Patent : Intellectual Property

- **Patent : A set of exclusive rights granted by a sovereign state to an inventor or their assignee for a fixed period of time (up to 20 years) in exchange for the public disclosure of an invention**

  - The winner takes it all.

- **Patenting of biopharmaceuticals** : Discovery and initial characterization of any substance of potential therapeutic applications or practical utility

- Detail information regarding drug's physicochemical characteristics, a production method, and its biological effects

  → Successful patenting

  -Usually filed after pre-clinical and phase 1 clinical trials

- **Inventor should make available a detailed technical description of the invention/innovation**
- **Encourage innovation by promoting R & D**
- **Physical asset** : Sold or licensed to third parties for cash
- **Not grant a right to utilize/sell the patented product** :

  - Should prove safety and effectiveness in subsequent clinical trials
  - Approval for general medical use by a regulatory authority

What is patentable ?

- **An innovation/invention must satisfy several criteria**

- **The most important four criteria**

  - Novelty

  - Non-obviousness

  - Sufficiency of disclosure

  - Utility

- **Novelty**

  - Invention/innovation should not be what is described as " prior art "
    It should not be something already known or described previously
  - Prior disclosure of the invention/innovation in a scientific journal or at the scientific meeting → makes the invention "prior art"
    → Hinder subsequent patent application

ex) Patenting is usually possible in the USA as long as the patent is filed in under 1 year after the date of publication

- **The " first to invent " principle** in the USA
  Availability of full and detailed laboratory notebooks or other records as to how and when the invention was made
- "**The first to invent**" policy is changed to " **The first to apply**"

- **Non-obviousness**

  - Invention/innovation must not be something that would be immediately obvious to somebody skilled in the art
  - Obviousness : a simple and logical progression of prior art
  - Non-obviousness : an additional ingredients of inspiration

- **Sufficiency of disclosure**

  - Sufficient technical detail must be provided in the patent application such that somebody of ordinary technical skill in the area could reproduce/repeat the innovation

- **Utility :** Practical applicability

  - Invention/innovation must have some applied use

Patent types

- **Product**

  - Specific substance is patented

    ex) New cytokine with applicability in cancer treatment

    Novel microorganism capable of degrading oils

- **Process**

  - Specific novel process, rather than an end product

    ex) New purification process of therapeutic proteins with higher yield

- **Use**

  - Novel application for a specific substance

Any patent type must also satisfy the four major criteria

Patent application

- **2-5 years from the initial filing date**
- **A national right, granted by government of the country in question**
- **Patent Trademark Office (PTO) : USA**
- **European Patent Organization : EuPO**

  - Any patent application approved by the EuPO can be enforced automatically in the constituent countries

- **International applications**

  - Traditional patent system : Direct application to designated country within 12 months after filing a domestic application

- **Patent Cooperation Treaty (PCT) application**

- A patent application filed under the PCT is called an international application, or PCT application within 12 months after a filing a local application.

- A single filing of an international application is made with a Receiving Office (RO) in one language.

- A search process is performed by an International Searching Authority (ISA), accompanied by a written opinion regarding the patentability of the invention.

- Initial review of the patent is undertaken by a single patent office

- **Initial assessment plays a major role in deciding whether to proceed with the patent application in individual PCT countries.**

- **Finally, the relevant national or regional authorities administer matters related to the examination of application (if provided by national law) and issuance of patent.**

- **A PCT application does not itself result in the grant of a patent, since there is no such thing as an "international patent", and the grant of patent is a prerogative of each national or regional authority.**

- **Patent application to designated countries within 30 months after filing a local application.**

- **In other words, a PCT application, which establishes a filing date in all contracting states, must be followed up with the step of entering into national or regional phases in order to proceed towards grant of one or more patents.**

- **The PCT procedure essentially leads to a standard national or regional patent application, which may be granted or rejected according to applicable law, in each jurisdiction in which a patent is desired**

Patenting process

- **Submission of a final draft to a patent office**
- **A formal filing date is issued after the patent application is briefly reviewed, given all the required information is provided**
- **A detailed examination of the patent by patent office experts based on four main criteria**
- **A report is issued accepting or rejecting the patent claims**
  → The opportunity to reply or modify the patent
  → Resubmit the patent for further evaluation

- **Patent application document**

- Title

- Abstract

- Background to patent application:
drawn from published research articles and pre-existing patents

- Outline of problems the innovation will solve

- Detailed technical description of invention

- The specific patent claims

Patenting in Biotechnology

- **Products of nature** : microorganisms, antibiotics, proteins

  - Simple discovery of naturally occurring substances on the earth

  → Un-patentable because of lack of novelty or any inventive steps

  - If a product of nature is purified and enriched to make the product available for the first time in an industrially useful format

