DOI: 10.38061/idunas.1038600

IDUNAS	NATURAL & APPLIED SCIENCES JOURNAL	2022 Vol. 5 No. 1 (1-13)

Academic Entrepreneurship and Technical Considerations for the Commercialization of Biomaterial-Based Medical Devices

Review Article

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DOI: 10.38061/idunas.1038600

Received: 19.12.2021; Accepted: 22.06.2022

Abstract

Academic entrepreneurship, which refers to the university-based initiatives to encourage commercialization on campus and in the surrounding community, has evolved considerably in the recent years. Increasing number of stakeholders have been interested in academic entrepreneurship, and institutions have established higher number of strategies to encourage this development. Universities are organizations that play an important role in modern society by teaching, as well as research and development activities to produce scientific knowledge. Many institutions have recently taken important steps to create a "third purpose", by fostering connections within knowledge and users through promoting technology transfer, sometimes at the request of policymakers. Commercialization of knowledge produced in the academia, which includes patenting and licensing of findings, together with academic entrepreneurship, has gained a lot of attention from both academics and policymakers among the multiple pathways available for forging these linkages. Because it represents direct, demonstrable market acceptance for academic research results, commercialization is seen as a rising model for achieving academic influence. Many institutions have built specialized organizations, such as technology transfer offices (TTOs), scientific parks (Technopolis), and incubators, to aid commercialization as well as supporting internal policies and processes. The linkage between the universities and the industry have massively strengthened through academic entrepreneurship. There has been a significant impact on the regional and economic development due to the technological patents and spinoff companies emerged as a result of the research activities in universities. In this comprehensive review, the recent patent applications in the field of biomaterials in Turkey, Europe, and the United States of America were also covered, highlighting the number of patent applications of different biomaterial subgroups.

Keywords: Academic entrepreneurship; Patent; Licensing; Technology Transfer Office; Technopolis; Biomaterials; Commercialization.

1. INTRODUCTION

Starting a business by taking several risks, either to gain profit or to endure the losses is considered as entrepreneurship. The term entrepreneurship includes all processes of marketing, planning, development strategies. Moreover, the definition is constantly evolving in line with the technological developments and sophisticated research and development (R&D) activities. As a result of all of the cumulative activities in the field, entrepreneurship is becoming one of the most popular topics of today. It actually plays a vital role in global and national economic growth. Entrepreneurship will benefit the community just as it will profit the individuals. Entrepreneurship plays a major role in the social and economic development of societies, providing benefits such as creating new jobs and employment opportunities, developing new products and new ideas, as well as creating national income [1, 2].

Every person who starts a business is called an entrepreneur. Entrepreneurs create changes in the society by seeking ways to turn crises into opportunities. The term “academic entrepreneurship” is similar; but there are slight differences. In specific, academic entrepreneurship is the process of commercializing and transforming knowledge into business ideas and organizations. In simple words, this means making use of knowledge, research and development towards starting innovative ventures.

Academic entrepreneurship is the “third mission” of the higher education, and it strives to connect academia, the commercial sector and R&D together. This is also known as “intellectual enterprise”, where the universities collaborate with institutions and communities to create business ideas and ventures. Academic entrepreneurship has diverse principles compared to other entrepreneurship activities as it moves slow, studies the problem in detail, functions in constraints, and focuses on patterns. In universities, academic entrepreneurship has a significant role to play as it involves scientific research. This scientific research helps in generating revenue as their findings have commercial applications. Therefore, universities foster entrepreneurial activity and revenue generation. These are central to the academic entrepreneurship phenomenon [3].

The three fundamental concepts of academic entrepreneurship can be summarized as:

- It is based on knowledge and revolves around technological development.
- It is an income activity that arises from technology development.
- A specific behavior is adopted to alter the pattern of research.

There are many definitions of academic entrepreneurship, as a term, which covers the scientific publication of research results, as well as the profit out of these results. Both these outcomes can happen through a patenting process, which itself is a non-commercial activity [4]. In many countries, university licensing, patenting and starting a young companies (start-ups) began to become very common.

Academic entrepreneur is a scientist or a university professor, a PhD student or a post doctorate fellow who starts and sets up a company to justify and commercialize the results of the research done in the laboratory. The results of the research are used to set up a business and direct link is created between academia and industry. Usually, academic entrepreneurship occurs within an academic institution or by group of individuals who are generally research scholars and who acts independently. Thus, an academic entrepreneur is similar to a business entrepreneur who gives practicality to his or her idea - which is in the form of results of the research and builds a business based on it. Both the R&D work and production and marketing work is done.

