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Commentary

Patenting medical diagnosis methods in Europe: Stanford University and time-lapse microscopy

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A B S T R A C T

In 2013, a European Patent for the technique of time-lapse microscopy was granted by the European Patent Office (EPO) to Stanford University and was subsequently opposed by Unisense FertiliTech A/S and by the European Society for Human Reproduction and Embryology (ESHRE), Sigrid Sterckx, Julian Cockbain and Guido Pennings. ESHRE et al.'s opposition was based on the argument that Stanford's patent was directed to a method of medical diagnosis, methods that are excluded from patentability by Article 53(c) of the European Patent Convention. The Opposition Division of the EPO rejected the oppositions in November 2015, and both opponents have now filed their appeals. In this paper, we comment on the Opposition Division decision and the grounds of appeal put forward by ESHRE et al.

Introduction

In October 2010, Stanford University applied for a European Patent for time-lapse microscopy, a technique for assisting a physician to choose which IVF embryo to implant in order to optimize the chance of a successful pregnancy, and which involves determining the cell division rate of embryos *in vitro*. In January 2013, Stanford was duly granted what is probably the dominant European Patent (Wong et al., 2013). Stanford has licensed this patent to the US company Progyny Inc., and, if the patent is upheld, physicians may have to use Progyny's product, use another licensed product, or face a patent infringement suit.

European patents can be opposed within 9 months of their grant, and Stanford's patent was opposed in February 2012 by Progyny's Danish competitor Unisense FertiliTech A/S on the basis that the subject-matter claimed in the patent was not new, lacked an inventive step, was insufficiently described and that subject-matter had been added. Unisense FertiliTech did not argue that the method claimed was inherently non-patentable as a method of medical diagnosis.

Following an article in *Reproductive BioMedicine Online* by Sterckx et al. (2014) arguing that Stanford's patent related to a method of diagnosis excluded from patent-eligibility by Article 53(c) of the European Patent Convention (EPC) (European Patent Office, 2013), and following Unisense FertiliTech's declining to add this ground to its own opposition, a further opposition to Stanford's patent was jointly filed in October 2013 by the European Society for Human Reproduction and Embryology (ESHRE) and the authors of the Sterckx et al. article.

The only ground of opposition argued by ESHRE et al. was that the patent claims were directed to a method of medical diagnosis excluded under Article 53(c) EPC which states that:

> 'European patents shall not be granted in respect of . . . diagnostic methods practiced on the human or animal body . . .' (European Patent Office, 2013)

The oppositions lead to a hearing at the European Patent Office (EPO) in November 2015 at which the Opposition Division decided to maintain the patent. The Opposition Division's written decision (European Patent Office, 2016), issued in February 2016, and was appealed by both opponents whose detailed arguments were filed in June 2016 (ESHRE *et al*, 2016; Unisense FertiliTech, 2016). The appeal has been given the number T-0990/16. In July 2016, Stanford University was invited to respond to the appeal arguments, and its reply can be expected at or towards the end of 2016.

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Unisense FertiliTech did not raise arguments under Article 53(c) EPC in its appeal, and is not entitled to do so other than as an *amicus curiae* ('friend of the court'). As the scope of the exclusion of diagnostic methods is the subject of this paper, we shall not, for example, comment on Unisense FertiliTech's arguments of lack of novelty.

The points at issue

In simplified form, the broadest claim of Stanford's patent (as granted) is directed to:

A method for assessing good or poor developmental competence of a human embryo comprising the following:

(i) (using time-lapse microscopy) measuring cellular parameters of a human embryo *in vitro*, those parameters including: (a) the duration of the first cytokinesis; (b) the interval between cytokineses 1 and 2; or (c) the interval between cytokinesis 2 and 3; and
(ii) determining that the embryo has good developmental competence when (a) is 0–30 min; (b) is 8–15 h; or (c) is 0–5 h.

