UNITED STATES PATENT AND TRADEMARK OFFICE (USPTO)
DEPARTMENT OF COMMERCE
Docket No. PTO-P-2021-0032

AIPPI's Comments Re: Patent Eligibility Jurisprudence Study

14 October 2021

AIPPI submits the following comments on certain Topics for Public Comment relating to the above-identified Patent Eligibility Jurisprudence Study.

A. INTRODUCTION TO AIPPI

AIPPI, the International Association for the Protection of Intellectual Property, was founded in 1897, and is dedicated to the development, improvement, and legal protection of intellectual property. The acronym of the organization was derived from its name in French: *AssociationInternationale pour la Protection de la Propriété Intellectuelle*. AIPPI is a non-affiliated, non- profit, politically neutral organization headquartered in Switzerland, having over 8,000 members representing over 130 countries. The members of AIPPI include lawyers, attorneys, and agents working across all fields of intellectual property in corporate and private practice throughout the world, as well as academics, judges, government officials and other persons interested in intellectual property. AIPPI is organized into 68 National and 2 Regional Groups.

The objective of AIPPI is to improve and promote the protection of intellectual property at bothnational and international levels. It does this by studying and comparing existing and proposed laws and policies relating to intellectual property and working with both government and non- government organizations for the development, expansion and improvement of international and regional treaties and agreements, and national laws.

B. AIPPI'S COMMENTS ON PATENTABLE SUBJECT MATTER

AIPPl's comments have been prepared with the benefit of input of members of, and work product prepared by, the Standing Committee on Pharma (AIPPI Pharma Committee), and approved by the AIPPI Bureau. AIPPI's comments are limited to the impact of the U.S. law on patentable subject matter on the diagnostics industry. In particular, AIPPI responds to questions #4 and #5 from the USPTO notice.

Q4:

Question #4 from the USPTO notice asks:

> Please explain how your experiences with the application of subject matter eligibility requirements in other jurisdictions, including China, Japan, Korea, and Europe, differ from your experiences in the United States.

U.S. caselaw on patentable subject matter prevents patent applicants from obtaining meaningful patent protection for most inventions covering diagnostics.

Other countries do not exclude diagnostic methods from patentability. In the EPO, there is a prohibition on patenting "methods for treatment of the human or animal body by surgery or therapy and diagnostic methods practised on the human or animal body." However, applicants can obtain claims that cover diagnostic inventions, but do not recite treatment or interaction with the human or animal body. For example, applicants can claim treatment of a sample or treatment *in vitro.*

The EPO Enlarged Board of Appeal in its decision of G1/04 sets out the phases that must *all* be present in a method for it to relate to an excluded/non-patentable diagnostic method:

(i) the examination phase, involving the collection of data,
(ii) the comparison of these data with standard values,
(iii) the finding of any significant deviation, i.e., a symptom, during the comparison, and
(iv) the attribution of the deviation to a particular clinical picture, i.e., the deductive medical or veterinary decision phase (diagnosis for curative purposes).

If one or more of these steps is excluded, the claim covers patentable subject matter. As a result, it is possible for innovators in the diagnostics industry to obtain meaningful patent protection for their inventions.

Japan also prohibits patenting methods of treatment, which include methods of diagnosis on the human body. Japanese law contains a statutory bar based on the main paragraph of Art. 29(1) of the Japanese Patent Act, which excludes claims directed to methods of diagnosis, if such a method includes a medical act solely made by a medical doctor. However, diagnostic inventions can be patented in Japan if the subject matter is rewritten as a product, or a method that is not limited to an act only made by a medical doctor.

In Korea, an industrially applicable invention is patent eligible under the main body of Article 29(1) of Korean Patent Act. In this regard, KIPO's Patent Examination Guidelines provide that a method of diagnosing a disease in a human subject is not considered as industrially applicable, and thus such diagnostic method claim is not patent eligible. However, subject matter eligibility can be satisfied by redrafting the claim to be directed to "a method of providing information for diagnosing ..." so that a clinical judgment by a medical practitioner can be excluded, or by amending "human subject" to "non-human subject".

In Australia, diagnostic method claims are patentable subject matter. This was recently confirmed in June 2021, in the case of *Ariosa Diagnostics, Inc v Sequenom, Inc (Sequenom 2021)* when the Full Federal Court of Australia upheld a decision to allow patents to diagnostic methods involving the practical application of natural phenomena (including nucleotides). The Federal Court found that the substance of the invention was not cffDNA itself (i.e., mere "naturally occurring information"), or the mere observation that cffDNA was present in maternal plasma or serum. Instead, the substance of the invention was found to lay in devising a new means for detecting foetal DNA without the need for invasive sampling, that overcomes difficulties involved in invasive sampling and using maternal blood. As such, it was held that the invention as claimed is not merely the output, but the detection process which yields the output and that this is the very type of subject matter considered to fall on the correct side of the line between discovery of a scientific fact or law of nature and invention (*Sequenom 2021: [154] – [167]*).

