Algorithm for business plan development for a new medical device

Simon Popelier, Jeff Maenhaut

Supervisor: Prof. dr. ir. Pascal Verdonck
Counsellor: Dr. Ewout Van Steenkiste (UGent)

Master's dissertation submitted in order to obtain the academic degree of
Master of Science in Industrial Engineering and Operations Research

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ALGORITHM FOR BUSINESS PLAN DEVELOPMENT FOR A NEW MEDICAL DEVICE

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MASTER DISSERTATION PARTNERS

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PREFACE

Billions of people worldwide depend on medical technology at home, at the doctor's or at the hospital. Medical technologies all contribute to living longer and better, and empower citizens to contribute to society for longer. This master dissertation presents a new developed simulation model, a tool to support newly established MedTech development teams. By doing so, developments in medical devices or new technologies should reach patients, caregivers and hospitals in a more faster way.

This master dissertation allowed us to discover the world of medical device start-ups in all its aspects. It was a pleasure to explore a whole new engineering field, supported by the knowledge of experienced people.

First, we would like to thank our promotor prof. dr. ir. Pascal Verdonck. Thanks for all the dedication and commitment to mentor us during the past year. This project would not have been possible without the time, enthusiasm and support that he invested in our master dissertation. We also want to thank all other members of MedTech Flanders, especially dr. Ewout Vansteenkiste and Karin Scheerlinck for their excellent guidance and support.

Finally, we would like to thank all companies and experts who shared their expertise with us and completed our evaluation tool. Without their passionate participation and input, the validation of the evaluation tool could not have been successfully conducted.

"It is not the strongest of the species that survives, nor the most intelligent,

but the one most responsive to change."

- Charles Darwin

Jeff Maenhaut, Simon Popelier

May 2017

ABSTRACT

Medical technology is any technology used to save lives of individuals suffering from a wide range of conditions. Medical devices are any instrument, apparatus, implant, in vitro reagent or any similar/related article that is used to diagnose, prevent or treat a disease or other conditions. A high-tech approach is needed to meet the future needs of medicine and healthcare with an aging population and increasing chronic conditions. In recent years, the medical device development process has become increasingly complex. As a consequence of these thresholds, many good ideas or new technologies do not reach the patient. In general, developments in medical devices or new technologies need to reach patients, caregivers and hospitals in a more faster way. This master dissertation presents a new developed simulation model, a tool to support newly established MedTech development teams with the early understanding of the complex development process of a new medical device.

Keywords

MedTech, medical devices, start-ups, development process, simulation model, evaluation algorithm, success rate

EXTENDED ABSTRACT

Algorithm for business plan development for a new medical device

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Abstract – **Medical technology is any technology used to save lives of individuals suffering from a wide range of conditions. Medical devices are any instrument, apparatus, implant, in vitro reagent or any similar/related article that is used to diagnose, prevent or treat a disease or other conditions. A high-tech approach is needed to meet the future needs of medicine and healthcare with an aging population and increasing chronic conditions. In recent years, the medical device development process has become increasingly complex. As a consequence of these thresholds, many good ideas or new technologies do not reach the patient. In general, developments in medical devices or new technologies need to reach patients, caregivers and hospitals in a more faster or efficient way. This master dissertation presents a new developed simulation model, a tool to support newly established MedTech development teams with the early understanding of the complex development process of a new medical device.**

Keywords – **MedTech, medical devices, start-ups, development process, simulation model, evaluation algorithm, success rate**

I. Introduction

Medical devices vary a lot in complexity and application. It can be very familiar, everyday objects such as spectacles, disposable gloves, pregnancy tests, hearing aids etc. Meanwhile, at the high-tech end of the scale, medical devices include total body scanners, implants, prostheses, medical imaging equipment or even software which assist in conducting medical testing. Nowadays also applications (smartphone, computer, wearable…) gain ground as medical device.

The overall aim of medical devices or medical technology is to provide better treatment options or a better quality life for the patient/user or even save their life. In the future, the technology will have more impact on the preventive, diagnostic and therapeutic possibilities of medicine and healthcare. This evolution is also driven by the breakthroughs in clinical practice of genetics and molecular medicine on the one hand and the development of advanced engineering technologies on the other.

The MedTech sector is one of the flagships of the medical industry. The high level of research and development within the industry and the close cooperation with the users result in a constant flow of innovations. It is estimated that small and medium-sized enterprises (SMEs) make up 95% of the industry, the majority of which employ less than 50 people. [1] The rapid MedTech innovations are the results of this particular business and research interaction model. Unfortunately, many SMEs are failing, making many new technologies never see the light of day.

Start-ups have difficulties with covering their negative cash flow during the early stages of the product development. There is less seed capital available for “early stage investments”. Many valuable ideas and concepts for new medical devices do not survive the so-called “valley of death”. On top of the many economical complications, medical technology start-ups are also facing a lot other challenges. They need to navigate through the complicated legislation for medical devices. In addition to complying with regulations (directives, CE-labels…), one must mostly set up a full quality system (ISO 13485 certification). The companies need a strategy about how they will protect their ideas and inventions (Intellectual Property protection, patents, keeping the technology as a black-box…). Clinical trials often make an important part of the product development process; these trials also involve a lot of regulations and strategic thinking.

The engineers, researchers and developers need early recognition and understanding of the complex valorisation trajectory to develop and launch a new medical device. In addition, the real needs of the patient population must be known to evaluate if the medical device fills up a clear unmet clinical need and has an added value for the patient, the healthcare system and the society. Also, the commercialization and implementation of the products are stumbling blocks. Knowledge, expertise and insights from various experts in the field of MedTech must be passed on to the new developers and researchers.

The purpose of this master dissertation is to develop a simulation model, a tool to support newly established MedTech development teams with early understanding of the complex development process of a new medical device.

On the one hand the tool should estimate the success rate potential of a start-up with the new product or service they have in mind. With the given knowledge and organizational structure of the start-up, one wants to predict the quantitative success rate of the idea. This tool should include a risk analysis of the product development cycle of a new MedTech product or service.