There has been a significant increase in the commercialization activities of academic knowledge and other technology transfer movements since the implementation of the "Bayh–Dole Act" in 1980 in the USA. The Act allows colleges to get the Intellectual Property Rights (IPR) of inventions created by their staff on campus. Besides the USA, other countries including Canada, Australia and other European and Asian countries have seen an increase in university licensing, patenting, and start-up development since then [5]. These commercialization endeavors have been referred to as "academic entrepreneurship" that differs from other types of entrepreneurships in several ways. For example, since in these entrepreneurial

ventures the academics devote their time and energy to the university, the university at least partially owns the intellectual property rights.

Academic entrepreneurship has evolved considerably since its first inception, specifically boosted by the launch of University Technology Transfer Offices (TTOs). There was a considerable emphasis on two essential characteristics of university technology transfer when these activities were originally started on campuses: patenting and licensing. The startup aspect received little attention because it would take focus away from the 'block-bluster' patent-licensing arrangements. Furthermore, because there were few entrepreneurship courses and programs on campus, people working in the research venture were unfamiliar with entrepreneurship and even remained not so connected to the entrepreneurial community. Additionally, academic entrepreneurship has just been introduced into the economic development missions of many universities [6].

This review article summarizes the basic concepts of academic entrepreneurship by specifically emphasizing its effects on the academia and on the industry, as well as the commercialization aspects of biomaterial-based products; mainly stemmed from the start-ups that fueled their development. Moreover, recent patents and commercialization activities within the academic entrepreneurship-based biomaterial development are also covered.

2. ACADEMIC ENTREPRENEURSHIP

Bayh-Dole Act

Bayh-Dole Act is a law, also known as Patent and Trademark Act Amendments. The act is a great help to promote the development of many start-ups and research organizations. This helps the universities, non-profit research institutes and small business enterprises to secure a patent. Through the act, these institutions can commercialize the inventions which was conducted within their organization. The act was a landmark development as it helped for the development of around 10k startup companies and around 200 drugs/vaccines and other medical products; with economical contribution in the level of $1.3 trillion to the U.S. economy since its implementation [7, 8]. The act provides rights for the university to retain its intellectual property (IP), which promotes the academic entrepreneurship. The act is, therefore, a gateway to promote academic entrepreneurship and has been a great success.

Progress of Academic Entrepreneurship

There are many ways by which academic entrepreneurship is being promoted by the universities. A popular way is to mandate entrepreneurship and connect the R&D of the faculty with creation of new patents. Research needs to be oriented towards IP rights. Another way is by offering grants for projects that address some technological or contextual problems that the local communities face, and thus create innovations that improve the lives of local communities. So, the process of academic entrepreneurship begins before a research project begins. Known as the incubation period of academic entrepreneurship, this period brings together like minded experts from different disciplines who share their ideas of opportunities and new collaborations that are feasible. Often in these cases, the university serves as the investor or as research makes significant progress, universities call on outside investors to participate in project presentations and updates. At this stage, when the product or idea is reaching completion, marketing becomes a very important aspect of the project.

Effect on Industry

Academia and industry are interconnected structures due to information exchange. This interconnectivity has further increased in recent years due to the increase in the frequency of academic

entrepreneurship. Academic initiatives affect the industry in terms of finding more funding opportunities when in collaboration with the academic research, since the reliability to the research and potential outcomes increase. In addition, academics generally have less difficulties in allowance. Universities have increasingly begun to increase competition in trade. With the growing ambition among universities, the number of members engaged in academic entrepreneurship in universities has increased.

The main effects of academic entrepreneurship on the industry can be summarized as follows:

- Academic entrepreneurship has provided assistance to the industry as various unsolved industrial problems have found solutions through the research carried out in the academia.
- Academic entrepreneurship has increased the importance and scope of the R&D departments in the industrial organizations.
- Academic entrepreneurship has increased the scope of innovation and creativity in the industry.
- Through innovative ideas and application of more sophisticated production techniques, upgraded systems can be applied in the industry that reduces waste and increases the efficiency of production.
- With a higher level of academic information, one can develop the industrial processes through innovative products, protocols and work environments.

Effect on Academia

Along with academic entrepreneurship, the ongoing debate about expanding the mission of universities beyond education and research for economic and social development has further revealed the need for a view of corporate entrepreneurship in the university environment. Universities have taken on a different mission through the "change" initiated. With this mission, expectations from academics have also changed. In today's academy, it is expected not only to produce intellectual knowledge, but also to create added value in the economy by using this knowledge. Many academics actively involved within disciplines of science, engineering, life sciences and medicine and has entrepreneurship activities are likely to apply their knowledge to their startup's benefit, and these concepts are frequently classified as high-tech fields [9].