Q5:

Question #5 from the USPTO notice asks:

> Please identify instances where you have been denied patent protection for an invention in the United States solely on the basis of patent subject matter ineligibility, but obtained protection for the same invention in a foreign jurisdiction, or vice versa. Please provide specific examples, such as the technology(ies) and jurisdiction(s) involved, and the reason the invention was held ineligible in the United States or other jurisdiction. following areas: a. Quantum computing; b. artificial intelligence; c. precision medicine; d. diagnostic methods; e. pharmaceutical treatments; and f. other computer-related inventions.

AIPPI has recognized several patent application families for which diagnostic claims have granted ex-U.S. while claims in the counterpart U.S. application remain rejected. The below examples are not unique or atypical, but rather characteristic of the situation - similar claims to diagnostic inventions have been consistently rejected by the USPTO.

U.S. Patent Application Serial No. 15/647,824
Patent Family: PCT/AU2013/001088 (WO2014/043763)
Title: Non-Invasive Determination of Methylome of Fetus or Tumor from Plasma
Applicant: The Chinese University of Hong Kong

U.S. Patent Application Serial No. 15/647,824 ("'824 application"), entitled Non-Invasive Determination of Methylome of Fetus or Tumor from Plasma," was filed on March 15, 2013, and claims priority to parent U.S. Application Serial No. 13/842,209. The applicant discovered that the methylation pattern of DNA of various tissues can be used to detect the presence of tumors, and to obtain information about the tumors. In the continuing '824 application, the applicant pursued claims in the U.S to a method of determining a type of cancer by analyzing DNA molecules from a biological sample of an organism, by the steps of obtaining sequence reads from cell free DNA molecules from the sample, analyzing the sequence reads to determine the amount of methylation, determining the methylation profile, and determining the type of cancer based in part on the methylation profile. The claims are subject to a final rejection, solely on the grounds that the claims are "directed to an abstract idea without significantly more." Specifically, the Examiner alleges that the steps of

analyzing the sequence reads to determine the amount of methylation, determining the methylation profile, and determining the type of cancer are each directed to abstract ideas.

The parent application to the ‘824 application granted as U.S. Patent No. 9,732,390, but the claims recite a method of measuring a first metalation profile of a first issue from a biological sample. The granted claims do not recite the diagnostic invention.

In contrast to the prosecution of the ‘824 application in the U.S., counterpart applications claiming a diagnostic invention have been granted in the national phase in several countries, including Australia (AU 2013317708 B2), Europe (EP 2 898 100 B1), and Japan (JP 6683752 B2; JP 6317354 B2), and has been allowed in Korea (KR 10-2020-7019527). The granted European patent has been opposed, but not on grounds of patentable subject matter. Exemplary granted Claim 1 of EP 2 898 100 is below:

1. A method of analyzing a biological sample of an organism, the biological sample including cell-free DNA originating from normal cells and potentially from cells associated with cancer, the method comprising:
   analyzing a plurality of cell-free DNA molecules from the biological sample, wherein analyzing a DNA molecule includes:
   determining a location of the DNA molecule in a genome of the organism; and
   determining whether the DNA molecule is methylated at one or more sites;
   for each of a plurality of sites,
   determining a respective number of DNA molecules that are methylated at the site;
   calculating a first methylation level based on the respective numbers of DNA molecules methylated at the plurality of sites;
   comparing the first methylation level to a first cutoff value; and
   determining a first classification of a level of cancer based on the comparison.

Hence, the applicant has been denied a patent for their diagnostic invention in the U.S. on patentable subject matter grounds, but has obtained patent protection for their diagnostic invention outside the U.S.

U.S. Patent Application Serial No. 14/122,754
Patent Family: PCT/US2012/040283 (WO 2012/166971)
Title: Method of Assessing Risk of PML
Applicant: Biogen Idec

In U.S. Patent Application Serial No. 14/122,754 ("'754 application"), the applicant discovered a method of assessing a patient's risk of developing progressive multifocal leukoencephalopathy (PML), by determining the level of anti- JCV antibody in a sample. The applicant pursued claims to a method of evaluating a patient's risk of developing PML, comprising the steps of determining anti-JCV antibody titer in a sample from the patient, where the index is determined to be above 1.5. Diagnostic method claims were finally rejected, in part under 35 U.S.C. §101 as unpatentable subject matter. The Examiner alleges that the method steps use "the natural relationship between those anti-JCV antibody titers/values and predetermined/control values to predict a patient's risk of developing PML." The '754 application was abandoned. A continuation application 16/211,154 is pending. However, the claims have been amended to recite a method of treatment, rather than a method of diagnosis.

