BIOMARKERS from the RESEARCH to the MARKET

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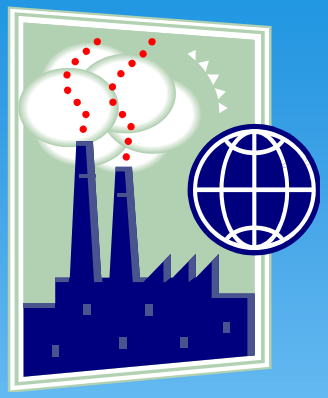


It is customary to say that an innovative start-up has two main assets:
its team
and its intellectual property

PART I

PATENTS PROTECTION

THIRD PARTIES RIGHTS & FREEDOM TO OPERATE

Patent Monopoly

Patent rights are exclusionary.

A patent does not give the patentee the right to practice the invention. No guarantee of Freedom To Operate.

The patent give the patentee only the right to sue someone else who practice the invention without permission.

Filling preserves patentee's place in line: right to enforce only when patent issues, which can take many years.

Patent Strategy

Three approaches to patent protection

The offensive patent strategy: entails filing patent applications for all reasonable inventions as soon as possible. This approach, allows to block competitors from using the invention, and to generate royalties by enforcing patent rights. This is an expensive strategy.

The defensive patent strategy: entails only filing patents to ensure the use of the innovations without the risk of competitors patenting it. This strategy will entail filing patents less often, and approaching the patent portfolio as an asset that provides negotiating power. This strategy is associated with lower costs, and is therefore more suited to SMEs.

Defensive publication or disclosure: Another approach can be not to file for patent protection, but rather to disclose the inventions so that they end up in the public domain. This will ensure that no competitors can patent the invention. This strategy can be valuable for SMEs if they do not need the particular patent in their portfolio to attract investors.

Patent Strategy

Key points:

Patent protection should be done with a clear view of the business, the growth strategy, the market, and the strategic position.

- Know the importance of the invention
- Know the related product
- Know the market and the potential commercial life of invention
- Know the competitors,
- Take into consideration national legal limits (patentability, scope of likely patent protection and enforceability)
- Consider Financing / Licensing

When to apply for patent protection?

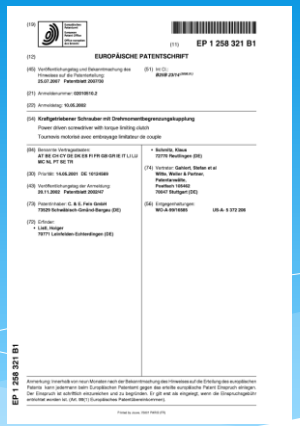
- Key considerations:
  - Timing of own disclosure. Ability to satisfy description requirements
  - State of development of technology

Want sufficient disclosure, but do not want too long and be blocked by somebody else.

Filing patent at the time of genetic discovery increases probability that funding can be found to develop clinical tests

Patentability of Diagnostic Methods in Europe and US

EUROPE

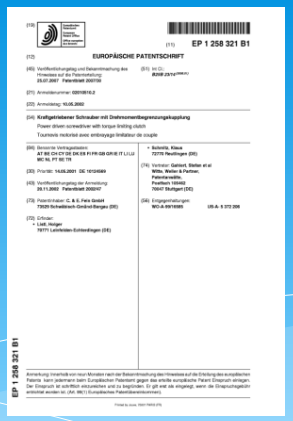

EP 1 258 321 B1

EUROPÄISCHE PATENTSCHRIFT

The European Patent Office (EPO) considers that the discovery of a natural phenomenon is not patent eligible. However the EPO takes the view that a patentable invention can derive from a practical use of that discovery such as its use in a method of diagnosis.

- **The discovery of a naturally-occurring correlation between a biomarker and a disease can be put to a practical use in the form of a method for diagnosing the disease. A claim directed to a method of diagnosing the disease involving detecting the presence or amount of that biomarker may be patentable at the EPO.**

EUROPE


EUROPÄISCHE PATENTSCHRIFT

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The main issue with diagnostic methods at the EPO is a general exclusion from patentability of diagnostic methods **that are practiced on the human or animal body (Article 53c EPC)** If the technical steps of the claimed diagnostic method can be carried out separately from the body, then the method can be patent eligible at the EPO.