With the spread of academic entrepreneurship, some universities began to be called as "entrepreneurial universities". The main goal of entrepreneurial universities is to instill entrepreneurial spirit in students and researchers. This creates many tasks for universities, such as including entrepreneurship courses in their curriculum. In addition, an entrepreneurial university should have a wide interface, such as technology office license, and a technology transfer office. As this requirement affects universities economically, it is inevitable that positive returns will be received in education after these requirements are done.

The main effects on academia on entrepreneurship are as follows:

- Academic entrepreneurship has increased the scope for academia in terms of quality research as more people are willing to carry out research so that can be land up being an entrepreneur.
- Academic entrepreneurship has increased the scope for academic researchers' profession as now they have the option to enter into corporates rather being into academics.
- Through academic entrepreneurship, institutions create a connection between education and commerce for the development of society.
- To widen the information towards academic goals.
- To establish expertise knowledge through different platforms, so as to learn and grow.

Effect and Impact of Academic Entrepreneurship

The main importance of academic entrepreneurship is:

- It creates a significant shift in the circulation of academic information.

- It provides a platform for academic experts to share their knowledge and work with the mass population.
- It creates opportunities for academic institutions in finding ways to tackle uncertainties.
- It helps to design innovative ventures right from the source of research and knowledge.

The advantages and potential disadvantages of academic entrepreneurship are discussed below:

Advantages

Academic entrepreneurship is a good measure to test the practical applicability of an idea or concept and it lets the academic know if their concepts can withstand in the real world; a good theory needs to have the ability of being adaptive. So, practical application lets academics know if their concept and are feasible or if changes are needed.

Another advantage is that if the entrepreneur chooses to use their academic skills for market situations and develop a revenue model, then they are decently compensated for the same and can capitalize on their ideas. This economically contributes to their careers helping them to raise funds for future studies or any other need in terms of their academic projects and even otherwise in nonacademic field.

Academic entrepreneurship is also extremely important as it helps in educating the students about various entrepreneurial activities. Apart from it, it also emphasizes training the students and create awareness regarding the entrepreneurial activities. The main essence of academic entrepreneurship is the rise in the number of academic startups and hence better scope for the commercialization of the innovative idea. When there is a rise in entrepreneurial activity then it will result in contributing to the economy in a positive way.

Disadvantages

It needs to be highlighted that if academics devote their attention to suiting the market needs and in capitalizing an idea, they might come in conflict with certain ethical standards within their fields of study. Sometimes some amount of confidentiality needs to be maintained in academic study which is generally neglected in market models. Also, market needs might modify an academic concept or idea to make it more "sellable" while compromising on the ethical value.

The second negative impact could be that in case of entrepreneurship the market and the sales targets, revenue etc., the prime benchmarks of the potentiality of an idea or concept can become the sales rather than its scientific impact. This means that valued peer reviews which are held in much high esteem in academic field are neglected so the intellectual value of an idea translates into merely with the same value of the idea.

3. TECHNICAL CONSIDERATIONS IN THE COMMERCIALIZATION OF BIOMATERIAL-BASED MEDICAL DEVICES

Biomaterials are basically defined as the materials that interact with the human body or body fluids for a therapeutic or diagnostic purpose. Living cells or synthetic materials such as polymers, metals or ceramics etc. can be used to create these materials as long as they are convenient in terms of biocompatibility. From the production of biomaterials to their sale, there are various regulatory requirements that must be followed, with the primary role of preserving human health by assuring product safety, efficacy and quality. First step for technical consideration is understanding the characteristics of the biomaterial and it is critical because each material has its own set of strengths and weaknesses, thus, has its own set of regulations, standards, and testing techniques. Second, intended use because in some cases, the same device is regulated differently depending on the indication. Third, knowing which regulations apply in the region where the product will be sold, as regulations change by country. These understandings are

crucial to a medical product's long-term success because if not properly addressed, regulatory rules can become challenges to commercialization but, on the other side, they can also be a great source of knowledge to help with the development process.

As previously stated, in the process of biomaterial commercializing there are many different technical requirements to be met and regulations which differs from country to country and material to material. Today, collaborative organizations such as the FDA (for the United States) and the EMA (for the European Union), or equals due to their aims, methodically create these guidelines. Before a product created may be put on the market, these institutions must approve it.

For the analysis of the regulatory requirements, biomaterials can be divided into two sub-headings. These are synthetic and biologically-derived biomaterials [10-13].