On the other hand, the simulation must help to gain insight and awareness among the product developers with the feasibility of the technological, economic and regulatory development process.

The experience of start-up engineering companies already affiliated with MedTech must be included in the algorithm. A simulation with the new simulation model should lead to a quantitative proposal of the success rate (expressed as a percentage) to go from an idea to a commercialised product or service. The solution model must be sufficiently robust to provide an investigator to gain insight on the basis of simulations into the feasibility of the technological and economic development trajectory of a clinical product.

The evaluation process consists of three major steps (Figure 1). First, there is a newly developed questionnaire presented to

the development team. Based on their selected answers, certain weights are allocated to the answers in a mathematical algorithm. This simulation algorithm has to generate a total success rate together with a report with strengths, weaknesses and pitfalls of the organisation and concept.

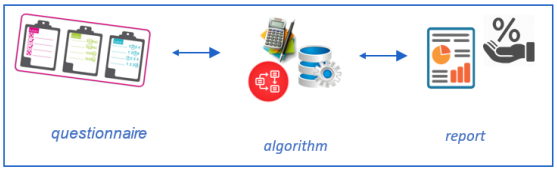

Figure 1: Structure of the evaluation process

II. Determining the Evaluation Framework with Appropriate Parameters

The protocol for the evaluation model construction entailed several steps. The first step is to find the right evaluation criteria and parameters. Both the degree of innovation of the new product or service as well as the internal organization of the start-up must be examined. At a later stage, these parameters should be queried in questions.

A. Medical device evaluation from different stakeholder perspectives

It is important to gain insights from the perspective of investors, hospitals, caregivers, patients, public health regulators and other stakeholders. The various actors in the MedTech network pay attention to other determinants when they evaluate new technologies. The stakeholders are seeking value through managing clinical benefit, increased access, improved life-quality and financial implications (cost-effectiveness, revenue, budget impact, financial stability…). There are many ways to investigate value proposition with different types of quality measures.

First, a review of existing medical device evaluation models from different stakeholder perspectives was made.

When **customers or patients** evaluate a product or service, they consider implicitly value against the price. It is difficult to pin down what consumers truly consider as value. A study of Bain & Company [2] identified 30 “elements of value” that fall into four categories: functional, emotional, life changing and social impact. The four categories extend Maslow’s “hierarchy of needs”. In general, the more elements provided in a presented product or service, the greater customers’ loyalty and the higher the company’s sustained revenue growth. For medical devices, a clear unmet clinical need is necessary to differentiate from different other devices. A preliminary market analysis needs to be performed to ensure there is a sufficient market opportunity for the clinical need.

Hospitals or caregivers evaluate medical devices from a different point of view. In 2013, Boston Healthcare Associates introduced a model with different evaluation criteria for a new healthcare technology adoption.[3] They proposed to establish Hospital Value Assessment Committees (VAC), including clinicians representing various specialities, nurses and hospital administrators. They need to make an assessment of the new technology based on some key review elements (revenue impact, return on investment, complication rate, accuracy, safety, OR (operation room) turnaround time, ease of use, price, patient outcome and length of stay). If the technology is deemed appropriate by the VAC, they refine the value proposition. Therefore, they have different value dimensions (clinical impact, economic impact, training and education, performance measurement and documentation, distribution and logistics, patient satisfaction and experience). After implementing the new technology, quality measures should be set to evaluate.

Evidently, **investors** have a completely different perspective on MedTech developments. Business Angels (BA), Venture Capitalists (VC) and investment funds attach importance to the business case of the new MedTech start-up. From conversations with a few investors (both inside and outside the MedTech field), one learned that most of them have the same approach to evaluate new opportunities. When there is room for new projects in the investment budget, they start the sourcing phase. The offering of the start-up should hold enough potential in a sizable market with a well-defined market gain and international scoop. The eight most important evaluation criteria are market potential, proof of concept, decrease of the healthcare costs, robust intellectual property protection, a cross-functional engaged team, a clear regulatory pathway, established reimbursement codes and exit possibilities.

In most western countries, the biggest payer for these products or services is a **public health insurance** or a national health system. The way reimbursement policies are developed is not very transparent nor predictable. Many decisions are politically driven and the criteria are not always well described. Many public health authorities conduct health-economic evaluations in the shape of comparative analyses of two or more interventions in care, taking into account both the costs and the health effects.[4] The PICO-framework (Patient or Population, Intervention, Comparison, Outcome) is frequently used to describe the new technology. The Incremental Cost-Effective Ratio (ICER) is calculated to summarise the cost-effectiveness of the new health care technology, defined by the difference in cost between the new intervention and the intervention that is currently reimbursed, divided by the difference in effectiveness of these interventions. [5]

To evaluate the product or service from a **manufacturers’** point of view, different steps in the development trajectory should be overviewed. The innovators want to know which factors at each of the development stages contribute to the success of the new product or service. They want to bring the medical device as fast as possible to the market, without making any mistakes. Several process representations of the medical device development already exist. There are waterfall models [6] with an iterative feedback loop for review, verification and validation steps. Next to this, there are also linear models [7][8] of the device development pathway. Also stage-gated representations are used.[9] To highlight the iterative nature of medical device development, the total product life cycle model is used. This model also emphasizes the importance of incorporating user needs and device experience into next generation device development. The iterative process does not always follow the linear idealised model, but rather involves fuzzy boundaries and reiteration between the different development stages. Some parts of the development project can already be in a more advanced phase, while certain activities of a previous phase need to be repeated at the same time.

B. Towards a new evaluation framework

Next to the different perspectives on medical device development, a lot of literature review on the complex

valorisation trajectory (regulatory affairs, directives, regulations, quality system management, health economics, reimbursement codes, marketing, post-market-surveillance, clinical trials etc.) is done.

