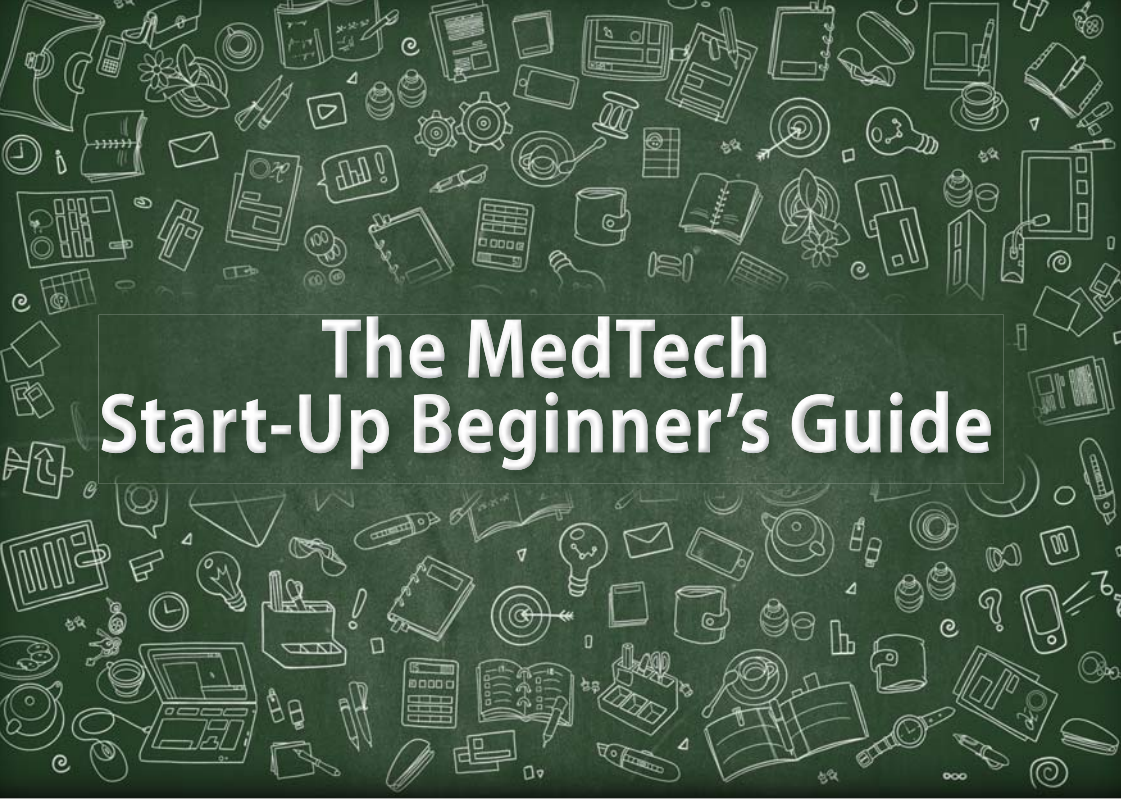

The MedTech Start-Up Beginner's Guide

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Bringing Business to Life

ICI meeting

Eureka - I've found it!!! I have an idea!! ... What next?

Congratulations! You've thought of an amazing idea for a new medical device that addresses a real need, will save lives, improve quality of life, ease the suffering of patients and save the collapsing health care system.

But what should you do now? Where do you start?

Let us start from the beginning…

Background: Medical Devices Development

The medical device development world is a fascinating one, poised on the cutting edge of technological innovation. If you are looking into this, it means that you want to deal with the real added value of things, with life itself, and your drive doesn't come from financial interests only.

The basic assumption: Medical device development is (very) expensive. And (very) long.

The duration and cost of developing and bringing a medical innovation to market are, on average, at least 2 or 3 times more than developing any other high-tech product.

The main difference lies in the fact that the product is intended to have an effect on, or come into contact with, the human body - an interaction that can affect a person's health, wellbeing and sometimes even life itself.

Hence, a medical device development process is closely regulated and controlled by global health and regulatory authorities to ensure its safety and efficacy. This process includes, amongst other things, laboratory tests, animal

safety trials and clinical trials on patients - all of which are lengthy and very expensive processes.