Regulations Related to Synthetic Biomaterials

Synthetic biomaterials are classed as ceramics, metals, synthetic polymers and their composites and are made utilizing a range of processing processes. There are two main regulatory pathways for commercializing these biomaterials: risk analysis and safety process, and efficacy process.

Risk Analysis and Safety: Since the goal of biomaterials is to diagnose, treat or cure a wide range of pathologies, the materials used in the product should not expose the patient to risk even though there is no such thing as zero risk. When a manufacturer chooses from the often-limited number of materials suitable for healthcare applications, the risk-to-benefit ratio must be taken into account in all cases. The initial step is to specify the risk classification and analysis, followed by biocompatibility tests, manufacturing process which is production, sterilization, packaging and quality to ensure safety.

Global Risk Classification and Analysis: Depending on the application, the risk classification terminology and different regulatory controls are required for biomaterials. These include the degree of surgical invasion or physical contact, the length of the service, the activity, and the energy sources or technologies employed. The risk classification differs from country to country.

Class II to IV and active implantable devices are the focus of nonclinical testing, which refers to in vitro or in vivo experiments in which test objects are evaluated prospectively in test systems under laboratory circumstances to determine their safety. Low-risk and noninvasive Class I or A medical devices, on the other hand, are rarely subjected to nonclinical testing. The classification of a device is usually the first step in determining the regulatory pathway and study requirements.

A rigorous procedure used throughout product development to establish what is required to show safety is known as risk analysis. One of the most often used methods is Failure Modes and Effects Analysis (FMEA). It is a strategy for systematically examining a process to determine where and how it could fail, as well as the relative impact of various failures, in order to determine which areas of the process require the most changes. The technical considerations that must be addressed in the context of safety can be identified using the FMEA framework. Most regulatory bodies believe that safety should be built into the development phase rather than the manufacturing process since it helps to minimize problems caused by changes that must be made prior to production. As previously said, FMEA is extremely beneficial at this stage because it not only ensures patient safety but also helps to avoid business implications [11, 13].

Regulatory Issues Related to Biologically-Derived Biomaterials

Natural biomaterials are commonly used to replace or restore the structure and function of injured tissues/organs because of their advantages such as biocompatibility, biodegradability, and remodeling. They can support cell adhesion, migration, proliferation, and differentiation effectively. Naturally generated biomaterials, when transplanted into a damaged area, can stimulate the adhesion and migration of cells from the surrounding environment, resulting in extracellular matrix synthesis and tissue repair. Some commercial

products were made from naturally derived biomaterials including small intestinal submucosa (SIS), Matrigel®, Alloderm®, etc.

Protein-based biomaterials (such as collagen, gelatin, and silk), polysaccharide-based biomaterials (such as cellulose, chitin/chitosan), and decellularized tissue-derived biomaterials are all examples of naturally generated biomaterials (decellularized heart valves, blood vessels, liver, etc). Biomaterials made of proteins and polysaccharides can be made in two methods. Solvents or enzymes dissolve protein and polysaccharide from living organisms. The fibrils are then precipitated and reconstituted. The removal of additional constituents of live creatures using solvents or enzymes is the second method for preparing protein and polysaccharide. All cells from native tissues/organs are removed to make decellularized biomaterials. To create a successful decellularization strategy, physical, chemical, and enzymatic techniques are utilized [14].

Biocompatibility Tests

By definition, biocompatibility is a measurement of a device's compatibility with a biological system. The goal of biocompatibility testing is to evaluate if a technology is fit for human usage and if it can cause any possibly hazardous physiological consequences. All biocompatibility testing for biomaterials takes place before any clinical testing. The International Organization for Standardization (ISO) sets the main regulatory standards for nonclinical biocompatibility and medical device testing (ISO). Some countries, on the other hand, utilize parallel national and regional standards such as FMEA.

Confirmation of the device's suitability for its intended purpose is at the basis of the ISO Standard. When learning about biocompatibility standards, the ISO Standard 10993, Biological Evaluation of Medical Devices, is a good place to start, and using it as a guide will make selecting the right test much easier. These tests can include everything from skin irritation and sensitization assays to hemocompatibility and implantation tests thus it is essential to choose the right ones [10, 11, 13].

Manufacturing

Manufacturing is a long, complex process that involves careful coordination and control at every stage which is production, packing, sterilization and quality control and assurance. This control process is carried out in accordance with a procedure known as Good Manufacturing Practice (GMP) as a sub-branch of Quality System Regulations (QSRs).

GMP is a concept that ensures that products are produced and subsequently controlled according to quality standards. The goal is to lower the risks associated with the manufacturing process. It includes all aspects of production starting from raw materials to related facilities and equipment, and to training and behavior of personnel.