Also a first round of interviews with MedTech experts (developers, manufacturers, doctors, investors…) took place. All interviewees were asked to share their perspective on the development process, funding or adoption of medical devices. The purpose of these interviews was to identify the decisive parameters to successfully develop and launch medical devices. Based on the literature review and interviews, an evaluation framework was made. The model consists of 11 evaluation stages as depicted in Figure 1.

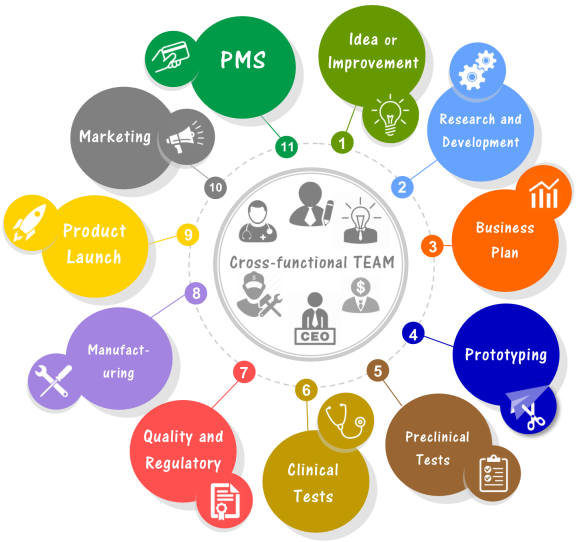

Figure 1: Evaluation model for MedTech ideas

A cross-functional engaged team with an experienced CEO should be at the heart of every start-up.

In a second round of interviews, the initial evaluation representation was presented to the MedTech experts, and feedback was obtained. Some additions and changes were continuously integrated. For each evaluation stage, different decisive parameters were listed. The evaluation parameters were casted in multiple choice questions. Some extra interviews are conducted to verify the listed questions. To limit the complexity of the model, only multiple choice questions are considered. Open answer questions are too difficult to identify and quantify when an automated computer algorithm is implemented without the use of artificial intelligence. The questions must be generic in the first version of the tool. The questionnaire can be filled in by development teams from all different types of (active) medical devices; also by software developers, designers of eHealth applications or manufacturers of patient specific prosthetics.

III. Building the Evaluation Tool

A. *Questions & rating of answers*

The algorithm should assign a weight to each possible answer of the multiple choice questions. The weight of the chosen answer must be stored. By doing mathematical calculations on all weights linked to the answers, a total success rate must be retrieved. The parameters linked to the questions that obtain a low score must be saved to be able to show the pitfalls of the organization or medical device. These weights are decimal number between zero and one and can be considered as a 'percentage'. To keep it organized, only four different 'classes' of weights were chosen.

A: 100% (1.00) B: 95% (0.95) C: 85% (0.85) D: 70% (0.70)

An example of a multiple choice question the manufacturing evaluation stage can be found in Table 1.

Table 1: Example of a multiple choice question of the manufacturing evaluation stage

Q: ISO environment: How long do you think it will take to get your workplace ISO 13485-certificated?		
Answer	Class	Weight
<3 months	D	0.70
<6 months	D	0.70
<1 year	D	0.70
<2 year	C	0.85
>2 year	A	1
We don't need an ISO certification	Does not Apply	DNA
The workplace is already ISO-certificated	A	1

A multiplicative model is chosen where all weights per stage are multiplied to receive a final stage score. In the example above, one states that if the ISO-certification of the workplace can be done within less than 6 months (class D answer), it is deemed they can only score 70% on the manufacturing stage. If all the other questions of this stage are answered with a class A answer. Answers on multifactorial questions are also converted to weights of a specific class, depending on the importance of the question and the selected number of answers. The questionnaire is implemented in an online tool, which is named "MedTech Compass" (Figure 2). Link: http://su.vc/medtech_compass

Figure 2: Logo MedTech Compass

B. *Product or service scenarios*

Medical device development teams usually have different long term objectives with their product or service. Some of them only want to prototype a very good idea, others want to build a solid company. The number of iterations in the development cycle can also be different. Some companies want to go to the market as soon as possible as they launch the new product or service and develop a second version based on customer feedback. Other companies want to be very confident of their product before they go to the market. These companies invest a lot of money and time in prototyping, biomedical tests and clinical trials. One immediately feels that there is a big difference between the two extremes concerning investments in time and money. Based on these considerations, four different product/service scenarios are formulated:

Scenario 1: Sell IP: Develop, design and prototype some product or technology. The technology will be intellectual protected with the intention to sell the intellectual property to another company.

Scenario 2: Early licensing: Going fast through the development cycle of the product or service with the intention to go very fast to the product launch. Next generations of products will be launched based on feedback of the users.

Scenario 3: Late licensing: Paying close attention to the prototyping and testing phases before the product is launched. The company is going slower through the development cycle because they want to be confident about their product before they launch it.

Scenario 4: Autonomous company: Paying close attention to all the phases in the development cycle and putting a lot of energy in the organization of a solid company next to the product development.

Depending on the product or service scenario, every evaluation stage gets a specific quotation allocated on how much it contributes to the final success rate score. The quotation for each stage corresponds with the quotation in the weighted arithmetic mean for the calculation of the total success rate.

Table 1: Quotation rules for every stage per product/service scenario

Stages	Scenario 1	Scenario 2	Scenario 3	Scenario 4
Idea or improvement	***	***	***	***
R&D	***	**	***	***
Business Case	***	***	***	***
Prototyping	*	*	***	***
Quality & Regulatory	***	***	***	***
Preclinical tests	***	**	***	***
Clinical tests	***	**	***	***
Manufacturing	*	***	***	***
Product launch	*	**	**	***
Marketing	*	**	**	***
Post Market Surveillance	*	**	**	***

C. *Evaluation moments*

Not every product development cycle of a start-up has the same duration. Depending on the moment the questionnaire is filled in during the development process, the team behind the start-up will have encountered a lot more or less knowledge. An average pattern traversed by most product development teams can be found in Figure 1.

