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PATENTABILITY OF DIAGNOSTICS UNDER THE EPC – GENERAL GUIDANCE FOR CLAIM DRAFTING

In the USA, recent landmark decisions *Prometheus* of the Supreme Court and *Myriad* of the Court of Appeals for the Federal Circuit have resulted in re-considerations of strategies for obtaining patent protection for inventions relating to diagnostic methods, biomarkers, and personalized medicine. Nevertheless, the decisions are not without clues for how to protect such technologies. The USPTO has released examination guidelines for method claims after *Prometheus*

These guidelines set forth a three-step test for determining patent eligibility under 35 U.S.C. § 101, comprising: (1) determining whether the subject matter is directed to a method; (2) determining whether it focuses on a natural principle; and (3) determining whether it includes additional elements that integrate the natural principle into the claimed invention such that the natural principle is practically applied. Hence, the key question to be answered relates to the identity of adequate "additional elements" for rendering the subject matter patentable.

From European perspective, the principle issue to be addressed is thus to be seen in the drafting of claims that are not only admissible under the EPC and in line with the case law of the EPO Boards of Appeal but also in compliance with (or at least adaptable to) the recent US decision, for example, when filing a PCT patent application.

The following summary provides some fundamental guidance for the drafting of claims being directed to diagnostic methods, biomarkers, and personalized medicine, taking into account the basic principles derivable from the EPO case law. However, it is to be emphasized that such general advice is not applicable, by default and without further adaptation, to any invention or subject matter for which protection is sought. A careful assessment of the factual circumstances underlying an individual case is highly recommended in order to obtain the broadest scope of protection possible under certain circumstances.

1. Diagnostic methods

According to Article 53(c) EPC, European patents shall not be granted in respect of methods of treatment by surgery, therapy, and diagnostic methods practiced on the human or animal body.

However, in relation to diagnostic methods, the EPO Enlarged Board of Appeal (EBA) held in decision G1/04 that the exclusion has to be interpreted narrowly. Accordingly, subject matter directed to a diagnostic method is only excluded from patentability if it includes all of the following steps:

(i) examination phase involving the collection of data;

(ii) comparison of these data with one or more references;

(iii) identification of a deviation from the normal (or desired) state;

(iv) attribution of the observed deviation to a particular clinical picture.

Furthermore, any step of technical nature (typically, the examination step) must be "practiced on the human or animal body". A specific type or intensity of interaction with the human or animal body is not required, neither the participation of a medical practitioner.

Notably, as confirmed in EBA decision G1/07, the three exclusions of Article 53(c) EPC are cumulative requirements. Thus, in order to be patentable, subject matter shall neither cover a surgical nor a therapeutic nor a diagnostic method.

Practical advice:

(i) Avoid interventional steps, such as "obtaining a blood sample" (Note: even a simple injection is considered surgery!).

(ii) Start or stop the method after or before surgical steps might be taken (for example, "providing a catheterized patient" rather then "catheterizing a patient").

(ii) Include method claims not covering all the above-referenced steps (or at least corresponding language in the description).

(iii) Include a claims being directed to an *in vitro* method, such as "analyzing a blood sample" or "analyzing a tissue specimen".

(iv) Avoid method of treatment claims. Instead, include purpose-restricted compound claims pursuant to Article 54(5) EPC) (and, as a "backup" in the description, classical Swiss-type claims).

2. Biomarkers / Personalized medicine

Personalized medicine refers to the "tailoring" of a medical treatment to the individual characteristics of each patient. Typically, such approach involves the analysis (presence and/or amount) of biomarkers for the selection of a collective of patients, e.g., for a better definition of a disease or its prognosis, for excluding patients at increased risk or for the prediction of a drug response (i.e., pharmacogenomics).

Claimed subject matter relating to personalized medicine can have many different formats, but is typically given as follows:

Compound X for use in treating disease Y in a patient with biomarker Z.