One of the technical concerns for manufacturing processes is sterilization. The purpose of sterilization is to render non-sterile medical devices sterile by inactivating microbial contamination. Sterilization can be accomplished through a variety of product and packaging sterilization methods. The sterilization techniques as either traditional (such as ethylene oxide or radiation) or non-traditional (such as hydrogen peroxide). The method and dose are determined by the product's structure and properties. The ability of biomaterials to be sterilized is critical for commercialization because non-traditional methods require more work to demonstrate their effectiveness and encounter regulatory oversight.

Another critical technical step in the biomaterial manufacturing is packaging. The package protects the device from external influences such as microorganisms during handling and shipping until the product is ready to use. General safety and performance requirements (GSPR), specifies the packaging requirements of medical devices. Because of packaging includes product identification, labeling, and user interaction, it must be properly prepared.

Finally, to ensure that devices manufactured and marketed are safe and effective for the intended user, manufacturers use a quality system known as a Quality Management System (QMS) that is compatible with regulatory criteria. A quality management system includes both quality assurance and quality control. Quality assurance ensures that a medical device's manufacturing process is free of faults. It occurs throughout the medical device manufacturing process, and their personnel ensures that it complies with the related regulations. On the other side, quality control finds defects in products after they have been manufactured but before they are distributed. Quality control checks individual products or batches of products to determine whether it satisfies specified product specifications. The goal is to identify defective products before they reach the end consumer [11].

Efficacy

The biomaterial's ability to achieve what it claims must be demonstrated. The FDA uses a number of tests such as animal testing to assess how effective and long-lasting products are and to establish the appropriate regulations. Test methods are promulgated by ISO or varieties and they must prove the efficacy of the product [11].

4. ROLE AND IMPORTANCE OF PATENTS FOR COMMERCIALIZATION OF BIOMATERIALS-BASED PRODUCTS

What is a Patent and How to Apply for It?

A patent is a document that states that the inventor has the right to prevent others from producing, using, selling, or importing the product which is subject to the invention, for a certain period of time.
Firstly, there are different kinds of industrial and intellectual property protections such as patent, trademark and copyright. It is important to know the differences between these protection types, since the inventor has to clearly determine the type of the property protection. In other words, the question: “Do I really need a patent?”, has to be asked by the inventor(s).

As a next step, a patent search is needed before applying for a patent, because a patent application cannot be filed if it has already been publicly disclosed. The search for foreign patents is also advisable. Depending on the invention, the type and route of the application will also be different. For instance, the European patent office (EPO) accepts applications done to the European Patent Convention (EPC) or the Patent Cooperation Treaty (PCT) [15]. However, there is no need to apply to the European patent office, if the inventors are seeking protection in only a few countries. In that case, an application for a national patent directly to each of the national offices (eg. Turkish or US Patent and Trademark Office - USPTO) will be proper. Patent applications are mainly composed of a request for grant, a description of the invention, claims, drawings (if any), and lastly an abstract. It is advisable to fill the applications in the official languages determined by the patent offices, otherwise an extra translation has to be submitted. Once the application is being filed, nothing new can be added to the application. With all necessary information and documentation and completed filing (eg. an indication that a specific patent is sought, details identifying the applicant, description of the invention etc.), the application may be accorded a filing date.
Within the process of examination, further determination whether the application meets the requirements of the patent office and whether it can be granted, is being investigated and a response (search report) about the claimed invention is sent to the applicant(s). The report may also include the appropriate fees (changing with the national laws) that must be paid previously within a time limit. During this process, a designated attorney who communicates with the office may represent the inventors. After the patent is being granted, maintenance fees have to be paid in order to maintain the patent, otherwise the patent will expire [16].

Another important subject for patent search is to know the classification system of the intended patent office. For example, Turkish Patent and Trademark Office uses International Patent Classification (IPC), which provides a hierarchical system using symbols instead of different languages. Cooperative Patent Classification (CPC) originates with the cooperation of USPTO and EPO to form a system that harmonizes the existing classification systems.
After the general search is completed and the classification system is understood, a detailed patent search using the patent office archives needs to be done. In the following Section, recent patent applications in "biomaterials" field were covered via Turkish Patent and Trademark Office (Türk Patent Enstitüsü; TPE), EPO, and USPTO.