The leading 'case law' of the EPO is G-1/04 *Diagnostic methods* (European Patent Office, 2006), an opinion given in 2005 by the Enlarged Board of Appeal (EBoA) of the EPO in response to a request that was made by the EPO's President since the decisions of the EPO's Technical Boards of Appeal were in conflict on the question as to whether or not a patent claim had to explicitly recite the 'decision' step of the diagnostic process, i.e. the step in which the physician decides on the basis of the information that she has gathered that a particular condition, e.g. a broken bone or influenza, is or is not present in the subject of the diagnosis (the patient). The G-1/04 opinion also addressed the question of whether the subject (patient) had to be present for at least one of the data-gathering steps that are the necessary precursor for the decision step. The EBoA confirmed that the decision step did have to be recited and that the subject did have to be present for at least one of the data-gathering steps. In this way, the EBoA confirmed that claims to *ex vivo* laboratory analysis and to pure data-gathering techniques (e.g. medical imaging techniques) were not excluded.

Therefore, to determine whether or not a claim is excluded by Article 53(c) EPC, the following points need to be addressed:

(i) is the subject a human or animal body?
(ii) is the method practised on that body?
(iii) does the method involve a data-gathering step?
(iv) does the method claim involve a step of diagnosis, i.e. a decision-making step based on gathered data? and
(v) does the recited step of diagnosis qualify as a method of diagnosis for the purposes of Article 53(c) EPC?

Whether an embryo is 'a human body' or not was not argued in the opposition hearing – the opponent's earlier submission that, for patent law purposes, it is, was unchallenged.

In its decision, the EPO Opposition Division confirmed that, in Stanford's case, the answers to (i) to (iv) were yes and that therefore the only point outstanding was point (v) and that this depended on two factors: the purpose of the diagnosis; and the nature of the condition being diagnosed. In G-1/04 *Diagnostic methods*, the EBoA had said that, to be excluded, the purpose of the diagnosis had to be curative (i.e. that the condition being diagnosed must be curable), and that the condition being diagnosed must be a disease. For readers who are not physicians, we must point out here that, for medical purposes, 'disease' means 'discomfort' – dis-ease – and thus that a broken arm would count as a disease.

The appeal and the request for referral of questions to the Enlarged Board

In the case of time-lapse microscopy, poor developmental competence (the condition being diagnosed under Stanford's patent) is currently not curable, and the pre-implantation embryo is clearly not capable of experiencing discomfort. Therefore, with the EPO's current interpretation as explained in the previous paragraph, the Opposition Division found that Stanford's patent was not directed to a method of diagnosis.

ESHRE et al. had argued that G-1/04 *Diagnostic methods* was incorrect in reading into Article 53(c) EPC the requirement that the diagnosed condition had to be curable and to be a disease. To this end, they had submitted statements from 29 physicians of a broad range of ages, nationalities, seniorities and specializations showing that the EBoA's interpretation of what conditions could be diagnosed was wholly incorrect from the physicians' point of view. These physicians had been asked to confirm their agreement with the following statements:

i. There can be a medical diagnosis of a condition in a human subject without that condition being a disease condition (examples that might be given are pregnancy and gender dysphoria).
ii. There can be a medical diagnosis of a condition (whether or not a disease condition) even if no curative treatment for the condition is known (examples that might be given are infection by Ebola virus and Huntington's disease).
iii. There can be a medical diagnosis of a condition (whether or not a disease condition) even when the subject currently has no obvious dysfunction but instead only has a poor prognosis (examples that might be given are: presymptomatic mutation carriers of neurodegenerative late-onset genetic diseases (e.g. Huntington's disease) and late-onset familial cancer syndromes (e.g. *BRCA1/2* mutation in hereditary breast and ovarian cancer).
iv. The result of a medical diagnosis of a condition may, for example, be that the subject has the condition, that the subject does not have the condition, that the subject is borderline for having the condition, or that the subject has the condition to a particular extent (e.g. degree of severity) (examples that might be given are abnormal blood pressure [e.g. hypertension]; and abnormal body weight [e.g. anorexia or obesity].