The question at issue is whether limiting a medical use by specifying the patient to be treated as having biomarker Z will confer novelty if (i) the prior art is silent about patients having biomarker Z but (ii) a treatment of at least one patient having biomarker Z appears inevitable (e.g., if Z is an SNP, a methylation profile, or the like). In other words, does limiting a medical use to a patient group that overlaps with, or is within, a patient group known from the prior art, render corresponding claimed subject matter novel?

Current EPO case law does not provide a uniform picture in this regard. In decision T233/96, a strict two-part test for novelty was established requiring (i) the patient groups (i.e. the new group claimed and the prior art group) to be non-overlapping and (ii) the new patient group to be non-arbitrary, that is, there must be a functional relationship between the physiological or pathological status of this group and the therapeutic effect observed. However, in subsequent decisions (e.g., T836/01, T1399/04, and T1642/06), a more lenient position was taken, allowing claimed subject matter where patient groups overlapped with the prior art provided that a different technical effect is accomplished or a new clinical situation identified.

Based on recent experiences it seems as if EPO is again taking a stricter view of the issue. If the EPO decides on applying a test which is based on the concept of a patient with the relevant biomarker ‘inevitably’ having been treated, presumably this is a prior use test, in which case it would be burdensome for applicants to locate evidence on what actually happened. However, if the test is similar to that used in T233/96, i.e., requiring that patient groups do not overlap, this should severely curtail patent protection for personalized medicines.

Based on current EPO practice the following consideration could be made:

(A) Claim format: *Compound X for use in treating disease Y in a patient with biomarker Z.*

In case, the biomarker Z is not known or is known but not its correlation with the therapeutic efficacy of compound X, novelty of the claimed subject matter will largely depend on the identity of compound X.

If compound X is a known drug approved for the treatment of disease Y, and if it is established that biomarker Z occurs in a significant portion of the patients being treated, the EPO will usually consider it beyond reasonable doubt that at least one patient suffering from disease Y has been treated, thus anticipating the claimed subject matter.

However, it might be reasonable to argue that the claimed subject matter represents a particular type of selection invention. However, for the time being, the first instance bodies of the EPO will presumably reject such claims. The assessment may change once any cases have been dealt with by the Technical Boards of Appeal.

(B) Claim format: *Compound X for use in treating disease Y in a patient, comprising: assaying a blood sample from a patient to determine if a patient has biomarker Z; and administering a therapeutically effective amount of compound X to the patient if biomarker Z is present*.

A novelty objection will likely be raised for the same reasons as for claim format (A). But: Based on the lines of argumentation provided in recent examination proceedings, it seems that the following claim wording should principally be considered as novel:

> *Compound X for use in treating disease Y in a patient, comprising: assaying a blood sample from a patient; determining if a patient has BIOMARKER A; and administering a therapeutically effective amount of compound X to the patient if biomarker Z is present.*

Hence, even small differences in the claim wording can have detrimental effects. Accordingly, it appears highly advisable to include multiple claim formats in a patent application in order to provide for various fallback positions. Nevertheless, novelty of this type

of claim hinges on whether an applicant can provide evidence that there is a link between the presence or absence of biomarker (physiological or pathological status) and any improvement in the treatment. Such evidence should ideally be from patients rather than animal models.

In general, the type of evidence that should be provided to the EPO may relate to safety (i.e., there are fewer side-effects of compound X in one patient sub-population than in the other(s)) or efficacy (i.e., compound X is more efficacious in one patient sub-population than the other(s)). Currently, it is not clear how many patients would be required for the evidence to be considered convincing (a collective of 5-10 patients will likely suffice).

Practical advice:

(i) Include different claims formats.

(ii) Include experimental data demonstrating that there is a link between the presence or absence of biomarker and the improvement in the treatment (efficacy or safety) and that the presence/absence of biomarker distinguishes the patient population with respect to the physiological or pathological status.