- **A diagnostic method that is carried out on an *in vitro* tissue sample is not carried out on the human or animal body can be patented** (T666/05).

- Although diagnostic methods practiced on the human or animal body are not patentable, **substances or compositions for use in such methods may be patented.**

United States

In 2012, the U.S. Supreme Court decided the landmark case of Mayo, which was hailed by some **as banning patents on methods of medical diagnosis. It appeared to be the end of the road for the development of personalized medicine in the US.**

Like the Supreme Court, the U.S. Court of Appeals for the Federal Circuit (CAFC) interpreted diagnostics inventions to concern three types of subject matter **that cannot be patented:**

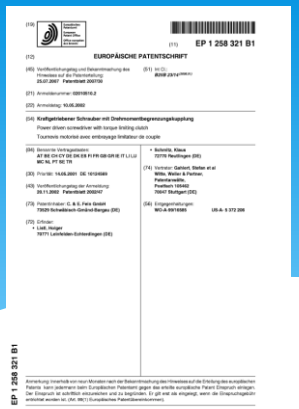
* **natural laws** (such as the relationship between an analyte and a disease),
* **natural phenomena** (such as genes),
* **and abstract mental steps** (such as reaching diagnoses based on observations).

United States

However, the lower courts have interpreted *Mayo* to still allow inventors to patent certain diagnostics and biomarkers, but only to a limited extent. 2018 has been a very active year for judicial decisions on this topic:

* *Classen* set a precedent that **methods of treatment or prevention of disease tied to diagnostic methods are eligible for patenting.**
* *Exergen* teaches, **a novel way to measure a recognized property or analyte can still be patented,** even if not tied to a diagnostic step
* The USPTO has taken the position that **steps to measuring an analyte can be patented.**

EP vs US



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EUROPÄISCHE PATENTSCHRIFT

(11) EP 1 258 321 B1

(12) EUROPÄISCHE PATENTSCHRIFT

(54) Kraftgetriebener Schrauber mit Drehmomentbegrenzungskupplung

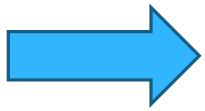
Power driven screwdriver with torque limiting clutch

Tournevis motorisé avec embrayage limitateur de couple

The United States of America

The Director of the United States Patent and Trademark Office

United States Patent



The approach to patenting diagnostics is very different in Europe to that in the United States.

THIRD PARTIES RIGHTS

REMINDER : A PATENT IS…

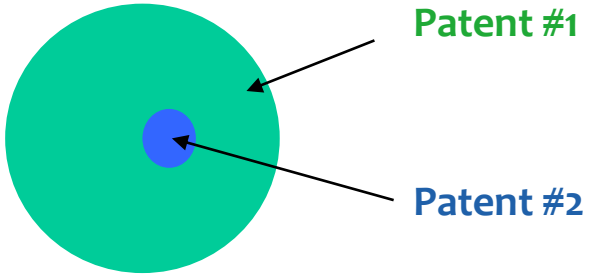
* A Patent is a legal right granted to the patentee by national governments
  * to exclude others from : making, using
    * selling

  the patented invention for the lifetime of the patent

* **But** not an automatic right to use the invention. Broader third party's patent may block narrower selection invention patent

FREEDOM TO OPERATE ("FTO")

* A patent does not give the patent owner the right to practice their invention. It is a right of exclusion. Broader third party patent may block narrower selection invention patent



  * Patent 1 can exclude owner of Patent 2 invention from practice of the Patent 2 invention
  * Patent 2 can exclude owner of Patent 1 invention from practice of the Patent 1 invention within scope of Patent 2

Freedom-to-Operate (Cont.)

Before any licensing-in agreement collaboration agreement or acquisition

* Review partner's own FTO search results
* Perform independent FTO search and analysis
  * For existing indications
  * For desired indications
* Consider reviewing non-infringement opinion

FREEDOM TO OPERATE ("FTO")

- From the beginning and during the life of a product, **it is crucial to identify and evaluate third party's rights.**

- If a third party's patent is **relevant for the FTO, the following options have to be evaluated :**
  - "Acquire" freedom-to-operate by license or assignment
  - Challenge the patent (opposition or nullity action)
  - Find another not infringing solution.