All the physicians confirmed that they fully endorsed those statements.

At the hearing before the Opposition Division in November 2015, ESHRE et al. pointed out that allowing the patenting of diagnostic methods for infectious and incurable diseases (such as Ebola virus infection had recently been) would run counter to the very justification that the EPO's Boards of Appeals had found for the exclusion of medical methods from patentability, namely to free the physician from fear of patent infringement while performing her profession, e.g. in the case of Ebola by isolating the patient and providing palliative (rather

than curative) treatment. In its decision, the Opposition Division seemed to accept that the requirement for curability was indeed incorrect.

The position of ESHRE et al. in the appeal is that, to fall under the exclusion of Article 53(c) EPC, a diagnostic method must merely inform the physician in her choice of action (or indeed inaction) and that it need not of itself be decisive in that regard, i.e. that the physician may still be left with a range of actions to choose from and that further data, e.g. age, sex, physical condition, other current medications being taken, may contribute to the subsequent decision as to what action to take. Simply put, diagnosis is not the act of deciding what action to take but of deciding whether a condition is present at all or to a particular degree. In medical diagnosis, there is a fundamental difference between a 'condition' and a 'symptom'. Diagnosis of a condition lays open a variety of (non)treatment options (e.g. you are pregnant, I could prescribe iron, folic acid, or both), whereas identifying a symptom merely adds to the clinical picture (e.g. you have high blood pressure, and you are old, but this may be due to the fact that you have run to the doctor's surgery or that you are afraid of medics, rather than that you have an underlying heart condition). The case law of the Boards of Appeal of the EPO makes it clear that a method of measuring a symptom (e.g. blood pressure or body temperature) is not an excluded method of diagnosis. Stanford's patent, however, relates to the diagnosis of a condition (i.e. poor chance of successful birth) rather than a symptom.

In their statement of grounds of appeal, ESHRE et al. have therefore asked the Technical Board of Appeal handling the case to refer three questions to the Enlarged Board in order that a better understanding of what is or is not diagnosis might be reached. These questions are essentially as follows:

A. Where a claim is directed to a method of diagnosis of condition X, must a curative treatment for the condition be available for the method to be a method of diagnosis excluded from patentability under Art. 53(c) EPC?
B. Where a claim is directed to a method of diagnosis of condition X, must the condition be a disease for the method to be excluded from patentability?
C. Where a claim is directed to a method of diagnosis of condition X, must the determination that the subject has (or does not have) the condition be in itself fully sufficient to determine the appropriate course of action (or inaction) to be adopted by the physician for the method to be excluded from patentability? (In other words, if other information may inform the physician's course of action, is the method still excluded?)

ESHRE et al. have asked that the question of what conditions can be the subject of an unpatentable method of diagnosis be dealt with before the more technical questions of novelty and inventiveness.

Conclusion

European patent law precludes the patenting of methods of medical diagnosis practised on the body (i.e. not laboratory blood tests and the like). Since the end of 2005, however, the position of EPO has been that diagnostic methods are patentable if the condition being diagnosed is incurable or is not a 'disease'. This interpretation of the law came about because questions were referred to the EPO's Enlarged Board of Appeal in proceedings which did not involve a public hearing and in which interested parties could only have a say by filing *amicus curiae* briefs, a procedure that we suspect is unfamiliar to most in the medical profession. In the event, most of the nine *amicus* briefs filed were filed by parties with an interest in the scope of patent-eligibility being as broad as possible and the curability and disease criteria seem to have been adopted with little discussion.

The purpose of Article 53(c) EPC is to allow physicians to carry out their professional duties without having to fear being sued for patent infringement. In opposing the Stanford University patent, and in appealing the Opposition Division decision, ESHRE et al. are seeking to ensure that this Article applies to all forms of medical diagnosis and not just to those concerning a curable disease. To this end, they have requested that the EPO's Enlarged Board of Appeal revisit its definition of what conditions can be diagnosed. The result will unfortunately not be known for 2 more years.

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