Therefore, before you quit your job and become a BioMed entrepreneur, make sure you've checked:

- ☐ **Have you already done your own initial due-diligence?**

Answer the following questions:

- ☐ **Is there a real clinical need for the product?** Consult with physicians in the field.
- ☐ **Is your suggested solution technologically feasible?** If you are not an engineer, discreetly consult with one.
- ☐ **Is your idea really a new one?** Check in Google... Maybe someone has already thought of it (even if it hasn't been patented)...
- ☐ **Can the invention be protected by a significant patent?** Even if your idea is patentable, there is no point in registering a patent if you will not be able to enforce its breaching, or if a competitor can solve the problem in another way which doesn't breach your patent.
- ☐ **Will the product serve the interests of the various parties involved in the medical environment (patients, physicians, nurses, hospitals, insurance companies)?** Might it potentially disturb or harm any of these parties?

If you've answered positively to all the above questions, you're ready for the big challenge!

Roll up your sleeves, let's get started!!!

Technological POC: Conducting Initial Proof-of-Concept

Demonstrating the technological feasibility of the product is an important step in reducing risk in development, raising money and increasing the company's value. This feasibility demonstration can be done as a

theoretical proof of concept (e.g. computerized simulations, literature survey, interviewing experts in the technological field, etc.), or, preferably - by a practical demonstration of a basic question concerning the ability to develop the product.

People: Building Company's Team and Advisory Board

One of the most influential elements of investors' decision whether to move forward is the quality of staff and their relevant experience. Select the partners and employees carefully, and also build a team of external experts and opinion leaders to make up the company's Advisory Board.

Product: Defining a Product - Application Selection

Often technology is presented as a platform that can adapt to many clinical applications (e.g. stent technology is suitable for cardiac, neurological, urological applications etc.). While on the one hand, presenting the technology as a platform is great for displaying the company's vision to investors, on the other hand, the investors also want to see that in the short term the company is focused on one application – the one that will penetrate the market in the shortest possible time and using the most limited resources.

Therefore, the application selection stage is an important step that should be given sufficient time and weight. Consult doctors and regulatory and other experts from various disciplines, prioritize the applications, and finally determine the initial application and focus only on that development.

However, the additional applications that were found in this process are worth displaying as second generation and future products in the midterm and long term plans of the company. It is also worth safeguarding by patents the full range of applications found.

IP: Intellectual Property

This is probably the most critical step. The company's main asset is usually its intellectual property, the aim of which is to protect the inventions and knowhow and enable the enforcement of a profitable business model as a result of the exclusivity that results from the patent(s).

It is important to consult a competent patent expert, whose job is to draft solid patents and to formulate a comprehensive patent strategy, in order to prevent potential competitors from developing competing products in the key countries without violating your patent.

Handling of intellectual property is a multi-stages process, which requires planning, executing and maintenance throughout the entire life of the project and patent. Main stages include:

Stage	Activity	Explanation
Pre-company	Extensive Online Search	Search engine check: Is it possible to find a patent, an article, a story, video etc. that sounds similar to your idea?
Seed	Professional Patent Survey	Make sure that your idea is not violating someone else's patent (Freedom To Operate). **This stage requires an initial investment of a few hundreds to thousands of dollars.**
Pre-patent filing	Confidentiality Agreement (CDA / NDA)	In order to enable discussing matters freely with third parties (experts, potential investors etc.) before filing the patent application, it is advisable to conclude a confidentiality agreement (CDA) with them.
Concept construction	Provisional Application	An initial submission (in the USA) in lesser detail, which protects the basic idea and safeguards the **Priority Date** of your invention so that no competitor will be able to get a patent filed after that date, on the same idea. A provisional patent application is a fast and relatively cheap process (a few hundreds to thousands dollars). It constitutes a basis for the full patent application. **It remains discreet (it is not published) and expires after 12 months.**
Within 12 months of the Priority Date	Full Patent Application - preferably an international patent application (PCT)	Filing a patent in full detail including the legal part, which determines the patent claims. PCT (Patent Cooperation Treaty) is a process conforming to an International Treaty, according to which applying for a patent through the PCT route in only one country enables applicants to simultaneously seek protection for an invention in 148 countries throughout the world. **The PCT application is widely published 18 months after the initial date.**
Within 30 months of the Priority Date	National Phase	Within 30 months from the filing of the provisional application, the patent applicant must decide in which countries he or she wants the patent to be examined and approved providing protection, and to file patent applications in each country individually. After that date the right for protection of the invention expires in other countries. This decision has wide financial, legal and commercial implications. **This step is very expensive and requires an average investment of tens of thousands of dollars, depending on the number of countries where the patent application is filed.**

The patent examination process is conducted in each country individually, and usually includes corresponding exchanges between the patent examiner of that country and the patent applicant, until the long-awaited approval is acquired separately in each individual country. After receiving the certificate, an annual fee needs to be paid in each country in order to keep the patent valid.