PART II

BIOMARKERS VALIDATION PROCESS

BIOMARKER VALIDATION PROCESS

Key points*

- A biomarker is a characteristic that is objectively measured and evaluated as an indicator of a normal biological process, a pathological process or a biological response to a therapeutic intervention.
- Biomarkers increase the success rate of drug development programs.
- The analytical validation phase of biomarker development is characterized by analysis of the performance metrics of the biomarker to ensure that the test is reliable, reproducible and of adequate sensitivity and specificity.
- Qualification is a graded evidentiary process that links a biomarker with biological and clinical end points.
- Utilization of biomarkers for clinical applications is dependent on their clinical utility for disease diagnosis, disease staging and treatment selection.

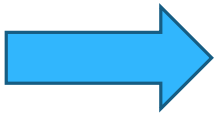
* **DOI:** 10.1038/s41584-018-0005-9

BIOMARKERS VALIDATION PROCESS

In the biomarker validation process every effort should be made **to ensure that a biomarker is relevant for its intended use**, a principle commonly referred to as "fit-for-purpose". The fit-for-purpose method validation is an umbrella terminology for distinct stages of the validation process including:

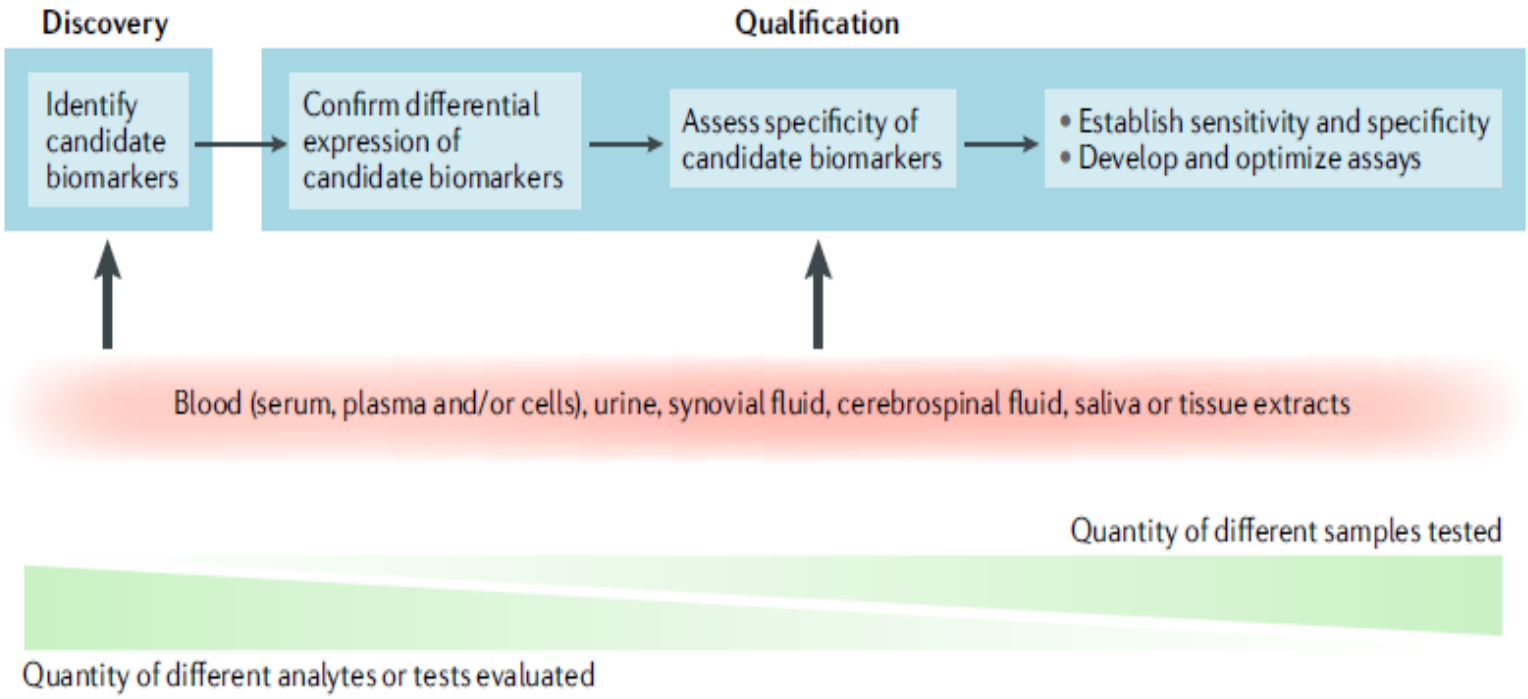
- the first and probably the most critical preanalytical validation stage (definition of purpose),
- exploratory purpose stage (the basic assay performance),
- in-study validation stage (further assessment of fitness-of-purpose and the robustness of the assay in the clinical context),
- and a more complete validation for advanced application stages (the formal performance of the assay, e.g., method robustness, extended specificity, and sensitivity).