  → Patentable

- **Policy in USA**

  - The PTO recognizes purity as a change in form of the natural product

  - Purification, modification for practical use → patentable

  - Purity alone facilitates patenting of a naturally occurring product

    ex) B_{12} : available in the form of crude liver extract

    → No therapeutic use

    → Pure, crystalline B_{12} : clinical use → patented

    ex) Pure cultures of specific microorganism, factor VIII, EPO ; patented

- **Technical advances → Complex patenting issues**

  - 1980s : Non-human multicellular organisms, including animals

    ex) Harvard mouse : first transgenic animal patented in 1988

  - Patenting of genes and DNA sequences

    -Some genes were granted largely on the basis of the use of cloned roducts

    ex) EPO, tPA

- **Application on partial human cDNA sequences of unknown function by NIH in 1992: rejected**

  - Patent protection only for nucleotide sequences that can be used for specific purposes, e.g., diagnostic biomarker or codes for protein product of medical value

  →Balance issues of public interest with encouraging innovation

- Patenting genetic materials or transgenic animal/plant remains a debating issue

- **A major step in patenting in biotechnology** : introduction of European patent directive in 1998

  - Naturally occurring biological materials are potentially patentable,

  but they must be isolated/purified or produced via a technical process, and have general patentability categories

- **Non-patentable substances**
  - Gene/genome sequences of unknown function
  - Human body
  - Cloning of humans
  - Use of human embryos for commercial purposes
  - Modifying germ line identity in humans

New drug development process

Overall process for a new drug development : ~ 10 years, $ 1 billion

1. **Discovery of a drug candidate based on underlying mechanisms of diseases**

2. **Initial characterization in terms of effectiveness for a targeted disease, pharmacokinetics(PK) and pharmacodynamics(PD)**
   - **Confirmation of efficacy :Preparation and application of Intellectual property**

3. **Preclinical trials (in animals) : to prove safety and efficacy and to get approval from a regulatory authority to commence clinical trials in humans (~ 3 years)**

4. **Submission of preclinical data to the regulatory authority**

   Approval for clinical trials in humans by regulatory authority

5. **Clinical trials (phase I, II, III) (more than 5 years)**

6. **Submission of clinical trials data and manufacturing process**
   to the regulatory authority : Manufacturing process should be also approved for the production

7. **Regulatory authority review the data and information**,
   and grant manufacturing and marketing licenses : **cGMP**
   (current good manufacturing practice)

8. **New drug goes to the market**

9. **Post-marketing surveillance** : to investigate any drug-induced side effects and to inspect the manufacturing facility

Patent issue

- **Patent battle regarding the gene-editing technology using CRISPR–Cas9**
- **In May 2012, researchers at UC Berkeley led by Jennifer Doudna and her collaborator, Emmanuelle Charpentier filed a patent application in the US CRISPR–Cas9.**
- **Seven months later, Feng Zhang, a researcher at the Broad Institute, filed a competing application that covered similar uses of the technology.**
- **Zhang's lawyers requested that his application be fast-tracked**

  - USPTO awarded one patent to Zhang in April 2014, followed by a dozen more in the subsequent 12 months.

- **Last April, Doudna's lawyers requested that the USPTO conduct a specialized legal trial, known as a patent interference, to determine the ownership of the US patents that cover the CRISPR–Cas9 system.**
- **This January, the USPTO formally agreed to carry out the proceeding**

- **In February 2017, U.S. Patent Trial and Appeal Board rejected UC's appeal to block patents already issued to the Broad Institute, Massachusetts, for making CRISPR work in human and other eukaryotic cells.**
- **Nonetheless, the patent by UC will be soon issued, and the debate over the patent will continue.**

Key issue : Obvious or non-obvious?

- The patent by Doudna and Charpentier demonstrated in test-tube experiments that CRISPR precisely cut DNA

- The patent by the Broad Institute claims the use of CRISPER/Cas system in human and other eukaryotic cells

- Would it obvious that the CRISPER technology by Doudna and Charpentier works in eukaryotic cells and that a person who had a "ordinary skill in the art" would have had " a reasonable likelihood of success ?

Why the issue is critical ?

- **Financial stakes are high.**
  - **The CRISPR–Cas9 patents are widely viewed to be worth hundreds of millions, if not billions, of dollars.**
  - **Both organizations have invested directly in spin-off companies that were co-founded by their researchers**
  - **The Broad Institute in Editas Medicine, co-founded by Zhang, and UC Berkeley in Caribou Biosciences, co-founded by Doudna.**
  - **More than 900 related patent applications are filed so far .**