals are not eligible.

5.1.3.1 A process for the production of plants or animals which is based on the sexual crossing of whole genomes and on the subsequent selection of plants or animals is excluded from patentability as being essentially biological. Products of these essentially biological processes are also excluded from patentability.

Illustrative Example 1

Claim: Method for the production of plants having trait X comprising crossing plants A and B and selecting progeny having marker X.

Analysis

The claim is patent ineligible because it includes crossing of plants which is an essentially biological process.

Illustrative Example 2

Claim: Use of a (transgenic) plant for generating further plants.

Analysis

The claim is patent ineligible because the conventional breeding includes an essentially biological process. *The claim is not explicit on the method of how further plants will be generated, hence it may be construed that conventional breeding methods will be applied.*

Illustrative Example 3

Claim: A seedless tomato produced from crossing tomato X and tomato Y.

Analysis

The claim is patent ineligible because it pertains to a product of an essentially biological process.

Illustrative Example 4

Claim: Use of a (transgenic) animal for breeding. (Same rationale as Example 2).

Analysis

The claim is patent ineligible because the conventional breeding includes an essentially biological process.

Illustrative Example 5

Claim: A livestock animal comprising a genomic modification from a horned allele to a polled allele, wherein the animal is a first breed of animal that has the horned allele and the polled allele is found in a second breed of animal.

Analysis

The claim is patent ineligible. Genetically modified livestock is basically a progeny of selecting and crossing two (2) different breeds which are polled and horned.

5.1.3.2 Moreover, where the process contains additional steps that are technical in nature, performed before or after the steps of crossing and selection, but such additional steps merely assist or enable the performance of crossing and selection, said process would still be considered as essentially biological, hence excluded from patentability.

Illustrative Example 1

Claim: Introgression of a (transgenic) trait X into a plant.

Analysis

The claim is patent ineligible because it includes a case where a gene is introduced by an essentially biological process like crossing.

Illustrative Example 2

Claim: Methods for plant breeding comprising the step of embryo rescue.

Analysis

The claim is patent ineligible since it includes a step of crossing two interspecific (two distinct species) or two intergeneric (two genotypically different organisms) that would normally produce seeds which are aborted.

5.1.3.3 If, however, such a process of sexual crossing and selection contains within it an additional step of a technical nature, which by itself introduces or modifies a trait in the genome of the plant or animal produced which cannot be the result of mixing of genes or gametes, then the process is not excluded.

Illustrative Examples

Claim A: Method of producing a (transgenic) plant having trait X by introducing a vector comprising the sequence of SEQ ID NO: 1.

Claim B: Method for selecting animals having phenotype Y by screening for the presence of a marker having the sequence shown in SEQ ID NO: 1.

Claim C: Use of the nucleic acid of SEQ ID NO: 1 to select a plant having trait X.

Claim D: A method for generating a transgenic plant from a population of plant protoplasts, the method comprising isolating a plant protoplast comprising a polynucleotide of interest, the method comprising: separating the at least one sodium alginate-encapsulated plant protoplast comprising the polynucleotide of interest and a fluorescent marker from the remaining plant protoplasts in a population of plant protoplasts by fluorescence-activated cell sorting (FACS); and culturing the separated sodium alginate-encapsulated plant protoplast(s) comprising the polynucleotide of interest and the fluorescent marker to regenerate a transgenic plant.⁶³

Claim E: A method of creating genetically modified livestock organisms comprising altering a native horned allele of a livestock primary cell, a livestock primary somatic cell, a livestock stem cell, a livestock

⁶³ EP 2893024 B1 (DOW AGROSCIENCES LLC) 04 December 2019

primordial germ cell, with horned allele being altered to a polled allele.

5.1.3.4 A process for the production of plants which is not based on the sexual crossing of whole genomes or through asexual propagation of plants is not excluded from patentability provided that technical intervention by man in the process plays a significant part in determining or controlling the result it is desired to achieve.

Illustrative Example 1

Claim: A grafting method for promoting asexual reproduction of *Populus euphratica*, characterized in that it comprises the following steps: preparation of bud slices: take young shoots of *Populus euphratica* to prepare bud slices; Bud piece treatment: soak the bud piece in the plant nutrient solution for 10min-120min before budding, and the plant nutrient solution includes rootstock extract; Rootstock treatment: select the Xinjiang poplar that grows vigorously as the rootstock, prepare the bud interface on the seedlings of Xinjiang poplar, spray the bud interface with the mixed solution, and in the volume of the mixed solution, the mixed solution contains red Mycin 100-500mg/L, indole-3-acetic acid 50-200mg/L, naphthaleneacetic acid 50-200mg/L, potassium dihydrogen phosphate 400-800mg/L and superphosphate 500-1000mg/L; Grafting bud pieces: inserting the bud pieces into the bud interface, binding the budding parts, and obtaining grafted seedlings; Soil treatment: adding a soil improver to the root of the grafted seedlings to complete the grafting; The rootstock extract has the following steps to prepare: High-pressure heating the rhizome of Xinjiang poplar and water with 5 to 10 times the mass of the root of Xinjiang poplar for 1 to 2 hours, and filtering to obtain filtrate and filter residue; Put the filter residue and filtrate in an airtight container, insert fermenting bacteria into the container and ferment for 4-6 hours; After the fermentation is completed, the rootstock extract is obtained by filtering; the soil conditioner, in parts by weight, its raw material components include: 100-150 parts of diatomite, 80-120 parts of fly ash, 70-90 parts of bentonite, 50-70 parts of kaolin, 80-120 parts of peat, 120-160 parts of plant straw powder, 12-20 parts of algae-containing carrier, 40-60 parts of organic fertilizer, 40-70 parts of humus, 20-35 parts of zeolite powder, 20-30 parts of glass microspheres, 18-25 parts of silica powder, 3-5 parts of hydrophobic resin, 20-30 parts of microbial bacterial liquid; 10-20 parts of polypropylene alcohol, 10-15 parts of urea, 8-10 parts of monoammonium phosphate, 30-40 parts of traditional Chinese

medicine waste residue powder, 20-40 parts of waste tea residue, 8-24 parts of fulvic acid concentrate, 40 parts of distiller's grains -60 parts, 30-60 parts of leaf humus, 40-60 parts of sawdust, 20-30 parts of husk ash, 10-30 parts of pine phosphorus, 50-70 parts of coconut peat and 30-40 parts of slow-release fertilizer.⁶⁴