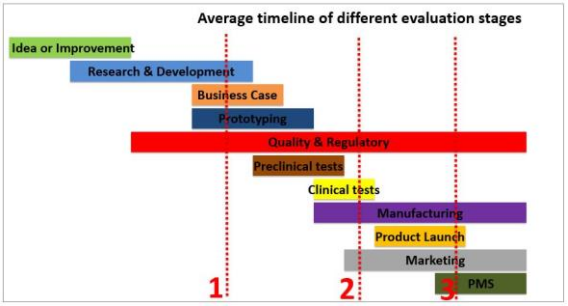

Figure 1: Three predefined evaluation moments for filling in the tool

Three evaluation moments were predefined at this tool. The users are asked to choose one of the evaluation moments that describes best their current situation. Depending on this moment, not all questions will partake in the algorithm to calculate the success rate. Some questions are not yet relevant for some development teams. Including them will give an irrelevant outcome for stage scores and moreover for the total success rate. For some start-ups it will be necessary to be able to skip an entire evaluation stage, because they have not yet enough insight on how they will approach this development phase. If an evaluation stage is not filled in, it has no contribution to the total success rate calculation.

D. *Benchmarking the score of an evaluation stage*

After linking weights to each answer of each question, it is time to calculate a total score for a stage. Until now, a simple multiplication of all answer related weights gives us a preliminary stage score. Since not all stages include the same number of questions, those scores should be adjusted to a certain benchmark.

$$s_i = \left(\prod_{k=0}^{K_i} w_{ik}\right)^{\frac{F}{K_i}} \quad (1)$$

$$with: \begin{cases} s_i = Total\ score\ of\ stage\ i \\ K_i = Total\ number\ of\ questions\ of\ stage\ i \\ w_{ik} = Weight\ of\ the\ k^{th}\ answer\ of\ stage\ i \\ F = Benchmark\ factor \end{cases}$$

E. *Total success rate*

To calculate the total success rate of the product or service, the total stage scores, evaluation moment and scenario must be taken into account. The total success rate is the weighted result of all the different stages, depending on the importance of a stage in the selected product or service scenario and the evaluation moments.

$$\text{Total success rate} = \frac{\sum_i^I x_i \sum_i^I b_i \sum_i^I \sum_k^{K_i} y_{ik} \left(\prod_{k=0}^{K_i} w_{ik}\right)^{\frac{6}{K_i}}}{\sum_i^I x_i \sum_i^I b_i \sum_i^I \sum_k^{K_i} y_{ik}} \quad (2)$$

$$with: \begin{cases} x_i = \begin{cases} 1 \text{ if stage i is included} \\ 0 \quad \text{otherwise} \end{cases} \\ y_{ik} = \begin{cases} 1 \text{ if the } k^{th} \text{ question of stage i is included} \\ 0 \quad \text{otherwise} \end{cases} \\ b_i = \text{product or service scenario weight of stage i} \\ K_i = \text{total number of questions of stage i} \\ w_{ik} = \text{weight of } k^{th} \text{ question of stage i} \end{cases}$$

F. *Generated report*

Once filled in the provided online tool, a report is generated were all relevant outcomes are discussed and shown. For each evaluation stage an indicator is presented, as depicted on the example in Figure 1. Also the total success rate is indicated on the example in Figure 2 and the total success rates in case another product or service scenario was chosen can be found in Figure 3.

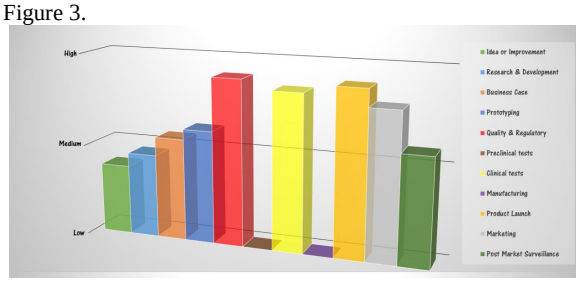

Figure 1: Indicators of all evaluation stages

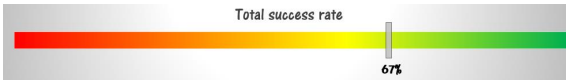

Figure 2: Total success rate indicator

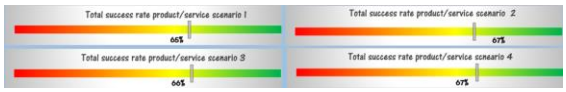

Figure 3: Total success rate indicators for all product/service scenarios

Next, the two evaluation stages with the lowest score are determined. Of these stages, four parameters that require urgent attention are displayed, like the example in Figure 4.

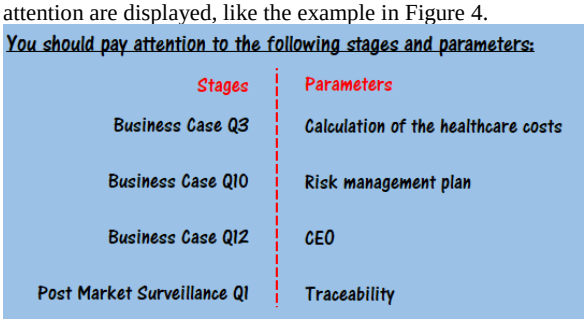

Figure 4: Four lowest scoring parameters related to the two lowest scoring evaluation stages

Finally, in Figure 5 the scores of the different evaluation stages are compared to the score they would achieve if they indicated a different evaluation moment in the product development cycle.

