Technology transfer: from the innovation to the exploitation:

a summary

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Technology transfer: from the innovation to the exploitation: a summary[1]

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Innovation is the successful exploitation of new ideas [1]: idea creation without innovation doesn't contribute to the development and to the performance improvement of a company. Hence, innovation collects all steps that are necessary to transform an idea into a project, and subsequently in a value.

Innovation process may involve R&D, production and marketing. Traditional **innovation management** was focused on research and development only, while TIM (**total innovation management**) regards different areas and aspects and in particular to the synergy among them [2]. There are many non-technological factors such as organizational structure, cultural characteristics, market, innovation strategy that may also have an important influence on innovation performance.

Traditional practice of IM consists of 2 separated stages: the first includes product innovation, the second the process innovation. At present, the dominant paradigm for total innovation management is to concentrate on product innovation first, then to pay attention to process innovation and finally to reach a steady balance between product and process innovation.

Innovation management has the goal to exploit ideas so it includes the management of all activities related to the project which develops this idea. Project management is defined as the planning, the organization, the management and the control of corporate resources to carry out activities aimed at achieving specific objectives in a defined interval of time. Each project must have a project plan which is a group of documents setting out objectives, activities, responsibilities, budgets, timetables, performances, risks and the closure. There are several tools that enable the description, the definition of all of these elements (gantt, network diagram, Work Breakdown Structure, etc.). The project charter is the project's "license to do business." This person is usually known as the project sponsor and in general he is someone outside the project with funding access and authority sufficient to support the project and to promote next phases asking resources, moneys, etc [3].

In biotechnology field projects leads to a new knowledge which may be represented by methods, scientific know-how, scientific results, technical expertise that may represent an internal value for the company. All steps included in the chain of the value creation may be considered as different technology transfer activities. Technology Transfer (TT) is the process of sharing of skills, knowledge, methods, manufacturing, facilities among governments and other institutions to ensure that technological developments are accessible to a wider range of users

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who can then further develop and exploit the technology into new products, processes, applications, materials or services [4]. To obtain a successful TT it is necessary select carefully science with commercial potential, secure intellectual property, establish frequent dialog with investigators and stakeholders, avoid conflicts of interest and practice good business principles [5]. Relations among universities, big pharma and biotech can be interpreted as TT activity. Problems in university, in biotech and big pharma may interrupt TT so it is necessary to understand exactly which are the interests of the parties and which role they are covering in the TT process in order to maximize returns [6]. CMO (contract manufacturing organization), CRO (contract research organization) agreements and cooperative R&D are TT activities that may help and promote relationships among organizations. The cluster environment may facilitate integration among parties too [7].

The commercial exploitation of a initial discovery needs the intellectual protection trough a patent filing or licensing before publication of scientific papers. The TT is only possible with a **formal protection of invention**. This step creates a value added from a initial discovery and it may represent a new immaterial good for the company, so it must be accurately managed.

IP (intellectual property) management process must: be defensive, control the costs, get profit, integrate, be visionary. It may be divided in 2 components [8]:

1. IP portfolio management which concerns patent life like patent procedure with patent offices, patent costs management;
2. IP portfolio evaluation which is quantitative and qualitative evaluation of the patent portfolio with the aim to define strategic recommendations.

Patents are not only a useful tool of IPR (intellectual property rights) to protect an invention but they are intangible assets which strongly contribute to improve the companies' value [9]. They represent a competitive advantage for companies and they are a source of potential revenues (out-licensing, sales, assertive licensing). IP management brings to company several advantages: protection against competitors, protection against infringement, valorization of company's services and products, protection of R&D investments, preserve market share, capture new markets, create new partnership, to attract potentials investors, get revenue doing licensing and to preserve technological advance [10]. IP management tools are focused to evaluate patents, to organize patent portfolio, to search patents in databases and to analyze patent information and to obtain statistics on different parameters.

Patent information includes content (description, drawings, claims, ecc.) search report, legal information and bibliographic part (inventors, applicants, abstracts and others). There are free and not-free databases enabling the access to these information (for example espacenet [11]). The use of these patent database enables to perform statistics and to establish strategic recommendations (patent intelligence). In addition the analysis of patent information may: avoid duplicating, determine the patentability of an inventions, avoid infringements, estimate the value, improve planning for business decisions (licensing technology, partnerships,, acquisitions), exploit technology, gain intelligence, predict future direction of business competitors.

Patent is a formal protection of a invention which permits to create value added from an invention. It is a right to exclude others from commercially making, using, distributing or selling

the invention without the patent owner's consent. It has an expiry date: it protects something for a limited period of time in a defined territory.