Illustrative Example 2

Claim: A method for producing a rooted cutting of a Pinaceae tree, comprising: A: adding a cytokinin to the outside of a shoot apex of a short shoot of a Pinaceae tree to induce a new scaly leaf and/or primary leaf which is grown to a length of 2 to 10 mm and into a form of a needle leaf to an extent that it touches an adjacent needle leaf; B: cutting out the short shoot in which the new scaly leaf and/or primary leaf having a length of 2 to 10 mm has been induced in A, and C: inserting the short shoot cutting into a rooting bed wetted with a carbon source-free liquid medium comprising nitrogen, phosphorus and potassium as essential elements, and then D: culturing the cutting at a humidity of 80% or more to root the cutting; wherein culturing the cutting is carried out at a CO₂ concentration of 300 to 1,500 ppm.⁶⁵

5.2 Novelty

In the case of plant or animal inventions the assessment of novelty shall be carried out in the same manner as for other inventions. An invention will be novel only if it is new in the light of prior art, or is not anticipated by prior art. *Sec. 21* requires an invention to be new in order to be patentable. *Sec. 23* gives a definition of novelty, i.e., that "an invention shall not be considered new if it forms part of the prior art".

5.3 Inventive Step

5.3.1 If the skilled person uses a known method for gene modification of a plant or animal and said gene is also previously disclosed, the resulting plant or animal does not have inventive step.

Illustrative Example

Overview of the Description:

The invention relates to a transformed organism such as an organism selected from plants, bacteria, and cells. The transformed organism

⁶⁴ CN 109220280 B (Northwest Institute of Eco Environment and Resources of CAS) 03 August 2021. Translation from Espacenet website.

⁶⁵ US 8,763,304 B2 (HIROSHI & CHIKAHIRO) 01 July 2014

comprises a DNA molecule, which comprises a DNA sequence encoding the *Bouteloua gracilis* transcriptional regulatory expression element group or EXP sequence derived from a putative ubiquitin gene selected from the group consisting of: a sequence with at least 85%, 90%, 95% or 100% sequence identity to any of SEQ ID NOs: 1-5 or 7 an expression cassette comprising the DNA molecule or a vector comprising the expression cassette, which may be stably incorporated into the genome of the transformed organism.

Claim 1: A transgenic plant comprising a recombinant DNA molecule, which comprises a DNA sequence encoding the *Bouteloua gracilis* transcriptional regulatory expression element group or EXP sequence derived from a putative ubiquitin gene selected from the group consisting of: a sequence with at least 85 percent sequence identity to any of SEQ ID NOs: 1-5 or 7; a sequence comprising any of SEQ ID NOs: 1-5 or 7; and a fragment of any of SEQ ID NOs: 1-5 or 7, wherein the fragment has gene regulatory activity; wherein said sequence is operably linked to a heterologous transcribable DNA molecule.

Prior Art D1: Describes a nucleotide sequence from the sugarcane ubi9 polyubiquitin gene promoter, which is capable of directing constitutive expression of a nucleic acid sequence of interest that is operably linked to it. The sugarcane ubi9 promoter is useful in regulating expression of a nucleic acid sequence of interest in monocotyledonous and dicotyledonous plants.

Prior Art D2: Describes a plant regulatory element and uses thereof in expression constructs for expression transgenes in plants. The regulatory element to be used is derived from *Bouteloua gracilis* ubiquitin 1 gene having a nucleotide sequence that is 85% identical to SEQ ID NO: 1.

Analysis

Although D1 failed to explicitly disclose the claimed sequences or 85% identical thereof, it was already known in the art that other ubiquitin regulatory elements, like the regulatory elements of the ubi9 gene, could be used in expression constructs as taught in D1. More particularly, the person skilled in the art would be motivated to utilize the *Bouteloua gracilis* ubiquitin gene of D2 in combination with the construct of D1, thereby expectedly arriving at the claimed invention. Also, transgenic plants cannot be considered inventive if the constructs are not inventive. Therefore, claim 1 is refused for lacking inventive step.

5.3.2 A claim to a transgenic plant or animal that is produced by a process that is not obvious for said plant or animal, or great hurdles were overcome to perform such process, or if the resulting plant or animal has distinct advantages over the wild species, then said claim to transgenic plant or animal is inventive.

Illustrative Example

Overview of the Description:

The invention relates to an engineered insecticidal protein comprising the amino acid sequence as set forth in SEQ ID NO: 40 with inhibitory activity against Lepidopteran insects encoded by a polynucleotide set forth in SEQ ID NO: 39; a bacterial host cell and a plant host cell comprising the polynucleotide of SEQ ID NO: 39; an insect inhibitory composition comprising the engineered insecticidal protein; a seed comprising the full length polynucleotide set forth in SEQ ID NO: 39; a method of controlling a Lepidopteran pest by contacting with an insect inhibitory amount of the engineered insecticidal protein; a transgenic plant or plant part comprising said engineered insecticidal protein; a commodity product comprising a detectable amount of the engineered insecticidal protein; and a method of producing a seed comprising the engineered insecticidal protein. The disclosure exemplified that the engineered Cry1Da1_Var protein with three specific mutations (S200V_Y250S_I300P) has 90% higher insecticidal activity against Lepidopteran insects such as *Spodoptera frugiperda*, *Trichoplusia ni*, *Ostrinia nubilalis*, and *Chrysodeixis includens* compared to the wild type Cry1Da1 protein.

Claim 1: An engineered insecticidal protein comprising the Cry1Da1_Var amino acid sequence as set forth in SEQ ID NO: 40.