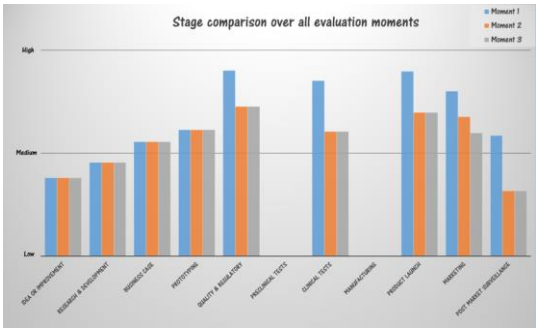

Figure 5: Stage indicator comparison over all evaluation moments

IV. THREE CASE STUDIES

A. *Case study 1: Evaluating established companies of the MedTech Flanders network as benchmark*

The evaluation questionnaire was implemented in an online platform and subsequently the mathematical algorithm was finished. Some of the interviewed MedTech experts were revisited to give their opinion on all weights, scores and quotation rules that are linked to the questions and evaluation stages.

Afterwards, three of the MedTech experts who were interviewed during the compilation of the questionnaire, were asked to complete the online tool. These experts did not see the final weights or quotation rules before they filled in the evaluation tool, to get an unbiased success rate determination of their company. They completed the MedTech Compass regarding their experience with the main medical device project in which they are involved. These are projects where the expert is the co-founder or CEO of the company. These companies already earned their spurs within the Flemish MedTech industry. Therefore, one expected them to score more than 75% for the success rate of MedTech Compass.

The three companies respectively achieved a success rate of 82%, 82% and 75%. The evaluation report was each time presented to the person who completed the tool. They confirmed that the indicators for the various evaluation stages represented the real strengths and weaknesses of the company.

Based on these three case studies at existing companies in the MedTech industry and the feedback of other experts, the tool was completed to its final form. The questions, weights and quotation rules were assessed by experts. Based on the results of this first case study, one could conclude that the benchmarking rules were very good.

B. *Case study 2: Evaluating start-ups participating the MedTech Flanders accelerator program*

Four start-ups participated in the first edition of the accelerator program of MedTech Flanders. These start-ups were creating different types of medical devices: a catheter monitoring system, a patient-specific implant, a recovery coach app and an In Vitro Diagnostic (IVD) device. Each development team completed the evaluation tool. The start-up working on IVD, quitted halfway the tool. Because the questionnaire is more focused towards “classic” medical devices, the questions were too far from the development phases they are currently undergoing. The reports were represented to the coaches of the accelerator program, they confirmed that the indicators for the various evaluation stages

and total success rates have the same results as they had in mind.

C. *Case study 3: Evaluating a start-up in the incubation phase*

As a final test, the evaluation tool was provided to an engineer who has plans to set up a medical device start-up in the near future. In fact, MedTech compass targets start-ups who can already submit a business case. An engineer or healthcare professional who is in the first phase of the ideation, does not yet have enough knowledge, information and insights about the development process of a new medical device. Nevertheless, it is interesting to present the questionnaire to a person or team in such a situation. The evaluation tool also has an educational facet that gives the development team new insights on the very complex valorisation process of a new medical device.

Despite the fact the project is still in the incubation phase, the evaluation scores for the different evaluation stages were quite high. But the developer had filled in many questions at his discretion. He confirmed that the MedTech Compass tool was very useful to get a picture on what is expected of a development team of a new medical device.

V. Future research & Conclusions

The goal of this master dissertation was to develop a simulation model to support newly established MedTech development teams with the early understanding of the complex valorisation process of a new medical device. The purpose was to estimate the success rate potential of a start-up with a new product or service. The simulation tool must also help to gain insight and awareness among the product developers with the feasibility of the technological, economic and regulatory development process.

The experience of start-up engineering companies already affiliated with the design of medical devices was implemented in the evaluation tool. Other MedTech experts (developers, doctors, investors etc.) were also interviewed to get important success evaluation factors from different perspectives. An evaluation framework with 11 stages was built. For each stage, various evaluation parameters were listed. These parameters were linked to multiple choice questions. Each picked answer of the questionnaire casted a weight to the mathematical algorithm. This algorithm calculated a score for every evaluation stage and finally a weighted total success rate. The calculations were represented in a automatically generated report.

A threefold case study was performed to test the evaluation tool on existing companies, start-ups participating an accelerator program and a new medical device incubation project. During the case-study on the start-ups, it was concluded that the evaluation framework is not suitable for IVD medical devices.

Based on this case study, the report generated by the evaluation algorithm appears to be representative to assess the strengths and weaknesses of a MedTech start-up. To establish the correctness of the success rate determination, a larger statistical analysis is needed. Because success is hard to measure, it is difficult to quantify if a calculated success rate gives a realistic view on the true success rate potential of a company.

The new evaluation tool should serve as a basis for future research. The questionnaires, weights and quotation rules are compiled based on literature and interviews with more than twenty Flemish MedTech experts. Medical technology is a fast growing industry. This simulation model will need to be continuously updated to accommodate the fast changing technologic progresses.

In addition to further elaborating the evaluation tool, it is possible to apply the evaluation algorithm to different questionnaires for more specific types of medical devices. (patient-specific medical devices, software and applications, IVD devices, drug-device combinations etc.) During the threefold case study, it became clear that the questionnaire certainly should be adjusted to be applicable for In Vitro Diagnostic medical devices.

Next to this, other types of HealthTech can be evaluated in a new tool based on the MedTech Compass evaluation algorithm.

Finally, the computer implementation of the evaluation tool can be further optimized. A visual basic script can be coded to automatically load the results into the algorithm. In the long term, a full web application can be developed to immediately return the results in an online tool.

The goal of this master's dissertation is achieved; a new evaluation framework is developed and successfully tested on various companies and concepts in the field of MedTech. The simulation report together with the questionnaire itself, gains insight and awareness among the product-developers with the feasibility of the technological, economic and regulatory development process.

The evaluation framework is composed based upon a lot of experience of various experts in the field of MedTech. Due to the generic approach during the composition of the algorithm, the possibility for further refinement and extension of the tool is afforded.

Acknowledgements

The authors would like to acknowledge the suggestions and feedback of all the MedTech experts and companies.