Recent Patent Applications in Biomaterials Field

The results of the search for patent applications in biomaterials field between 2019 – 2021 are being graphically represented in this Section [17, 18]. During the investigation, the patents were grouped according to the type of biomaterial described in the patent. Three different graphical representations were created in order to examine the similarities and/or differences among the patent offices which were taken under consideration (TPE, EPO and USPTO). In general, when the overall patent application numbers are compared, it is seen that the numbers are very similar for applications to USPTO (409) and EPO (406) during these years. In other words, there is an equal request to both patent offices. On the other hand, the number of applications in TPE is very low (11), compared to both EPO and USPTO.
It can be observed in **Figure 1** that applications to USPTO is majorly filed in the field of "implantable biomaterials". The category following it is the "polymeric biomaterials", and "composite materials" is the next one. On the other hand, it was observed that a significantly lower number of patent applications were filed in the fields of biodegradable, biomimetic, or injectable biomaterials to USPTO between 2019-2021.

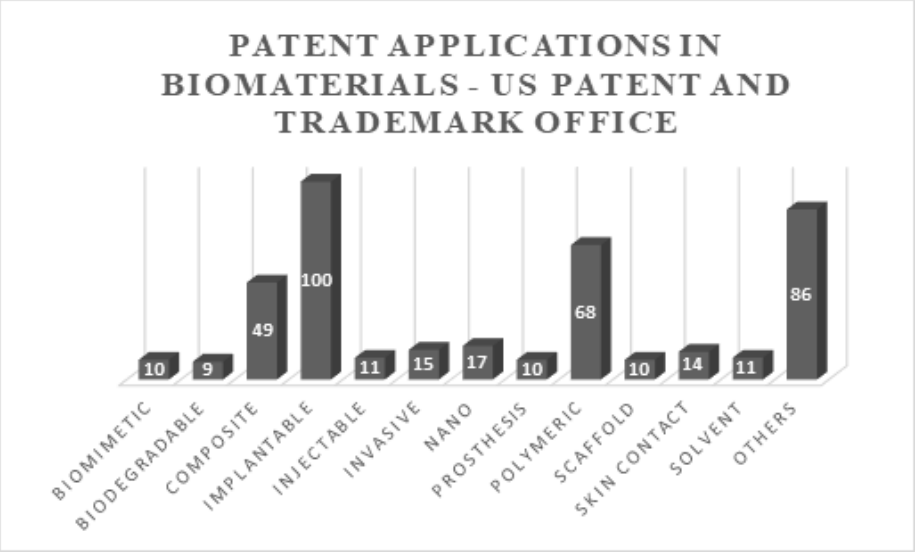

Figure 1. Graphical representation of the patent applications filed to USPTO between 2019-2021.

The trend in the applications to EPO was similar during this time period (**Figure 2**); composite, polymeric and implantable biomaterials are also the leading sub-groups [19]. Furthermore, applications for especially "coating materials" are seen in the EPO database, which was not grouped for USPTO. In other words, the range of biomaterial types are expanded in EPO. However, the main in-demand groups or types of biomaterials in USPTO as well as in EPO are equal.

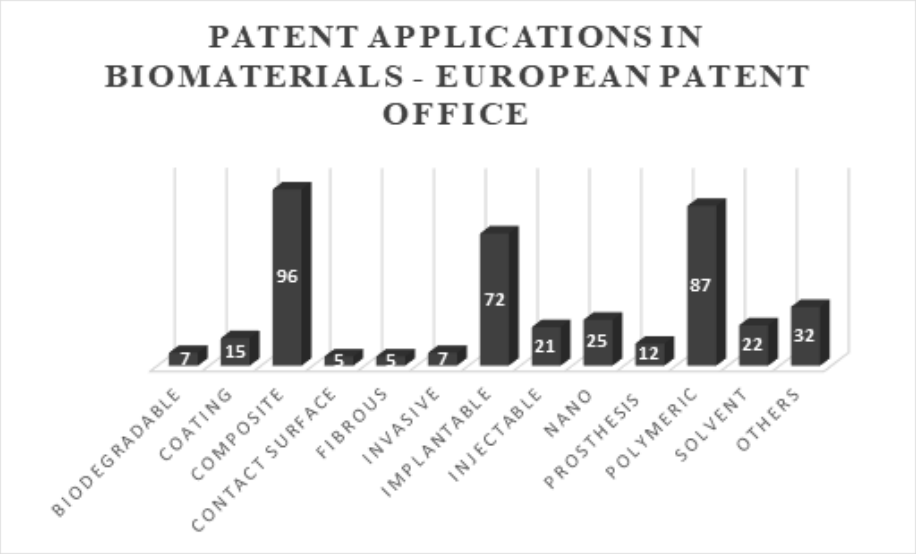

Figure 2. Graphical representation of the patent applications appealed to the EPO between 2019-2021.