Everything is not patentable. The general patentability criteria are: novelty, originality [12], unity [13], disclosure [14] and claims (independent and dependent) [15]. The protection of IPRs is ruled by several national laws which differ in relation to the countries. Hence, there are different types of a patent (in example National, European, Eurasian patents) and specific procedures for each of them. In Europe, the European patent procedures were performed by EPO (European Patent Office) [16]. A opportunity to exploit international agreements is the procedure offered through the Patent cooperative treaty (PCT) which consists of a single procedure to file a patent application simultaneously in a wide numbers of countries (144 States). One of the main advantage of this approach is the "Option of filing" within 30 months from the priority date in all countries members of the Convention. PCT enables to obtain a positive or negative opinion (International Search Report, IPR) concerning patentability (novelty, originality and industrial application) followed by a publication of international application [17].

Valuation of patents are important during fusion, acquisition of company, negotiation of patents, damages in case of dispute, infringements, IP portfolio management [18]. The valuation of a patent may be qualitative or financial. The qualitative valuation includes specific indicators (contents, bibliographic, procedural, novelty, inventiveness, scope). Chronological availability is a value indicator too. There are specific models that enable the qualitative analysis of a patent (in example: Intellectual Property Quotient, IPQ proposed by OCEAN TOMO, the Patent Factor Index, PFI™ by PANTROS IP; and TAEUS' model – by TAEUS WORKS). As regard financial methods to valuate IP the most important approach are: comparable, cost and income [19]. Each of them has advantages and disadvantages. An other method is risk adjusted net present value (rNPV) approach [20]. In biotechnology rNPV approach seems to be the best one. In this field it is always essential to consider, separately and together, clinical development and risky business [21].

An essential element in TT related to biotechnology is the **relationship between organizations** (in particular between university in which scientific results are developed and industry in which scientific results may be exploited). These relationships may be represented by **licensing**, **partnering** and **strategic alliances**.

A **licensing** agreement is a TT contract which permits to generate revenues. A license is the right to use something but with some limits. There are different types of licensing agreement: out-license (from University to Company, usually IP transfer); cross-license (from Company to Company; usually Joint Venture or strategic partnership); sub-license (from Company to Company, usually product development or marketing). Before to start negotiations about a license it is necessary to evaluate the value of patent(s) and the strategy of the company which is usually determined by several factors: market, competitors/collaborators and geographical components (territorial rights, registration, minority territories, ecc.).

Alliance is a legal relationship between institutions (University vs Industry, Biotech vs University, Biotech vs Industry, Industry vs Industry) which usually has a strategic intent based on defensive, discovery or offensive motivations. There are different types of alliances: bilateral, multi-lateral, "hub & spoke". The main activities/tools of alliance management are contract Research, shared Resources and pooled IP.

Partnering is a relationship between institutions which has the main goal to develop a product (drugs, medical devices, ect). Partnering activities and tools are quite similar to those applied in alliance strategies.

Alliances and partnering are both TT activities and, as licensing, represent for companies long-term strategies useful for the optimization of their main assets. For this reason, it is strongly requested an accurate due diligence (IP audit) which identifies and valuates all immaterial goods with the purpose to perform a internal and external analysis also called SWOT (strength, weakness, opportunity and threats) analysis. This check is generally focused on the identification of the central assets of the company and it is necessary to determine the strategy definition [22].

Industry and University seek both profits but in a different way. In general when industry finds a solution to a problem wants: a well developed solution, an easy implementation, a confined expenditures of capital, a significant disruptions to operations, not or little risk of failure – it needs to work the first time. University often seeks a balance between profit and image but it seldom respects all the abovementioned criteria in the problem solving strategy.

Innovation in life sciences is the exploitations of ideas in all sciences that have to do with 'organisms', like plants, animals and human beings. So it regards value creation in the field of biotechnology, pharmaceuticals, biomedical technologies, life systems technologies, nutraceuticals, cosmeceuticals, food processing, environmental, biomedical devices, and organizations and institutions that devote the majority of their efforts in the various stages of research, development, technology transfer and commercialization.

Biotechnologies may be applied to different fields: red (health care), green (agriculture and veterinary), white (industry, environment) and blue (marine and aquatic application).