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CONTENT

LIST OF FIGURES

LIST OF TABLES

LIST OF ABBREVIATIONS

AIMD	Active Implantable Medical Devices
AIMDD	Active Implantable Medical Device Directive
BA	Business Angel
BOM	Bill Of Materials
CareTech	Care Technology
CB	Competent Body
CE	Conformité Européene (European Conformity)
CEO	Chief Executive Officer
CRM	Customer Relationship Management
EU	European Union
FDA	Food and Drug Administration (US)
FMEA	Failure Mode and Effect Analysis
GLP	Good Laboratory Practice
HealthTech	Health Technology
ICER	Incremental Cost-Effectiveness Ratio
IP	Intellectual Property
IPO	Initial Public Offering
ISO	International Organization for Standardization
IVD	In Vitro Diagnostic
IVDD	In Vitro Diagnostic Directive
IVDR	In Vitro Diagnostic Regulation
MD	Medical Device
MDD	Medical Device Directive
MDR	Medical Device Regulation
MEDDEV	Common approach guidance on medical device development
MedTech	Medical Technology
METC	Medical Ethical Committee
NB	Notified Body
OR	Operation Room
PEST	Political, Economic, Social & Technological
PICO	Patient, Intervention, Comparison & Outcome
PMS	Post Market Surveillance
POC	Proof Of Concept
QALY	Quality-Adjusted Life Years
QMS	Quality Management System
R&D	Research & Development
RIZIV	Rijksinstituut voor ziekte- en invaliditeitsverzekering (Belgian Public Health Authority)
ROI	Return On Investment
SMEs	Small and medium-sized enterprises
SWOT	Strengths Weaknesses Opportunities & Threats
VAC	Value Assessment Committee
VC	Venture Capital or Venture Capitalist
US	United States
UK	United Kingdom

I. INTRODUCTION

1 Medical Technology, a driver for innovative health care

"Health technology" is one of the six essential building blocks considered by the World Health Organization (WHO) to be of main importance for the realization of stable and sustainable global health systems. Health technology covers the application of scientific knowledge, techniques and technologies in the domain of health care. In this master dissertation however, health technology is limited to "medical devices".

Medical technology is any technology used to save lives of individuals suffering from a wide range of conditions. A medical device is an instrument, apparatus, implant, in vitro reagent or any similar/related article that is used to diagnose, prevent or treat a disease or other conditions. The purposes may not be achieved through some chemical action within or on the body, which would make it a drug. Drugs or pharmaceuticals achieve their principal action by pharmacological, metabolic or immunological means. While medical devices act by other means like physical, mechanical or thermal means. Medical devices vary a lot in complexity and application. It can be very familiar, everyday objects such as spectacles, disposable gloves, pregnancy tests, hearing aids etc. Meanwhile, at the high-tech end of the scale, medical devices include total body scanners, implants, prostheses, medical imaging equipment or even software which assist in the conduct of medical testing. Nowadays also (smartphone, computer…) applications gain ground as medical device.

The overall aim of medical devices or medical technology is to provide better treatment options or a better-quality life for the patient or even save their life. There are more than 500,000 registered medical technologies currently available. Medical technologies have a beneficial impact on health, quality of life and society as whole. They contribute to living longer or better and empower citizens to contribute longer to the society. In this respect, good health is a prerequisite for well-being and economic prosperity. Medical technology or MedTech helps people live longer, healthier, more productive, more socially active or independent. It can also reinforce employability. In doing so, MedTech contributes to economic growth through better health of the workforce.

In the future, the technology will have an even more dramatic impact on the way preventive, diagnostic and therapeutic possibilities of medicine and healthcare. This evolution is also driven by the breakthroughs in the

clinical practice of genetics and molecular medicine on the one hand and the development of advanced engineering technologies on the other. A high-tech approach is needed to meet the future needs of medicine and healthcare. More and more engineers focus on research of new medical technologies. According to the European Patent Office, medical technology is globally the sector with the highest number of patent applications. [1] The sector is the engine of innovation and this will continue the coming decades. [2]

Note: *At most publications about MedTech (this master dissertation included), 'Europe' refers to the EU28 countries (still including UK) together with Norway and Switzerland, unless specified otherwise.*

1.1 Definitions

When talking about 'Health technologies' there should always a distinction be made between MedTech and CareTech.

CareTech

Assistive technology and technological tools for supporting people who suffer from limitations as a result of sensory, motor, cognitive, emotional or psychological problems. There are several fields of application like mobility (such as wheelchairs, lift and transfer systems, scooters…), communication and information (such as personal alarm systems, remote communication systems…), environment (such as ergonomic furniture, accessibility of buildings, security and access control…) or personal care (such as custom made beds, incontinence pads, household appliances…). [3]

MedTech: Medical Technology

Medical technology can be medical devices, in vitro diagnostics, imaging equipment or e-Health solutions used to diagnose, monitor, asses predispositions and treat patients suffering from a wide range of conditions. [3] [2].

Medical device

One speaks about a 'medical device' when it fits to the European regulations, defined in two directives.

1. The **Medical Device Directive (MDD)** 93/42/EC of 14 June 1993 defines a medical device as: "any instrument, apparatus, appliance, software, material or other article, whether used alone or in combination, including the software intended by its manufacturer to be used specifically for diagnostic and/or therapeutic purposes and necessary for its proper application, intended by the manufacturer to be used for human beings for the purpose of:
   - diagnosis, prevention, monitoring, treatment or alleviation of disease;
   - diagnosis, monitoring, treatment, alleviation of or compensation for an injury or handicap;

- investigation, replacement or modification of the anatomy or of a physiological process;
- control of conception;

and which does not achieve its principal intended action in or on the human body by pharmacological, immunological or metabolic means, but which may be assisted in its function by such means." [4]

2. According to the **Council Directive** 90/385/EEC of 20 June 1990 relating to **active implantable medical devices (AIMD)** a 'medical device' means: "any instrument, apparatus, appliance, material or other article, whether used alone or in combination, together with any accessories or software for its proper functioning, intended by the manufacturer to be used for human beings in the:
   - diagnosis, prevention, monitoring, treatment or alleviation of disease or injury,
   - investigation, replacement or modification of the anatomy or of a physiological process,
   - control of conception,

   and which does not achieve its principal intended action by pharmacological, chemical, immunological or metabolic means, but which may be assisted in its function by such means" [5]

In Vitro Diagnostics (IVD)

One speaks about 'in vitro diagnostic medical devices' when it fits to the European regulations, defined in two directives.