Claim 2: A transgenic plant or plant part comprising the engineered insecticidal protein of claim 1 and a polynucleotide having the nucleotide sequence as set forth in SEQ ID NO: 39, wherein said engineered insecticidal protein is present in an insect inhibitory amount.

Prior Art D1: Teaches a method of mutagenizing a Cry1Da1 polypeptide to increase the insecticidal activity of said polypeptide against a Lepidopteran insect; an isolated nucleic acid segment that encodes said polypeptide; polypeptide composition; transgenic plant or part which expresses said nucleic acid; method of producing thereof; and method of controlling Lepidopteran insects which are susceptible to said composition.

Prior Art D2: Teaches engineered Cry1Ba (eCry1Ba) proteins having improved toxicity to Lepidopteran insect pests and a method of making the engineered Cry1Ba proteins and methods of using the eCry1Ba nucleic acid sequences, for example in transgenic plants.

Analysis

There are no teachings or suggestions in D1 or D2 alone, or in combination thereof that could make the claimed engineered Cry1Da1_Var protein with three specific mutations (S200V_Y250S_I300P) and its offered surprising technical effect i.e., 90% higher insecticidal activity against Lepidopteran insects compared to the wild type Cry1Da1 protein which leads to a transgenic plant having an enhanced Lepidopteran inhibitory spectrum obvious to any person skilled in the art at the time of filing of this application. Therefore, the transgenic plant is considered to involve an inventive step.

5.4 Enablement/Full Support

5.4.1 A claim to a transgenic plant or animal may be considered enabled or fully supported by combining a name of the plant or animal, a typical gene and characteristics of the plant or animal, or a production process of the plant or animal.

If the plant or animal gene is deposited (*Sec. 35 of the IP Code, Rules 408 and 409 of the 2022 Revised IRR*), the plant or animal may be specified by the accession number.

Illustrative Example 1

Claim: A transgenic corn plant comprising a) a transgene encoding a dsRNA for suppression of an essential gene in a target pest; and b) a transgene encoding a bacterial insecticidal protein exhibiting biological activity against said target pest; wherein said target pest is a Western Corn Rootworm.⁶⁶

Analysis

The claim satisfies the enablement requirement because the specification describes and contains sufficient and clear disclosure of the transgenic corn plant comprising the identified transgenes including the process of making or producing the same, as well as a characteristic of the transgenic corn.

⁶⁶ US 10,787,680 B2 (BAUM et al.) 29 September 2020

Illustrative Example 2

Claim: A plant belonging to *Castanea crenata* (Japanese chestnut) having the accession number of ATCC-XXXX whose bark contains catechol tannin and pyrogallol tannin in the ratio of (X1 to X2): (Y1 to Y2) and has the content of catechol tannin of Z1 to Z2 ppm (weight ratio), or its mutant having said characteristics.

Analysis

The claim satisfies the enablement requirement since the plant according to the claim has a depository accession number designated as ATCC-XXXX.

5.4.2 A claim directed to or comprising a transgenic plant or animal selected from a wide array of Species, Genera, Families, Orders, Classes, or any Taxa, without a clear and detailed description of at least one way of doing the same using working examples shall be refused for lacking enabling disclosure and/or full support. Rule 406.1 of the 2022 Revised IRR requires that an enabling disclosure shall contain a sufficient and clear disclosure of the technical features of the invention including the manner or process of making, performing, and using the same, leaving nothing to conjecture. Rule 416b also requires that each claim shall be supported by the description.

Illustrative Example

Overview of the Description:

The invention relates to an isolated polypeptide X; DNA constructs and/or transgenic plant cells comprising said polypeptide; and method of producing transgenic plants comprising at least one of said polypeptide X, DNA constructs, or transgenic plant cells. The invention enumerates that the transgenic plant is preferably selected from the genera consisting of *Oryza*, *Zea*, *Sorghum*, *Zizania*, *Gossypium*, *Hordeum*, *Triticum*, *Glycine*, and *Solanum*. However, the description more particularly, the Examples, only provides sufficient and clear disclosure of transforming *Zea mays* and *Sorghum arundinaceum* plants.

Claim 1: A transgenic plant comprising a transgenic plant cell, expressing a polypeptide X, wherein said plant is selected from the Genera consisting of *Oryza*, *Zea*, *Sorghum*, *Zizania*, *Gossypium*, *Hordeum*, *Triticum*, *Glycine*, and *Solanum*.

Claim 2: A method for producing a transgenic plant comprising transforming an exogenous cell with an expression construct, comprising a heterologous gene of interest; and a nucleotide sequence encoding a polypeptide X, wherein said plant is selected from the Genera consisting of *Oryza*, *Zea*, *Sorghum*, *Zizania*, *Gossypium*, *Hordeum*, *Triticum*, *Glycine*, and *Solanum*.

Analysis

Claims 1 and 2 do not satisfy the enabling disclosure and full support requirements because the claims are directed to or comprise a transgenic plant selected from a wide array of Genera; whereas the description only provides a sufficient and clear disclosure, and full support to the manner or process of making or transforming transgenic *Zea mays* and *Sorghum arundinaceum* plants. Thus, the claims directed to a transgenic plant selected from the Genera consisting of *Oryza*, *Zea*, *Sorghum*, *Zizania*, *Gossypium*, *Hordeum*, *Triticum*, *Glycine*, and *Solanum* are considered mere conjectures and not fully supported by the description.

5.4.3 Due to Mendelian inheritance, the progeny of a transgenic plant may not contain the claimed transgene.

Illustrative Example

Claim 1: A transgenic plant comprising a recombinant insecticidal polypeptide having at least 80% sequence identity to the amino acid sequence of SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 384 or fragments thereof having insecticidal activity.

Claim 2: A progeny of the transgenic plant of claim 1.

Analysis

Claim 2 is refused for lacking full support in that the progeny of a transgenic may not contain the claimed transgene.