The number of applications in Turkey are very low compared to the other two offices as previously described. The leading group for applications to TPE between 2019-2021 is "nanomaterials" that are followed by "metallic materials" (**Figure 3**). An important notice is that, there was no reported group in particular for metallic materials neither in USPTO nor in EPO.

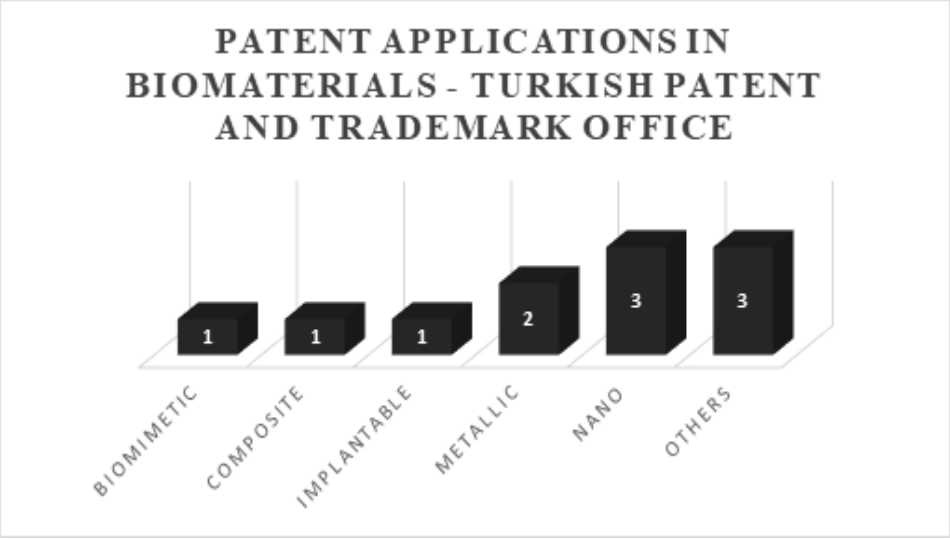

Figure 3. Graphical representation of the patent applications appealed to the Turkish Patent and Trademark Office between 2019-2021.

Figure 4 and **Figure 5** are representing the applicants (countries) that filed an application to USPTO and EPO, respectively. In both the USPTO and the EPO, the United States is the country that made the most applications and; therefore, the most inventions in biomaterials. Following the US, Japan and Korea are the second and third countries that has the highest number of applications. Additionally, the USPTO, as well as EPO, received one application from Turkey in the area of biomimetic biomaterials between 2019-2021.

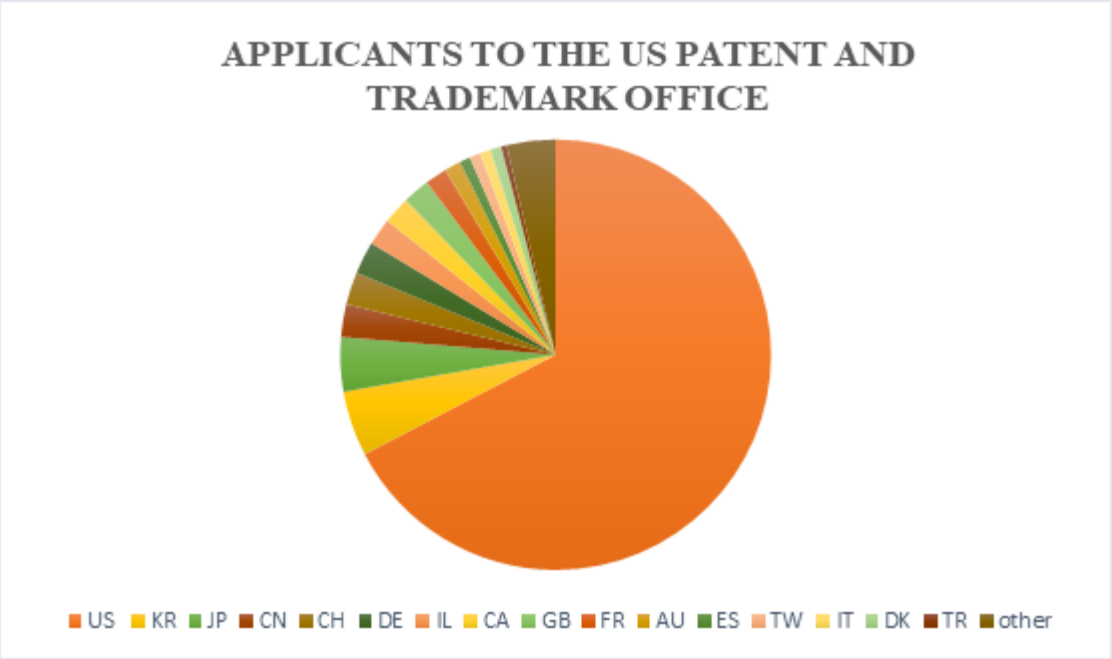

Figure 4. Graphical representation of the applicants (countries) to the USPTO between 2019-2021.