1. The **Medical Device Directive (MDD)** 93/42/EC of 14 June 1993 defines a 'in vitro diagnostic medical device' as: "any medical device which is a reagent, reagent product, calibrator, control material, kit, instrument, apparatus, equipment or system, whether used alone or in combination, intended by the manufacturer to be used in vitro for the examination of specimens, including blood and tissue donations, derived from the human body, solely or principally for the purpose of providing information:
   - concerning a physiological or pathological state, or
   - concerning a congenital abnormality, or
   - to determine the safety and compatibility with potential recipients, or
   - to monitor therapeutic measures.

   Specimen receptacles are considered to be in vitro diagnostic medical devices. 'Specimen receptacles' are those devices, whether vacuum-type or not, specifically intended by their

manufacturers for the primary containment and preservation of specimens derived from the human body for the purpose of in vitro diagnostic examination." [4]

2. According to the **Council Directive** 98/79/EC of 27 October 1998 relating to **in vitro diagnostic medical devices (IVDD)** 'an in vitro diagnostic medical device' is: "any medical device which is a reagent, reagent product, calibrator, control material, kit, instrument, apparatus, equipment or system, whether used alone or in combination, intended by the manufacturer to be used in vitro for the examination of specimens, including blood and tissue donations, derived from the human body, solely or principally for the purpose of providing information: concerning a physiological or pathological state; or concerning a congenital abnormality; or to determine the safety and compatibility with potential recipients; or to monitor therapeutic measures." [6]

The **Global Medical Devices Nomenclature Agency** (GMDN) divides all medical technology within 16 product categories.

Code	Product Category	Examples
01	Active implantable technology	Cardiac pacemakers, neuro stimulators
02	Anaesthetic and respiratory technology	Oxygen mask, gas delivery unit, anaesthesia breathing circuit
03	Dental technology	Dentistry tools, alloys, resins, floss, brushes
04	Electromechanical medical technology	X-ray machine, laser, scanner
05	Hospital hardware	Hospital bed
06	In vitro diagnostic technology	Pregnancy test, genetic test, glucose strip
07	Non-active implantable technology	Hip or knee joint replacement, cardiac stent
08	Ophthalmic and optical technology	Spectacles, contact lenses, intraocular lenses, ophthalmoscope
09	Reusable instruments	Surgical instruments, rigid endoscopes, blood pressure cuffs, stethoscopes, skin electrodes
10	Single use technology	Syringes, needles, latex gloves, balloon catheters
11	Technical aids for disabled	Wheelchairs, walking frames, hearing aids
12	Diagnostic and therapeutic radiation technology	Radiotherapy units
13	Complementary therapy devices	Acupuncture needles/devices, bio-energy-mapping systems/software, magnets, moxibustion devices, suction cups
14	Biological-derived devices	Biological heart valves
15	Healthcare facility products and adaptions	Gas delivery systems
16	Laboratory equipment	Most IVD which are not reagents

Table 1: The 16 medical technology product categories according to GMDN (2010) [2]

2 Regulatory Framework for medical devices

2.1 EU Directives

In the early 1990s there was a harmonization process through European directives in how medical devices were regulated. Previously there was a great diversity amongst the regulations in the different European countries. The regulation for medical devices was mostly evolved within the pharmaceutical regulatory framework before ultimately splitting into a legally autonomous framework. During the 1990s, the European Union ("EU") created a regulatory framework for Medical Devices based one three directives:

- Directive 90/385/EEC, active implantable medical devices ("AIMDD");
- Directive 93/42/EEC, medical devices ("MDD");
- Directive 98/79/EC, in vitro diagnostic medical devices ("IVDD").

Active Implantable Medical Device Directive (AIMDD)

Active medical devices are medical devices relying for its functioning on a source of electrical energy or any source of power that is not directly generated by the human body or gravity. An active implantable device is any active medical device which is intended to be surgically or medically introduced into the human body or by medical intervention into a natural orifice. It is intended to remain after the intervention or procedure.

Medical Device Directive (MDD)

This directive covers most other medical devices (active and non-active) and their accessories that are not covered by the first or third directive. This directive scopes a large number of products ranging from walking aids to prosthetic heart valves.

In Vitro Diagnostic Medical Device Directive (IVDD):

The In Vitro Diagnostic Medical Device Directive covers any reagent, reagent product, control material, kit, medical device, instrument, apparatus or system which is intended to be used in-vitro for the examination of substances derived from the human body.

There are some fundamental aspects to these current directives. First, private organizations competent in the standardization area have the duty of drawing up technical specifications required for the production and placement on the market of products that are in conformity with the 'essential requirements' specified in the Directives. Second, these technical specifications maintain their status as voluntary standards. Third, although non-mandatory national authorities will presume conformity with the 'essential requirements' if products are manufactured in conformity with these harmonized standards.

The 'Medical Device Survey 2015' of The European Association for Medical Devices Notified Bodies (TEAM NB), confirms that the largest percentage (91%) of the medical devices approved during 2015 belongs to the remit of MDD. IVD represents 7% and AIMD only 2% of all medical Devices. [7] The primary guidelines that regulate the medical devices sector are these three directives. Since they are directives and not regulations, the way they are implemented in national legislation plays an important role. Another important part of the rules are guidance documents that promote common approach to the implementation of the procedures as laid down in the Directives.