V. SUPPLEMENTAL DISCUSSIONS

Unity of Inventions Issues

Rule 605(a) of IRR:

The requirement of invention shall be fulfilled only when there is a technical relationship among those inventions involving one or more of the same or corresponding special technical features. The "special technical features" shall mean those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art;

Lack of Unity

"A priori"

"A priori" is based on general knowledge of the skilled person, i.e., before consideration of prior art, if the claims falling in different groups do not share a same or corresponding technical feature.

For Example:

Claim 1: An antibody defined by SEQ ID NO: 1 comprising Feature A and C.

Claim 2: An antibody defined by SEQ ID NO: 1 comprising Feature B and D.

An antibody defined by SEQ ID NO: 1 is the **common feature**, however, said common feature is not a **"special technical feature"**. Therefore, there is **a lack of unity a priori**.

The determination of a priori lack of unity is independent of any knowledge of the relevant prior art. Thus, respective inventions need to be assessed to determine whether they each involve one or more of the same or corresponding special technical features. If they include one or a group of such features then prima facie the inventions will possess unity a priori.⁶⁷

"A posteriori"

"A posteriori", is based on knowledge from a particular prior art document. i.e., after a search of the prior art, if the shared technical feature fails to make a contribution over the prior art.

⁶⁷ paragraph 2, <https://manuals.ipaustralia.gov.au/patent/1.1.4.8-a-priori-and-a-posteriori-lack-of-unity>

For Example:

Claim 1: An antibody defined by SEQ ID NO: 1 comprising Feature **A**.

Claim 2: An antibody defined by SEQ ID NO: 1 comprising Feature **B**.

*Note: an antibody defined by SEQ ID NO: 1 is disclosed in a particular **prior art** document.*

An antibody defined by SEQ ID NO: 1 is the **common feature**, however, said common feature is already disclosed in a prior art. Therefore, there is **a lack of unity a posteriori**. Feature **A** and Feature **B** may make a contribution to the prior art, but they are **not** common to both inventions.

A determination of lack of unity a posteriori can arise where relevant independent claims have features in common but those features appear not to be novel given the prior art, thus leaving the claims without a single general inventive concept.⁶⁸

On the other hand, a claim lacks **novelty**⁶⁹ if every element or step is explicitly or inherently disclosed. PSA must be able to identify that all the features are disclosed. **Prior art**⁷⁰ must enable PSA to carry out the claimed invention.

A Priori Determination of Unity of Invention

Illustrative Example 1

Claims:

1. A method of expanding and differentiating pluripotent cells in a dynamically agitated suspension culture system comprising culturing pluripotent cells to aggregated cell clusters in a planar adherent culture and differentiating the pluripotent cell clusters in a dynamic agitated suspension culture system, wherein the step of differentiating comprises use of a Cyp26 inhibitor.
2. The method of claim 1, wherein the method increases the percentage of cells in a GO/G1 phase of the cell cycle.

⁶⁸ paragraph 8, <https://manuals.ipaustralia.gov.au/patent/1.1.4.8-a-priori-and-a-posteriori-lack-of-unity>

⁶⁹ An invention shall not be considered new if it forms part of a prior art (Rule 203, 2022 Revised IRR for Patents, UMs and IDs)

⁷⁰ Everything made available to the public anywhere in the world by means of a written or oral disclosure, by use, or in any other way, before the filing date or the priority date of the application claiming the invention (Rule 204, 2022 Revised IRR for Patents, UMs and IDs)

3. A method of increasing the percentage of cells in GO/G1 phase of the cell cycle comprising expanding pluripotent to aggregated cell clusters in a planar adherent culture in an environment that includes from about 0.1% to about 2% of bovine serum albumin, transferring the clusters of pluripotent stem cells from the planar adherent culture to a dynamic suspension and culturing the cells in the dynamic suspension in a media supplemented with small molecule and optionally a TGF β family member.
4. The method of claim 3, wherein the small molecule is MCX and wherein the TGF β family member is GDF-8.⁷¹

Analysis

The subject matter of claims 1-4 does not relate to a single invention, or to a group of inventions linked so as to form a single inventive concept as per Rule 604 of the Revised IRR on Inventions. Thus, claims 1-4 contain following groups of inventions:

Group 1 Claims 1 and 2 directed to a method of expanding and differentiating pluripotent cells comprising the use of a Cyp26 inhibitor.

Group 2 Claims 3 and 4 directed to methods of expanding and differentiating pluripotent cells with bovine serum albumin.

Upon examination, the identified features may have the potential to make a contribution over the prior art but are not common to all the claimed inventions and therefore cannot provide the required technical relationship. Therefore, there is no special technical feature common to all the claimed inventions and the requirements for unity of invention (Rule 605 of the Revised IRR on Inventions) are consequently not satisfied a priori.

A Posteriori Determination of Unity of Invention

Illustrative Example 1

Claims:

1. Method for increasing the induction of brachyury comprising culturing pluripotent cells as aggregated cell clusters in a dynamic suspension culture in a medium supplemented with a small molecule.

⁷¹ Derived from PH 1/2016/500783 A (Withdrawn)

2. Method for differentiating pluripotent cells as aggregated cell clusters in a dynamic suspension culture through definitive endoderm in 18-30 hours wherein the culture media is free of activin A, WNT3A or any TGF β family member, wherein the method comprises a medium supplemented with a small molecule.⁷²

Analysis

Claims 1-2 contains the following inventions or groups of inventions, which are not so linked as to form a single general inventive concept as per Rule 604 of the Revised IRR on Inventions. Thus, claims 1-2 contains the following groups of inventions:

Group 1 - *Claim 1 is directed to a method for increasing the induction of brachyury comprising culturing pluripotent cells as aggregated cell clusters in a dynamic suspension culture in a medium supplemented with a small molecule. This combination of features is specific to this group of claims.*

Group 2 - *Claim 2 directed to a method for differentiating pluripotent cells as aggregated cell clusters in a dynamic suspension culture through definitive endoderm in 18-30 hours wherein the culture media is free of activin A, WNT3A or any TGF β family member, wherein the method comprises a medium supplemented with a small molecule. This combination of features is specific to this group of claims.*

The only feature common to all of the claimed inventions and which provides a technical relationship among them is culturing pluripotent cells as aggregated cell clusters in a dynamic suspension culture in a medium supplemented with a small molecule. However, this feature does not make a contribution over the prior art because it is disclosed in D1 and D2:

D1 discloses expanding human pluripotent stem cells in dynamic suspension culture, generating aggregated cell clusters, and differentiating into pancreatic progenitors in differentiation media supplemented with various small molecules including activin A, WNT3A.