- *The average duration for patent approval is 3-4 years from the submission of the provisional / first application.*
- *The average cost for registering and maintaining a single patent in 3-5 major market countries can reach $100k or higher over the life of the patent (20 years).*
- *Approximately half of this expense will be spent during the first 3 years, and the rest over the life of the patent.*

Regulation: Receiving Marketing Clearance

Receiving marketing clearance (FDA clearance/approval in the US, CE Mark in Europe, AMAR in Israel) from the various regulatory authorities is mandatory for obtaining a permit to sell the product in the market. The regulations and requirements applicable to your medical device have a great impact on the time and cost required for obtaining a certificate, as they may include laboratory tests, animal studies and clinical studies on humans. These requirements are affected, among other factors, by the product classification (e.g. in the US: Class I - Class III) and the relevant regulatory route (510k, PMA, etc.) for the device. The classification is risk-based: The riskier the product is perceived, the higher the requirements will be.

Some of the various parameters that need to be taken into consideration include: the intended use of the product; the clinical indication; the risk that the product might pose to the patient or user; the length of time the product is intended to be used; the product's level of invasiveness; the product uniqueness compared with other products on the market, and more.

It is recommend to consult a regulatory expert right from the initial steps to get a clear understanding of your product's classification and regulatory route. The consultant will also assist you in reviewing the product's regulatory requirements (standards, pre-clinical & clinical tests, etc.) and formulating a regulatory plan. The consultant may later assist you in guiding the actual implementation of the plan, working with the regulatory authorities and preparing the submission binder to the regulatory authorities.

Reimbursement: Insurance Coverage

The matter of insurance coverage for the product in the target countries is an important question, which may significantly impact market penetration of the product and the extent of its use (the project's sales potential). For instance, a product may not reach sales even though it may have received FDA/CE certifications, only because of the lack of insurance coverage.

It is important to ascertain whether the use of the product will be covered by the health insurers (national health services, private insurance companies, etc.), or whether the treatment will be paid for by the patient. Treatment covered by the primary insurers (e.g. Medicare coverage for senior citizens over the age of 65 in the US) is likely to be more widely used than other treatments. It is important to understand whether there is coverage in place for the treatment your product is made for - will it be reimbursed, or alternatively whether you need to try to convince the insurance agencies to include the product in their insurance coverage; and if covered, whether the payment that will be paid by the insurance companies constructs a profitable model for the company.

The work involved in securing insurance coverage is very lengthy and expensive (similar to regulation). Therefore it is important to begin the initial investigation as soon as possible, so as to minimize uncertainty and risks for investors, and to run in tandem with the regulatory processes in order to be ready to launch the product upon receipt of regulatory and reimbursement approvals.

Pre-Clinical and Clinical Trials

In light of the recommendations of your strategic regulatory plan, you will be able to determine whether testing on animals (pre-clinical) and/or in humans (clinical trials) is required in order to obtain marketing clearance.

Pre-clinical animal tests are designed to test the product on animals'organs to establish the safety of the product and be used as proof of its efficacy before testing on humans. These experiments may be carried out both outside (in vitro) and inside (in vivo) the body. The tests may be performed on different types of animals (small animals such as rats or larger ones such as pigs), all according to regulatory requirements and standards.

Clinical trials are usually the longest and most expensive part in the development of a medical product. This stage is designed to test the safety and efficacy of the medical device in achieving its clinical objective before going to market. These tests require thorough preparation and careful planning by experts. Many professionals are involved with the clinical

Tip: It is recommended to conduct a preliminary examination with a reimbursement specialist before starting a clinical trial in order to make sure that its protocol includes the relevant economic cost-benefit data, which will be required to making a convincing case for insurance coverage of your product.

trials' approval, performance and management processes: the Sponsor Company, the medical staff at the medical centers, the subjects who volunteer to participate in the clinical trial, the Institutional Review Boards (IRBs), the Health Authorities, etc. The success of a clinical trial depends on the knowledge, experience and adherence of all the parties involved to the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines and any other relevant local laws.

Before starting the clinical trial, it should be carefully planned in advance by regulatory consultants and clinical experts (such as CROs - Contract Research Organizations).