Red biotechnology is a field of applied biology that involves the use of living organisms and bioprocesses in engineering, technology, medicine and other fields requiring bioproducts. Red biotechnology leads to finding more solutions with respect to those based on traditional methods as well as therapeutic solutions. An other aim of red biotech is to reduce times required for medicine development, which are extremely long using traditional methods. Two examples of solutions are genetically modified animals (adopted in drug validation phase) and nanotechnology (for drug delivery). In terms of economic impact, the main applications concern production activities focused on developments of more effective and efficient technologies, and the use of the so-called molecular farming, namely the production of substances grown in plants and animals. Innovative solutions are related to biomedicine (macromolecular and small drugs), innovative therapeutic techniques (cell therapies, genetic therapies, anti-sense and interference RNA), vaccines, and diagnostic (proteins and nucleic acids) [23]. Biotech are usually associated with drugs. An other application of biotech are the development of new delivering biologic techniques (drug delivery). Emerging fields of red biotech regards development of small drugs, personalized medicine (pharmacogenetics) and medical devices. Pharma adopt strategies with a higher risk respect to those adopted by industrial biotech, but they may have a greater economically return [24]

The challenge of **drug R&D** is the production of molecules that are safe and efficacious across age, gender, weight and across racial and ethnic groups. The ideal drug must appeal the global markets, pass global regulatory review and overcome the different phases of development. There

is a sort of scale-up procedure. From a high number of targets (5000) a very low percentage of these become an approved drug. Most of these come from genomic studies. There is a bottleneck about lead generation and target validation. The road to a new medicine is long and for this reason the decision to develop a drug may be considered as a risky business [25]. This process consists of three phases plus a preclinical phase which regards target validation in a "in vitro" or "in vivo" model. Phase I regards safety and PK (pharmacokinetics) and PD (pharmacodynamics) and metabolism evaluation. Phase II regards activity and efficacy Phase III regards efficacy but tested on a larger population. After these phases there is the regulatory approval which can take 2 years. After drug commercialization further studies about collateral effects may be carried out forward (phase IV).

Marketing is the process by which companies determine what products or services may be of interest of customers and the strategy to use in sales, communications, and business development. It is integrated process through which companies create value for customer relationships in order to capture value from customer in return [4]. The main aspects of marketing are product, promotion, place, and price. Product is value proposition you are going to offer. "Value proposition" is a clear statement, in line with your market's challenges and desires, communicating the unique contribution your company, product and services provide to your market different than your competitors. For the customer product may have a collection of need satisfying attributes. In general, products need to satisfy a need/solve a problem. The collection of need satisfying attributes is the value proposition. In TT field, product is technologies/molecules available for filing patent/licensing. The marketing process grouped several activities with a common objectives consists of customer satisfaction. The marketing process includes internal and external analysis also called SWOT (strength, weakness, opportunity and threats) analysis [26]. This check is generally performed before the choice of marketing target which consequently will determine the strategy definition. To develop a marketing strategy you must consider technology platform, competitors and to enhance value preposition; strengthen negotiating position, market size (competitive profile, value range) and strengthen negotiating position (target the right companies and the right contact within companies). It also necessary to choose which kind of technology can fit your market: "me too", incremental improvement, disruptive or platform. Other useful information to determine your strategy are: size (Europe vs. U.S. vs. worldwide), competing products (number of products, patent life vs. time to market), gaps (inventor(s) might help, consistence of Value Proposition), growth trends, barriers to entry (regulatory requirements, other factors, i.e. pricing) and potential licensees (strong franchise in area of technology, products already on the market). Datamonitor [27] may represent a toll to gain insight all these aspects.

TT activities may also result into the creation of a start-up. Before to create a **new company** it is essential to write a business plan which is a document that analyzes carefully all the issues involved with the creation and strategy of a company, define framework for operations and set objectives and milestones. It is a sort of road map of the company. Essential elements for successful biotechnology companies are: having a milestone focused, having a deep network with the top scientists in the field (academia and industry); having a solution to significant problem in large and growing market; identifying customers who adopt, and pay for the value that you provide; differentiate your product or service; creating sustainable competitive advantage [28].

There are different ways of financing, it depends on the maturation stage of the company: venture philanthropy (non-profit organizations) and government grant, angels, venture Capital and Strategic Alliances.

Start-ups have to develop a sound **business model** in order to survive and growth, Business models in biotechnology are chosen on the basis of the strategy and must be well defined. The main important business models for life sciences companies are [29, 30]:

1. RIPCO (royalty-income pharma company) which are start-ups that research and develop a new drug to finally license it to a big pharma company in exchange for a royalty on sales
2. FIPCO (fully integrated pharma company) which are start-ups that launch their own drug.
3. TPCO (technology platform company) which are start-ups that rent/sell their technology to pharma companies (technology platform model)
4. NRDO (no research-development only) which are start-ups that buy a "discarded" promising drug from big pharma and use their technology to bring it to market.
5. DRCO (Drug Repositioning Company) which are start-ups or established Biotech companies that identify an opportunity to develop an already approved drug for novel and patentable new indications.

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