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Paper 166
Entered: September 2, 2014

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

ARIOSA DIAGNOSTICS,
Petitioner,

v.

ISIS INNOVATION LIMITED,
Patent Owner.

Case IPR2012-00022[1]
Patent 6,258,540

Before LORA M. GREEN, FRANCISCO C. PRATS, and JEFFREY B. ROBERTSON, *Administrative Patent Judges*.

GREEN, *Administrative Patent Judge*.

FINAL WRITTEN DECISION
35 U.S.C. § 318(a) and 37 C.F.R. § 42.73

I. INTRODUCTION

A. Background

Petitioner, Ariosa Diagnostics ("Ariosa"), filed a Petition for *inter partes* review of claims 1, 2, 4, 5, 8, 19–22, 24, and 25 of U.S. Patent No. 6,258,540 ("the '540 Patent") pursuant to 35 U.S.C. §§ 311–319. Paper 1 ("Pet."). Patent Owner, Isis Innovation Limited ("Isis"), filed a Preliminary

[1] This Case has been joined with IPR2013-00250.

Response. Paper 18 ("Prelim. Resp."). On March 19, 2013, we instituted trial as to all of the challenged claims. Paper 24 ("Dec. Institute").

After institution of trial in IPR2012-00022, Ariosa filed a second Petition for *inter partes* review of claims 3, 8, 12, 13, 15, and 18 of the '540 patent. IPR2013-00250, Paper 1. Ariosa also filed a Motion for Joinder, seeking joinder of that proceeding with IPR2012-00022. IPR2013-00250, Paper 4. On September 3, 2013, we instituted trial as to all of the claims challenged in the second Petition (IPR2013-00250, Paper 26), and joined the proceeding with IPR2012-00022 (IPR2013-00250, Paper 25). Thus, claims 1–5, 8, 12, 13, 15, 18–22, 24, and 25 are subject to *inter partes* review in the joined proceeding.

Isis filed a Patent Owner Response in the joined proceeding. Paper 89 ("PO Resp."). Isis filed also a contingent Motion to Amend by submitting proposed substitute new claims 28–30, or substitute new claims 31–33, for claims 1, 24, and 25, respectively. Paper 88 ("Mot. to Amend"). Ariosa filed a Reply to the Patent Owner Response (Paper 114; "Reply"), and also an opposition to Isis's Motion to Amend (Paper 115; "Opp."). Isis then filed a Reply in support of its Motion to Amend. Paper 130 ("Reply Mot. to Amend").

Isis filed a Motion to Exclude. (Paper 135; "Isis's Motion to Exclude"); and Ariosa filed an Opposition to that Motion (Paper 155). Oral hearing was held on January 24, 2014. Paper 165[2] ("Tr.).

[2] We note that the pages of the oral hearing transcript are not numbered. We, thus, designate the first page on which argument appeared, entitled "PROCEEDINGS," as page 1, and number the remaining pages sequentially therefrom.

The Board has jurisdiction under 35 U.S.C. § 6(c). This Final Written Decision is issued pursuant to 35 U.S.C. § 318(a) and 37 C.F.R. § 42.73.

Ariosa has demonstrated, by a preponderance of the evidence of record, the unpatentability of claims 1, 2, 4, 5, 8, 19, 20, 24, and 25 under 35 U.S.C. § 102(b). Ariosa, however, has not met its burden to show by a preponderance of the evidence of record that claims 3, 12, 13, 15, 18, 21, and 22 are unpatentable under 35 US.C. § 103(a).

Isis's Motion to Amend is *denied.*

B. Related Proceedings

Claims 1, 2, 4, 5, 8, 19–22, 24, and 25 of the '540 patent were declared invalid in *Ariosa Diagnostics v. Sequenom*, Civ. No. 12-00132-SI (N.D. Cal.). Paper 107, 1 (citing Ex. 2224). The district court granted summary judgment on the basis that the claims were drawn to patent ineligible subject matter under 35 U.S.C. § 101. Ex. 2224, 20. The district court's decision is currently on appeal to the Court of Appeals for the Federal Circuit in *Ariosa Diagnostics, Inc. v. Sequenom, Inc.*, Appeal Nos. 14-1139, 14-1142, and 14-1144. Paper 163, 1.