Business Plan

The company must formulate, both for itself and for investors, a solid business plan which translates to the economic justification for embarking on this great venture. The business plan must address many questions in addition to the aforementioned professional issues, including inter alia:

- Formulating a business model: What constitutes the projected revenues? (the sale of capital equipment, disposables, accessories etc.)
- Identifying the client: Who is the customer for the product? Who is the buyer? Who is the end user? Who may affect the purchase decision (nurses, doctors ... other people involved in the chain)?

  Ideally, your product should contribute to all components of the system. For example:

  - For the patient: cure; healing; improving quality of life; prolonging life expectancy; reducing recovery time; reducing pain; reducing risk of complications.
  - For hospitals: high economic cost effectiveness; reducing the risk of complications; improving profitability and increasing efficiency.
  - For the insurer/payer: high financial cost effectiveness; reducing the risk of future complications.
  - For the doctor: improved efficiency; reducing the risk of complications; increasing profitability; prestige; convenience.
  - For nurses: easing workload; convenience.
- Who is the competition? SWOT analysis.
- The potential market size – from this figure the annual sales potential of the product and the return of investment (ROI) can be projected.
- Sales & marketing:
  - Recruiting opinion leaders (scientific recognition)
  - Establishing an independent marketing force, or forming a strategic partnership with an existing strong marketing partner.
  - Licensing, distribution, strategic collaboration, etc.

Maximum attention should be given to preparing the documents for investors, including writing an executive summary (1-pager), presentation, business plan, etc.

Financing: Sources of Funding for a Start-Up Beginner

In choosing a source of financing at the seed stage, the availability of funds must be taken into account, together with the limitations associated with each source, the advantages and disadvantages of each one, and implications of choosing a particular funding source regarding prospects for future fundraising rounds and setting a company value.

Among the major funding sources available to the beginner entrepreneur:

- Angels: private investors, investing relatively small amounts (usually tens to hundreds of thousands of dolars). They may be from the relevant field (investors with added value), or financial investors. Angel investors can be found as individuals, or as part of angel clubs, such as the Angel Club with a medical focus - Angel MD.
- Crowdfunding sites: mass recruitment sites, a growing popular funding source, bypassing traditional investors and going directly to the general public, inviting large numbers to invest small amounts in order to get first pick of the product or some other bonus, but usually not for shares. An example of this is KickStarter.
- Venture capital companies (VCs): the primary source of funding for start-up companies, usually in amounts greater than a million dollars. This track is usually more suitable for companies at a more advanced stage.
- Incubators: a unique government track for beginner entrepreneurs with projects that receive backing and a considerable R&D budget for two years in return for shares (in Israel, approximately $ 650k in return for 30-50% of the company's shares).
- R&D grants: Non-diluting governmental grants, usually in return for a commitment to pay royalties from future sales. There are many tracks and you should choose the one most suitable for you.
    - In Israel: these grants are under the auspices of The Israel Innovation Authority, previously known as the Office of the Chief Scientist (OCS) in the Ministry of Economy;
    - In Europe: the flagship track for grants is the European technological cooperation program HORIZON 2020;
    - Bi-lateral funds – parallel agreements between two countries, for governmental support of a joint product

development by two companies from the two countries. For instance, BIRD-F supports joint R&D projects between US and Israeli companies.

You are advised to consult with grant experts concerning the most suitable source for your project, and to take into consideration the different obligations the company is taking upon itself with respect to each funding program.

About Shizim

Shizim is a leading Israeli-based biomed holding group, with companies active in the fields of R&D, clinical research, marketing and business development.

Shizim's Accelerator, ShizimXL, is one of the leading medical device-focused accelerators in Israel.

ShizimXL's portfolio companies take advantage of the high quality infrastructure, facilities, network, know-how and professional support from Shizim Group's diversified experienced personnel and consultants, in order to cultivate the best initiatives towards successful commercialization.

We are looking for exceptional innovative ideas and initiatives, with special focus on medical devices, targeted at real unmet needs, led by talented and enthusiastic entrepreneurs, who are people's people.

What's in it for you?

- Professional business, clinical, marketing and managerial support
- Professional mentoring in various fields, such as Regulatory Affairs, Intellectual Property, Industrial Design, Legal Consultation and more
- Assistance in networking and fundraising efforts
- Shizim's central logistics platform (IT, graphics, accounting, rent, office services)
- Co-sharing work space, meeting room and conference room

Contact us, and we will help you bring your vision to life!

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Note: This guide is a merely a short version guide, which may not include the entire relevant process and tips. You are advised to consult with experts

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