D2 discloses culturing embryonic stem cells in suspension culture with agitation (dynamic) and supplementing with a differentiating culture condition such as a growth factor (small molecule) which allows for the formation of hES-derived cell aggregates in suspension.

Therefore, in light of the documents, the common feature between the above-mentioned groups cannot be considered as a special technical feature.

⁷² Derived from PH 1/2015/501477 A (Withdrawn)

The unity of invention is treated to be fulfilled only when there is a technical relationship among inventions involving one or more of the same or corresponding special technical features. Thus, claims 1 and 2 failed to meet the requirements of Rule 605 of the Revised IRR on Inventions. Consequently, the requirements for unity of invention are not satisfied a posteriori.

Illustrative Example 2

Overview of the Description:

The specification discloses anti-CD47 monoclonal antibodies (anti-CD47 mAbs) with distinct functional profiles, methods to generate anti-CD47 mAbs, and methods of using these anti-CD47 mAbs as therapeutics for the prevention and treatment of solid and hematological cancers, ischemia-reperfusion injury, cardiovascular diseases, autoimmune diseases, inflammatory diseases or as diagnostics for determining the level of CD47 in tissue samples.

Claim 1: A monoclonal antibody, or an antigen-binding fragment thereof, which:

- a. binds to human CD47,
- b. blocks SIRPa binding to human CD47,
- c. increases phagocytosis of human tumor cells; and
- d. induces death of human tumor cells.

Claim 2: A monoclonal antibody, or an antigen-binding fragment thereof, which:

- a. binds to human CD47
- b. blocks SIRPa binding to human CD47,
- c. increases phagocytosis of human tumor cells,
- d. induces death of human tumor cells; and causes no agglutination of human red blood cells (hRBCs).

Claim 3: A monoclonal antibody, or an antigen-binding fragment thereof, which:

- a. binds to human CD47,
- b. blocks SIRPa binding to human CD47,
- c. increases phagocytosis of human tumor cells,
- d. induces death of human tumor cells; and
- e. causes reduced agglutination of human red blood cells (hRBCs).

Claim 4: A monoclonal antibody, or an antigen binding fragment thereof, which:

- a. binds to human CD4 7,

- b. blocks SIRPa binding to human CD47,
- c. increases phagocytosis of human tumor cells
- d. induces death of human tumor cells, and
- e. has reduced hRBC binding.

Claim 5: A monoclonal antibody or an antigen-binding fragment thereof, which binds to CD47, wherein the antibody or antigen-binding fragment comprises a combination of and variable heavy chain CDRI (HCDRI), variable heavy chain CDR2 (HCDR2), and variable heavy chain CDR3 (HCDR3), wherein the combination is selected from the group consisting of: XXXX ⁷³

Prior Art D1 discloses a monoclonal antibodies that bind CD47, the monoclonal antibodies that recognize human CD47 are also cross-reactive for at least one other nonhuman CD47 protein, such as, by way of non-limiting example, non-human primate, these anti CD47 monoclonal antibodies inhibit the interaction between human CD47 and human SIRPC;

Prior Art D2 relates to monoclonal antibodies that recognize and bind to CD47, particularly human CD47. The antibodies of the invention are capable of modulating, e.g. , blocking, inhibiting, reducing, antagonizing, neutralizing or otherwise interfering with CD47 expression, activity and/or signaling, and these antibodies do not cause a significant level of hemagglutination of human red blood cells, also referred to herein as erythrocytes [0002, 0004, Abstract] and;

Prior Art D3 which teaches an alpha-SNAP-23 antibody comprising a heavy chain variable domain (VH) and a light chain variable domain (VL) that selectively binds to a SNAP 25 having a carboxyl-terminus at the P residue of the BoNT/A cleavage site scissile bond [Abstract, 0059].

Analysis

Lacks unity a posteriori; Too many independent claims

The requirement of invention shall be fulfilled only when there is a technical relationship among those inventions involving one or more of the same or corresponding special technical features. The expression “special technical features” shall mean those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art. However, the special technical feature of a monoclonal antibody that

⁷³ WO/2017/049251 - Therapeutic CD47 Antibodies

binds to CD47 is already taught in the above-indicated prior art, the application lacks unity a posteriori.

Additionally, an application may contain one (1) or more independent claims in the same category (product, process, apparatus, or use), where it is not appropriate, having regard to the subject matter of the application, to cover this subject matter by a single claim which shall define the matter for which protection is sought.⁷⁴ The above-enumerated claims have too many independent claims. The present application may have claims which fall within the same category; however, the unnecessary proliferation of independent claims should not be allowed.⁷⁵

Illustrative Example 3

Overview of the Description:

The five nucleic acids encode dehydrogenases that include a conserved sequence motif defining the catalytic site and the dehydrogenase function of these proteins. The nucleic acids were isolated from five different sources such as a mouse, rat, guinea pig, feline and human.

The description clearly shows that these five nucleic acids are homologous based upon their overall sequence similarity (85-95% identity) at both the nucleotide and amino acid sequence levels.

Claim: An isolated nucleic acid selected from SEQ ID NO: 1, 2, 3, 4, or 5.

Prior art: A nucleic acid molecule isolated from monkeys, which has high sequence similarity (e.g., 90%) to SEQ ID NO: 1. The monkey nucleic acid encodes a dehydrogenase that includes the catalytic site defined by the conserved motif.

Analysis

The claimed nucleic acids would be considered as having the same or corresponding technical feature if the alternatives had a common property or activity, and shared a significant structural element that is essential to the common property or activity.