BIOMARKERS VALIDATION PROCESS



Consequently, method validation is an ongoing, iterative process, which critical steps lean on the predefined purpose of the biomarker. Typically, the objectivity of method validation should increase from the initial discovery/validation to more advanced validation and should be customized according **to biomarker type**, **the intended use of the biomarker application** (pharmacodynamics, monitoring, prognostic, predictive, surrogate, etc.), **variability, and prevalence**.

BIOMARKERS VALIDATION PROCESS



BIOMARKERS VALIDATION PROCESS

The FDA and European Medicines Agency (EMA) have developed similar processes for the qualification of biomarkers intended for use as companion diagnostics or for development and regulatory approval of a drug or therapeutic.

All these data have to be secured as they constitute one of the major assets of the company.

PART III

MARKET NEEDS COMPETITION FOLLOW UP

Diagnostic field

The diagnostic field includes:

* Large entrenched participants
* Stand alone IVD companies
* Companies affiliated with pharmaceutical or medical device companies
* Large diagnostic laboratories.

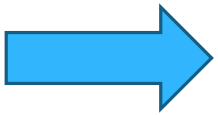
Business models.

Different Business models:

- ❑ Build a business
- ❑ License out
- ❑ Partnering model

Appropriate business model very often depends *inter alia* on patent portfolio.

MARKET NEEDS
COMPETITION FOLLOW UP



Market need and Competition identification and follow up are very important items of the market analysis.

Market analysis is a key part of any business plan.

MARKET NEEDS

* For SMEs, Market Need evaluation is very important as it is where SMEs show their potential investor that they have an intimate knowledge of their market.

  Drivers that competition has not been focussing on have to be identified and highlighted.

* Market research is essential to unify end user opinions, especially KOLs, and to use quantitative and qualitative research to find the best direction for product or service designs.

COMPETITION FOLLOW UP

* Identify competition from the beginning and have a fair view of the situation.
* Analyse competitor's performances and angle to the market in order to find a weakness that your product will be able to use in its own market positioning.
* One way to carry the analysis is to benchmark competitor's product against each of the key drivers of demand for the market (performances, price, quality, add-on services, etc.).

PART IV

AGREEMENTS WITH THIRD PARTIES DURING THE DEVELOPMENT

PROTECT YOUR ASSETS

FOR KNOW HOW / TRADE SECRETS and NOT STILL PATENTED INVENTIONS, DATA, BIOLOGICAL MATERIAL:

⇒**Nondisclosure agreements (NDA).**

FOR KNOW HOW / TRADE SECRETS

⇒**Restricting distribution:** The best thing for companies is to make sure that trade secret information **is only disseminated to those people who have a real need to know the information.**

Discussing with an other party

* **Secrecy agreement (CDA)** is for evaluation is not for a starting development
    * To protect confidentiality
    * To keep ownership of data and in most case, define IP in general
    * Will define general objectives prior to the supply or collaboration agreement
    * Enumerate et secure the received information

* **Material Transfer Agreements (MTAs)** are contractual documents used for the acquisition of various biological and research materials, and occasionally, data.
    * Define clearly the IP, ownership of the results and the right to the patent

Discussing with an other party

* **Supply or Collaboration agreement**
    * Will define clearly the objectives
    * Define clearly the IP, ownership of the results and the right to the patent (to protect competitive advantages, to protect independence)
    * Investigate third party ownership or co-ownership of the related IP

THANK YOU FOR YOUR ATTENTION

ANY QUESTION