C. The '540 Patent

The '540 patent issued on July 10, 2001, with Yuk-Ming Dennis Lo and James Stephen Wainscoat as the listed co-inventors. The '540 patent is drawn to "prenatal detection methods using non-invasive techniques," and,

in particular, "to prenatal diagnosis by detecting foetal nucleic acids in serum or plasma from a maternal blood sample." Ex. 1001,[3] col. 1, ll. 6–9.

According to the '540 patent, it was unexpected that fetal DNA "is detectable in maternal serum or plasma samples." *Id.* at col. 1, ll. 50–51. The concentration of fetal DNA in serum or plasma samples has been measured from 0.39% (early pregnancy) to 11.4% (late pregnancy), whereas the concentration of fetal cells in the cellular fraction is generally from 0.001% to 0.025%. *Id.* at col. 1, ll. 59–64. The '540 patent thus "provides a detection method performed on a maternal serum or plasma sample from a pregnant female, which method comprises detecting the presence of nucleic acid of foetal origin in the sample." *Id.* at col. 2, ll. 1–4. "[P]renatal diagnosis" is defined by the '540 patent as covering the "determination of any maternal or foetal condition or characteristic which is related to either the foetal DNA itself or to the quantity or quality of the foetal DNA in the maternal serum or plasma." *Id.* at col. 2, ll. 6–10.

The '540 patent also teaches that the "preparation of serum or plasma from the maternal blood sample is carried out by standard techniques," and that "[s]tandard nucleic acid amplification systems can be used." *Id.* at col. 2, ll. 26–27 and ll. 43–47. Polymerase chain reaction ("PCR") is one of the standard nucleic acid amplification systems disclosed by the '540 patent. *Id.* at col. 2, ll. 44–48. According to the '540 patent, "[s]ex determination has successfully been performed on pregnancies from 7 to 40 weeks of gestation." *Id.* at col. 3, ll. 60–62.

[3] Throughout the decision, quotations to the '540 patent (Ex. 1001) include the British spelling of several words. We, otherwise, use the American spelling; for example, "foetal" versus "fetal."

The ’540 patent teaches further that the plasma or serum-based prenatal diagnostic method may be used to determine fetal rhesus D status in rhesus negative mothers, such that the detection of the rhesus D gene in the negative mother is indicative of a rhesus D positive fetus. *Id.* at col. 2, l. 57–col. 3, l. 3. The diagnostic methods may be used also to detect haemoglobinopathies or other paternally-inherited DNA polymorphisms. *Id.* at col. 3, ll. 4–24.

According to the ’540 patent, the non-invasive methods may be used also to screen for Down’s syndrome and other chromosomal aneuploidies. *Id.* at col. 3, ll. 25–28. The ’540 patent teaches that it was known that the level of circulating fetal cells is higher in pregnancies with chromosomal aneuploidies, such as Down’s syndrome, and it was further determined that the level of fetal DNA in maternal plasma and serum is also higher. *Id.* at col. 3, ll. 30–40. Thus, the ’540 patent teaches that quantitative detection of fetal DNA in maternal plasma or serum may be used to screen for fetal aneuploidies. *Id.* at col. 3, ll. 40–43. Another method disclosed by the ’540 patent for use in screening fetal aneuploidies is quantifying fetal DNA markers on different chromosomes, such as quantification of fetal chromosomal 21-derived DNA. *Id.* at col. 3, ll. 44–51.

Example 2 of the ’540 patent describes quantitative analysis of fetal DNA in maternal serum, wherein the pregnancy is an aneuploidy pregnancy. *Id.* at col. 5, ll. 55–57. Plasma and serum samples were obtained from pregnant women undergoing prenatal testing, and DNA was extracted from those samples. *Id.* at col. 6, ll. 14–34. The DNA then was amplified using real time quantitative PCR using primers for the SRY gene. *Id.* at col. 6, l. 35–col. 7, l. 3. The inventors report that the concentration of fetal DNA is

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