A corresponding technical feature is shared among the claimed nucleic acid molecules resides in their common property that is, encoding dehydrogenases

⁷⁴ Rule 416(b) of the revised IRR on Patents

⁷⁵ MPEP, Chapter III, 3.2 and 3.3

and their shared structural element essential to the common property is the conserved motif.

However, a prior art disclosed a nucleic acid molecule which *encodes a dehydrogenase* and contains the shared structural element which has already been isolated from a different source (monkeys). Thus, the technical feature is not special because the functional and structural similarity between the claimed molecules cannot form the contribution that the group of inventions as a whole makes over the prior art. Therefore, the claimed nucleic acids lack unity of invention *a posteriori*.

Groupings would be:

Invention 1: Nucleic acid of SEQ ID NO: 1

Invention 2: Nucleic acid of SEQ ID NO: 2

Invention 3: Nucleic acid of SEQ ID NO: 3

Invention 4: Nucleic acid of SEQ ID NO: 4

Invention 5: Nucleic acid of SEQ ID NO: 5

On the other hand, if the prior art disclosed a nucleic acid molecule encoding a dehydrogenase but lacked the catalytic site defined by the conserved sequence motif, the technical feature would be special and SEQ ID NOs: 1, 2, 3, 4 and 5 would have fulfilled the requirement for unity of invention.

Sequence Claims

A claim to a polynucleotide sequence that was available to the public or already known before the priority date, lacks novelty, even if the activity or function of the said sequence of the polynucleotide has not been previously determined. A claim to a specific polynucleotide fragment may be considered novel, but only if it satisfies the requirements for inventive step and patentability.

Even without any indication of its action, a prior disclosure of the same sequence as the claimed sequence would *prima facie* constitute anticipation to the novelty of the claimed sequence. The explanation is that the activity of the claimed sequence is inherent in the earlier sequence. **If any sequence of a polynucleotide/polypeptide from a prior art does not exactly match with the claimed sequence of polynucleotide/polypeptide, the subject matter of such claims cannot be deemed to be anticipated by the prior art sequence.**

However, such sequences of polynucleotide/polypeptide of the prior art would be relevant for deciding inventive step or patentability.⁷⁶

Requirement of submission of a computer-readable file containing WIPO Standard ST. 26 compliant sequence listings through the use of the WIPO sequence suite available through this link:

<https://www.wipo.int/standards/en/sequence/index.html>

Assessment of animal suffering vs. potential medical benefit

Three matters to consider in balancing suffering and medical benefit:

- 1) Animal suffering
- 2) Medical benefit to humanity
- 3) The necessary correspondence between the two in terms of the animals in question. The usefulness of the transgenic organism in furthering research for the purpose of medicine must outweigh moral concerns about the consequences that may be brought to the organism.

Organs and tissues

Organs and tissues (whether of plant or animal origin) are generally not considered to be manufactures or compositions of matter. Organs and tissues are in general created by complex processes, elements of which require no technical intervention, and do not consist of ingredients or substances that have been combined or mixed together. However, organs and tissues which are genetically modified to exhibit meaningful medical utility may be eligible.

Illustrative Example

Claim: A genetically engineered heart isolated from a pig wherein said heart is engineered to express human cell surface antigens.

Analysis

This claim satisfies the eligibility requirement since the organ is genetically modified and has medical utility.

⁷⁶ Guidelines for Examination of Biotechnology Applications for Patent (Intellectual Property of India) 2013).

Artificial organ-like or tissue-like structures generated by technical intervention by combining various cellular and/or inert components may be considered, on a case-by-case basis, to be manufacture or composition of matter and therefore to be statutory subject matter.

Illustrative Example

Claim: An artificial heart valve comprising polymeric scaffold material configured in the shape of a human heart valve, said scaffold material seeded with human myocytes derived from a human myogenic stem cell line.

Claim Construction

1. "For use"

- o Substance XYZ for use in the treatment of disease ABC. *This claim is acceptable if substance XYZ is novel and inventive (provided it is for the first medical use).*

2. "Use of"

- o The use of substance XYZ to treat disease ABC. *This claim format is not acceptable since this may be construed as a method of treatment claim disguised as use claim.*
- o The use of substance XYZ for the manufacture of a medicament for the treatment of disease ABC. *This claim format is acceptable because it is a Swiss-type claim which is acceptable for first and subsequent uses.*

3. Product-by-process

Substances appearing to be claimed by performing a series of steps or methods are product-by-process claims. However, such claims should be construed as claims pertaining to the product *per se*, regardless of the methods employed to attain such.

- o Substance XYZ obtained by method of...
- o Substance XYZ derived from the process of...

4. Subject-Matter

The object of the definition in the claim, the entity or activity that is being claimed.⁷⁷ Determination of the subject matter of a claim requires special attention as a misconstruction of the subject matter affects all aspects of the examination.

Entity- something that has separate and distinct existence and objective or conceptual reality.⁷⁸

⁷⁷ IPOPHL Clarity Guidelines 2018

⁷⁸ Merriam-Webster, 2022

-something that exists apart from other things, having its own independent existence.⁷⁹

Therefore, different entities should be considered as preferred embodiments or subject matter to be protected which must be recast and claimed separately. More so, *Rule 416a of the 2022 Revised IRR* states that a claim must particularly point out and distinctly claim the part which the applicant regards as their invention. Thus, in no instance shall the claim present alternative designations of the subject-matter. A claim shall be refused for lacking clarity including but not limited to the following:

Illustrative Example 1

Claim 1: A transgenic plant, cell, tissue, and/or part thereof comprising a polynucleotide in SEQ ID NO: 1...

Claim 2: A transgenic plant, cell, tissue, and/or seed/progeny thereof comprising a polynucleotide in SEQ ID NO: 1...

Remarks: In claims 1 and 2, the transgenic plant will naturally consist of cells, tissues and any part thereof comprising the polynucleotide. Furthermore, a plant, a cell, a tissue or a seed have distinct morphological and physiological characteristics from each other. Hence, if the applicant desires protection for any part of the plant per se, then the claim must be recast specific to said part or entity.