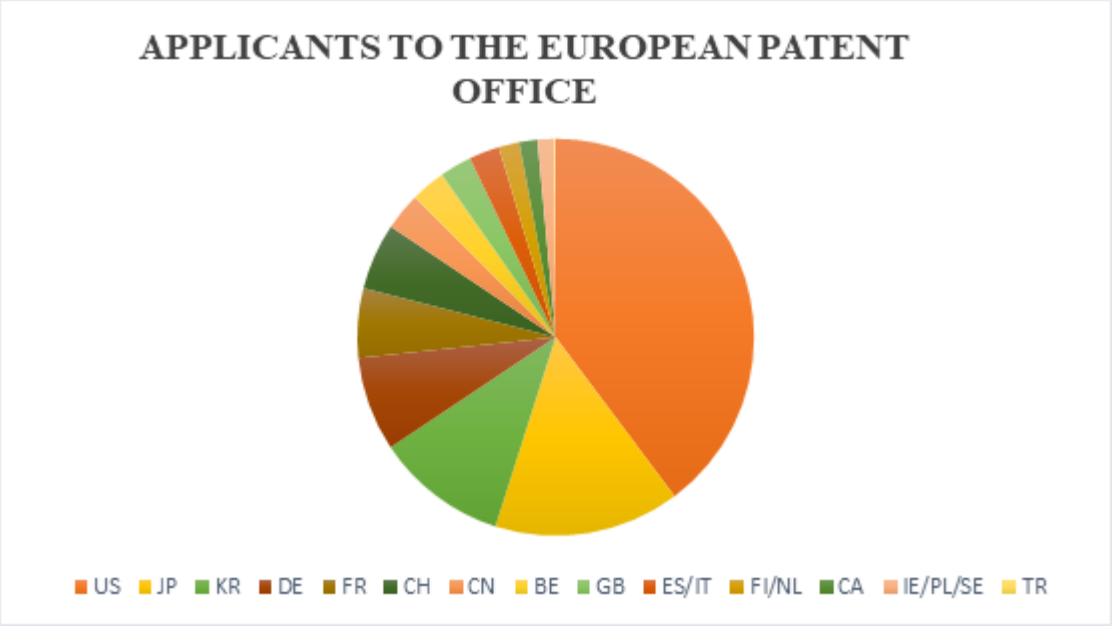

Figure 5. Graphical representation of the applicants (countries) to the EPO between 2019-2021.

5. CONCLUSION AND FUTURE PROSPECTS

Academic entrepreneurship, depending on the development of knowledge-based economies and the changing role of universities, is the sum of commercial activities of academics in their field of new essential technologies, new products or processes, and services that also contribute to development. In this review, academic entrepreneurship was discussed in a general framework and evaluated both for its processes and pros/cons. One of the biggest influences of academic entrepreneurship on the industry is the number of companies and the variety of products.

The interaction of human beings with biomaterials starts from prehistoric times. Biomaterials, which are used in almost all medical fields today, will appear in different forms in different fields in the future.

For this reason, biomaterials must be produced, sold and used in surgeries with care and within the framework of certain rules. Considering its importance for humanity, biomaterials should be subjected to various tests and inspections. Commercialization of biomaterials is a lengthy and difficult process involving multiple stakeholders and numerous issues beyond the technical characterization of the biomaterial, and in this process, the assistance of experts in this field should be sought, and the production and sale of the biomaterial should be carried out in accordance with the guidelines.

Patents are among the first cornerstones in the road to academic entrepreneurship. In this review, we have done a comprehensive patent search in biomaterials field between 2019-2021; for the patents filed to USPTO, EPO and TPE. Our findings were used to prepare number-based charts for USPTO, EPO, and TPE, as well as country-based charts. Based on these charts the following conclusions can be drawn:

- There is an intense recent interest in specific biomaterial types including implantable, polymeric and composite biomaterials.
- There are neglected areas in the field of biomaterials that might need improvement in the future, such as nano-, injectable-, biodegradable-biomaterials.
- The countries that file the most applications are US, Japan and Korea which implied the recent sources of inventions in the field of biomaterials.

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