Counterpart applications have been granted in the national phase in several countries, including Australia (AU 2012262122B2), European Patent Office (EP 2715352B1) and Japan (JP 6663396B2; JP 6243838B2) and Korea (KR 10-2039751-00000), with claims to the diagnostic invention. The granted European patent has been opposed, but not on grounds of patentable subject matter. Exemplary claim 1 of the Korean Patent (English language translation) is below:

1. A method of evaluating a patient's risk of developing Progressive Multifocal Leukoencephalopathy (PML), the method comprising:
   determining an anti-JC Virus (JCV) antibody titer expressed as an index in a sample of serum or plasma from the patient, wherein
   if the index is determined to be above 1.5, the patient is determined to be at a high risk of developing PML, and wherein
   the index is determined by normalizing an optical density (OD) value of the sample in a test, such as an enzyme-linked immunosorbent assay (ELISA), to a cut-off calibrator, where the cut-off calibrator is adjusted to have an OD value of 1.

Hence, the applicant has been denied a patent for their diagnostic invention in the U.S. on patentable subject matter grounds, while securing patent protection for the diagnostic invention in important markets outside the U.S.

U.S. Patent Application Serial No. 15/827,176
European Patent Application No. 17153745.9
Title: New Test for Monitoring Renal Disease
Applicant: Helena Laboratories

In U.S. Patent Application Serial No. 15/827,176 ("'176 application"), the applicant discovered a method of monitoring disease development in a patient by determining the amount of carbamylated serum albumin in a blood or plasma sample of the patient. The applicant discovered a relationship between carbamylated serum albumin and renal diseases. The claims were finally rejected on several grounds, including 35 U.S.C. §101, and the application was abandoned. In the final rejection, the Examiner stated that Claim 1 "is rejected under 35 U.S.C. 101 because the claimed invention is directed to a law of nature and an abstract idea without significantly more."

In contrast, the counterpart European patent application granted with claims covering a diagnostic method, in EP 3 355 058 B1. Exemplary claim 1 is below:

1. Method for monitoring renal disease in a subject, comprising subjecting a serum sample comprising albumin from that subject to electrophoresis, wherein carbamylated albumin is used as a bio-marker for the monitoring of the renal disease, wherein the monitoring comprises determining the symmetry ratio of the electrophoresis serum albumin peak.

Hence, the applicant has been denied a patent for their diagnostic invention in the U.S. on patentable subject matter grounds. In contrast, the applicant has obtained claims to the diagnostic invention in the EPO.

U.S. Patent Application Serial No. 15/308,328
Patent Family: PCT/US2015/058614 (WO 2015/165779)
Title: Small NCRNAS as Biomarkers
Applicants: Stichting VU-VUMC; Universidad de Granada

In U.S. Patent Application Serial No. 15/308,328 ("'328 application"), the applicants discovered the role of a small noncoding RNA biomarker in the detection of disease. The applicants claimed a method for identifying a small noncoding RNA biomarker pair, methods of determining the quantity of two different varieties of the noncoding RNA in samples from patients, and the ability to use that information to diagnose disease. However, claims to a diagnostic method remain finally rejected on grounds of 35 U.S.C. §101 (the claims are also rejected on obviousness grounds). The applicants filed a request for continued examination in an effort to pursue this subject matter.

In contrast, the counterpart European application granted as EP 3 137 626. Exemplary Claim 5 of the granted European patent is below:

1. A method for classifying the health status of an individual
using a small non-coding RNA (ncRNA) biomarker pair, the method comprising determining
the quantity of the biomarker pair in a bodily fluid sample from said individual,
determining the ratio of the biomarker pair in the bodily fluid sample,
and comparing the ratio to the ratio of the biomarker pair in a bodily fluid from a reference sample,
wherein the presence or absence in a difference in the ratio between the individual and the reference sample classifies the health status of said individual,
wherein the biomarker pair consists of two different varieties of an ncRNA
wherein the first and second varieties are selected from the canonical ncRNA; the ncRNA trimmed at the 5' or 3' end and/or extended at the 5' or 3' end;
and the ncRNA with a 3' non-templated nucleotide addition, optionally trimmed at the 5' or 3' end or extended at the 5'or 3'end;
wherein when said ncRNA is not an miRNA the first variety is selected from the canonical ncRNA and
the ncRNA with a 3' non-templated nucleotide addition

and the second variety is the ncRNA with a 3'
non-templated nucleotide addition, wherein the ncRNA
is selected from miRNA, tRNA, and Y-RNA

Hence, the applicants have been denied a patent for their diagnostic invention in the US on patentable subject matter grounds. In contrast, the applicants have obtained granted claims to the diagnostic invention in the EPO.

Respectfully submitted,

International Association for the Protection of Intellectual Property (AIPPI)