Illustrative Example 2

Claim: A vector, host cell, and/or composition comprising a recombinant polypeptide...

Remarks: In the present case, a vector and a host cell are clearly distinct from each other, and the composition being claimed could be any entity comprising other components which is not necessarily the claimed vector or host cell.

5. Acceptable claim format when claiming virus strains

Claim 1. A Porcine Reproductive and Respiratory Syndrome Virus (PRRSV) of a European type, which is of the strain deposited with European

⁷⁹ Cambridge Dictionary, 2022

Collection of Cell Cultures (ECACC) under the Accession Number ECACC 11012501.

or

Alternative drafting

Claim 1. A PRRS virus having a nucleotide sequence that is at least 95% homologous with the sequence set forth in either SEQ ID NO:1 or SEQ ID NO:10.

or a broader scope:

Claim 1. A PRRS virus having a nucleotide sequence that is set forth in either SEQ ID NO:1 or SEQ ID NO:10.

The Budapest Treaty

The *Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure* (The *Budapest Treaty*) was established in 1977. The Treaty is administered by WIPO and obliges contracting states to recognize the fact and date of a deposit of biological material for patent purposes, when it is made in a depositary which has acquired official status under the Treaty. Such a depositary is known as an International Depositary Authority (IDA). An applicant who is making multiple patent filings need only make one IDA deposit to satisfy the deposit practice in all contracting states.

The term “microorganism” is not defined in the Treaty so that it may be interpreted in a broad sense as to the applicability of the Treaty to microorganisms to be deposited under it. Whether an entity technically is or is not a microorganism matters less in practice than whether deposit of that entity is necessary for the purposes of disclosure and whether an IDA will accept it. Thus, for example, tissue cultures and plasmids can be deposited under the terms of the Treaty, even though they are not microorganisms in the strict sense of the word.

Where to Make a Deposit?

A list of International Depositary Authorities and their specific requirements is available at the following site:

<http://www.wipo.int/export/sites/www/treaties/en/registration/budapest/pdf/idalist.pdf>

New and Substitute Deposits

After an original sample of biological material has been deposited in an IDA (an original IDA deposit), circumstances may necessitate that a new sample of the same material be deposited in either the same or a different IDA (Article 4 of the *Budapest Treaty*) or that the sample be transferred to a substitute IDA (Rule 5 of the *Regulations Under the Budapest Treaty*).

If an IDA cannot furnish a sample of deposited material because it is no longer viable, a depositor must make a new deposit in the same IDA.

If an IDA cannot furnish a sample of deposited material because the sample must be sent abroad and this is prevented by export or import restrictions, a depositor may make a new deposit in another IDA.

To maintain an original IDA deposit date, a new deposit must be made within three months of the depositor receiving notice from an IDA that a sample is no longer viable or cannot be sent abroad, or that the IDA's status has changed. The deposit must be accompanied by a statement that the newly deposited material is the same as that originally deposited. If a new deposit is not made in accordance with Article 4 of the *Budapest Treaty*, the application is treated as if no deposit had ever been made.

If an IDA temporarily or permanently discontinues any of the tasks required of it as an IDA such that samples of deposited biological material can no longer be provided, the defaulting IDA is required to transfer samples of deposited materials to another IDA.

The new IDA is referred to as a substitute IDA and the deposit is known as a substitute deposit.

In order to access a deposited biological material, a request must be made. Where a restriction has been made by the applicant and is in effect, only the independent expert may make such a request. When such a restriction is not in place, or no longer applicable, any person may request access to the deposited material.

Suggested Readings

A. Patentability of Plants

• T 1729/06 (Seedless watermelon/SYNGENTA) of 17.9.2014

-The appeal was lodged by the applicant against the decision of the examining division to refuse European patent application 03744126.8 with the title "Enhanced pollenizer and method for increasing seedless watermelon yield" on the ground of being drawn to an essentially biological processes for the production of plants which was a corresponding application of International application PCT/US03/05720 on 25 February 2003 and published as WO 03/075641.

-It was decided that the claimed uses and methods constitute a "technical process" for which it foresees patentability.

Allowed Claims⁸⁰

1. Use of a diploid watermelon plant comprising a gene *e* as pollenizer for triploid watermelon plants in a process of producing triploid seedless watermelon fruit, wherein the fruits of the diploid watermelon plant are in a size range of between 0.9 to 3.2 kg and the fruit rind is brittle breaking under a pressure in the range of 90 to 150 g/mm².
2. Use according to claim 1, wherein the diploid watermelon plant is planted in a field of triploid watermelon plants and said triploid seedless watermelon fruit is harvested.
3. Use according to claim 1, wherein unharvested fruits of the diploid watermelons plant are eliminated from further reproduction through conventional crop disposal such as disking and plowing.
4. A method for producing triploid, seedless watermelon fruit comprising the steps of:
 - a) planting a field with rows of triploid watermelon plants;
 - b) planting said field with rows of diploid watermelon plants comprising a gene *e* and small fruits in a size range of between 0.9 to 3.2 kg with a brittle rind breaking under a pressure in the range of 90 to 150 g/mm²; and

⁸⁰ Derived from EP 1 487 256 B1 (2016)

- c) allowing pollination of said triploid watermelon plants by pollen of said diploid watermelon plants to obtain triploid, seedless watermelon fruit.
5. A method of increasing the yield of triploid, seedless watermelons plants, wherein the method comprises the steps of:
- a) obtaining diploid watermelon plants for pollenizing said triploid, seedless watermelon plants, which diploid watermelon plants comprise a gene *e* and small fruits in a size range of between 0.9 to 3.2 kg with a brittle rind breaking under a pressure in the range of 90 to 150 g/mm²;
 - b) planting said diploid watermelon plants in a field of triploid watermelon plants;
 - c) allowing pollination of said triploid watermelon plants by pollen of said diploid watermelon plants to obtain triploid, seedless watermelon fruit; and
 - d) harvesting said triploid, seedless watermelon fruit.
6. The method of claim 5 comprising the additional step of
- e) eliminating the unharvested fruits of the diploid watermelon plant from further reproduction through conventional crop disposal such as discing and plowing

B. Patentability of Animals

• T 0315/03 (Transgenic animals/HARVARD) of 6.7.2004

- The appeal was lodged by the applicant against the decision of the examining division to refuse European patent No. 0169672 in amended form the patent is based on European patent application No. 85304490.7, entitled "Method for producing transgenic animals" on the grounds of being drawn to animal variety and that it involved an extrapolation from mice in particular to mammals in general. Although the title and early versions of the claims refer to animals, the only embodiments disclosed relate to mice and the subject-matter of the patent has come to be referred to as the "oncomouse".

-It was decided that with claims limited to "mice," to fulfil the requirements and the request is accordingly allowable.

Allowed Claims⁸¹

1. A method for producing a transgenic non-human mammalian animal having an increased probability of developing neoplasms, said method comprising chromosomally incorporating an activated oncogene sequence into the genome of a non-human mammalian animal.
2. A method as claimed in claim 1 wherein the chromosome of the animal includes an endogenous coding sequence substantially the same as the coding sequence of the oncogene.
3. A method as claimed in claim 2 wherein said oncogene sequence is integrated into a chromosome of said animal at a site different from the location of said endogenous coding sequence.
4. A method as claimed in claim 2 or claim 3 wherein transcription of said oncogene sequence is under the control of a promoter sequence different from the promoter sequence controlling the transcription of said endogenous coding sequence.
5. A method as claimed in any one of claims 2 to 4 wherein said promoter sequence controlling transcription of said oncogene sequence is inducible
6. A method as claimed in any one of claims 1 to 4 wherein said activated oncogene sequence comprises a fused gene comprising an oncogene sequence fused to an activating viral or synthetic promoter sequence.
7. A method as claimed in claim 6 wherein said viral promoter sequence comprises a sequence selected either from an MMTV or an RSV promoter.
8. A method as claimed in any one of claims 1 to 7 wherein said oncogene sequence comprises a coding sequence of a c-myc gene.
9. A method as claimed in any one of claims 1 to 7 wherein said activated oncogene sequence comprises a DNA sequence selected from the oncogenes src, yes, fps, abl, ros, fgr, erbB, fms, mos, raf, Ha-ras-1, Ki-ras 2, Ki-ras 1, myc, myb, fos, ski, rel, sis, N-myc, N-ras, Blym, mam, neu, erbA1, ra-ras, mht-myc, myc, myb-ets, raf-2, raf-1, Ha-ras-2, or erbB.
10. A method as claimed in any one of claims 1 to 8 wherein said activated oncogene is derived from a plasmid.
11. A plasmid selected from the group comprising plasmids ATCC 39745, 39746, 39747, 39748, 39749.
12. A method as claimed in claim 1 wherein the activated oncogene sequence is derived from a plasmid as defined in claim 11.
13. A method as claimed in any one of claims 1 to 12 wherein said chromosomal incorporation is at a stage no later than the 8-cell stage.

⁸¹ Derived from EP 0 169 672 B1 (1992)

14. A method as claimed in any one of claims 1 to 12 wherein said chromosomal incorporation is at a stage no later than the 1-cell stage.
15. A method as claimed in claim 1 which comprises injecting into the male pronucleus of a fertilized one-cell mouse egg a linearized plasmid as defined in claim 11.
16. A method of testing a material suspected of being a carcinogen which comprises exposing an animal produced according to the method of any one of claims 1 to 15 to said material and detecting neoplasms as an indication of carcinogenicity.
17. A method of testing a material suspected of conferring protection against the development of neoplasms, said method comprising treating an animal produced according to the methods of any one of claims 1 to 15 with said material and detecting a reduced incidence of development of neoplasms, compared to an untreated animal, as an indication of said protection.
18. A method as claimed in claim 17, further comprising exposing said treated and untreated animals to a carcinogen prior to, after or simultaneously with treating said animals with said material.
19. A transgenic non-human mammalian animal whose germ cells and somatic cells contain an activated oncogene sequence as a result of chromosomal incorporation into the animal genome, or into the genome of an ancestor of said animal, said oncogene optionally being further defined according to any one of claims 3 to 10.
20. An animal as claimed in claim 19 which is a rodent.
21. An animal as claimed in claim 19 or claim 20 wherein said chromosomal incorporation is at a stage no later than the 8-cell stage.
22. An animal as claimed in claim 19 or claim 20 wherein said chromosomal incorporation is at a stage no later than the 1-cell stage.
23. A chromosome of an animal as claimed in claim 19, which comprises an oncogene as defined in any one of claims 3 to 10.
24. A method of providing a cell culture comprising providing a transgenic non-human mammalian animal as defined in any one of claims 19 to 22 and culturing a somatic cell thereof.
25. A cell derived from a somatic cell obtained from a transgenic non-human mammalian animal as defined in any one of claims 19 to 22.

C. FUNK BROTHERS SEED V KALO INOCULANT ⁸²

“Mixed cultures of root-nodule bacteria for leguminous plants fall under ‘discovery’, hence, not patent eligible.”

D. DIAMOND V CHAKRABARTY ⁸³

“Naturally-occurring microorganisms are not patent eligible.”

“Genetically- modified microorganisms are patent eligible.”

E. AMP V MYRIAD ⁸⁴

“Naturally- occurring genes are not patent eligible.”

“Mere isolation does not make a gene patent eligible.”

“Isolated DNA is not patent eligible.”

“cDNA is patent eligible due to ‘human intervention’ removal of introns constitute human intervention.”

⁸² <https://supreme.justia.com/cases/federal/us/333/127/>

⁸³ <https://supreme.justia.com/cases/federal/us/447/303/case.html>

⁸⁴ <http://www.genomicslawreport.com/index.php/category/badges/myriad-gene-patent-litigation/>

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