Nowadays, MEDDEV (Medical Device Guidance Documents, published by the European Commission) is the most used guideline for manufacturers of medical devices. It promotes a common approach to the implementation of the procedures as laid down in the Directives. The present MEDDEV is part of a set guidelines relating to questions of application of EU Directives on medical devices. They are not legally binding! Only the European Court of Justice can give authoritative interpretation of community law.

Active implantable medical devices and *in vitro* diagnostic medical devices are covered by separate directives. The European Commission periodically publishes interpretative documents that clarify provisions of these directives. They also are the prime movers in undertaking legislative amendments and revisions of the regulatory structure and they are hosting a number of stakeholders groups that author the guidance documents. The other public regulators are the National Competent Authorities (NCA), they draft the national implementing legislations and publish national guidelines on the implementation of the directives

2.2 New EU regulations

The MedTech industry has grown rapidly in recent years. This technology will have an even greater impact on the preventive, diagnostic and therapeutic possibilities of medicine and healthcare. The developments of the MedTech industry have vastly outpaced the regulatory framework for medical devices. Future medicine and healthcare require a high-tech approach, with the human component always in mind. The European regulators therefore considered that a change was needed. A scandal with the 'Poly Implant Prothèse' (PIP) in 2012 putted the negotiations on the fast track. [8] The breast implants came under increased scrutiny of the European Environment Committee when 500,000 women were believed to have been affected by the use of low-grade silicone in breast implants produced by the French manufacturer PIP. The European Parliament had been pushing for better rules for over 20 years, adopting a resolution in 2001 and a report in 2003. Certain initiatives have already been taken under the current regime to minimise the risk to patients' by increasing scrutiny on notified bodies. After several years of discussion, the European Commission published in 2012 two new proposals for regulations to replace the existing directives:

- a proposal for a regulation on medical devices ("MDR"), to replace the AMDD and MDD directives;
- a proposal for a regulation on in vitro diagnostic medical devices ("IVDR"), to replace the IVDD directive.

By shifting from directives to regulations a wider scope of protection and more effective implementation of the rules can be ensured. The new regulations have been published on May 5, 2017 in the Official Journal of the EU. The new rules will only apply after a transitional period. Namely, 3 years after entry into force for the Regulation on medical devices (spring 2020) and 5 years after entry into force (spring 2022) for the Regulation on In Vitro Diagnostic medical devices. [9]

The two new regulations altered their scope without introducing major changes. The scope of the MDR is largely equivalent to the directives MDD and AMDD but some considerable changes to the existing definitions are introduced, resulting in the inclusion of certain products that are currently not classified as a Medical Device. Products intended for cleaning, disinfecting or sterilising Medical Devices for example were previously considered to be accessories to Medical Devices. While the definition of 'accessories' was also enlarged whereby it includes devices that specifically or directly assist another device in its intended purpose. The MDR clarified that software which is used for medical purposes will be qualified as a Medical Device, while software for life-style and well-being applications are not Medical Devices.

The scope of the regulatory framework for the IVDR is also extended compared to the current IVDD. Some important concepts are better clarified so the IVDR now includes tests to provide information about the predisposition of a medical condition or disease and tests to provide information to predict treatment response or reactions. The scope of accessories was also enlarged and medical software is now explicitly mentioned in the definition of IVDs. For more information about the major changes involving the new regulations, please consult the proposal for the regulation (MDR or IVDR).

For Manufacturers it is important to check the qualifications of their existing products against the new rules and determine whether they are in or out of scope with the new rules and definitions. The changed scope of the definitions has an impact on the existing regulatory requirements. The EU wants to make sure that medical devices and in vitro diagnostic medical devices are safe while allowing patients to benefit of innovative health care solutions in a timely manner. They want to strengthen the rules on placing devices on the market and tighten surveillance once they are available. [10]

2.3 Classification

It is not feasible economically nor justifiable in practice to subject all medical devices to the most rigorous conformity assessment procedures available. There is no 'one-size-fits-all' solution because every device

requires a customized approach due to the wide variety of possible applications. Because a fully customized approach is practically impossible, a graduated system of control is more appropriate. The European legislator established a classification concept which is essentially based on potential hazards related to the use and possible failure of devices. In such a system, the level of control corresponds to the level of potential hazard inherent in the type of device concerned. Before a product becomes available, the appropriate safety measures should be put in place depending on the risk classification. [2] [11]

It is important that manufacturers are able to determine the classification of their product as early as possible during the device development. Therefore, a system of classification rules was needed so each manufacturer could classify its own devices. This classification should be a 'risk based' system based on the vulnerability of the human body taking account of the potential risks associated with the devices.

Classification for Medical Devices

The classification rules are set out in the MEDDEV directive (annex IX) and are corresponding to the classification rules of the Global Harmonization Task Force (GHTF). The MDD operates based on risk classification of the medical device. Products are categorized into four risk classes starting from lowest to the highest risk category because the vulnerability of the human body: classes I, IIa, IIb and III. The manufacturer of the medical device can choose the risk classification for their devices. Generally, class I devices is under the sole discretion of the manufacturer, for class IIa devices notified bodies need to be consulted at the production stage and for classes IIb and III (high risk) notified bodies need to review the design and production of the devices. Class I also has two additional subclasses: Class I sterile and Class I measuring function. Classification of a medical device will depend on upon a series of factors, including:

- how long the device is intended to be in continuous use,
- if the device is invasive or surgically invasive,
- whether the device is implantable or active,
- whether the device contains a substance, which in its own right is a medicinal substance and has action ancillary to that of the device.

Active implantable medical devices are typically subject to the same regulatory requirements as Class III devices. (https://www.emergogroup.com/nl/resources/europe-process-chart). For all devices except Class I (non-sterile, non-measuring), a Quality Management System in accordance with Annex II or V of the MDD should be implemented. Most companies apply the ISO 13485 standard to achieve QMS compliance. For Class I (non-sterile, non-measuring) a QMS is not formally required. However, a PMS procedure is required though not likely to be audited by a Notified Body.

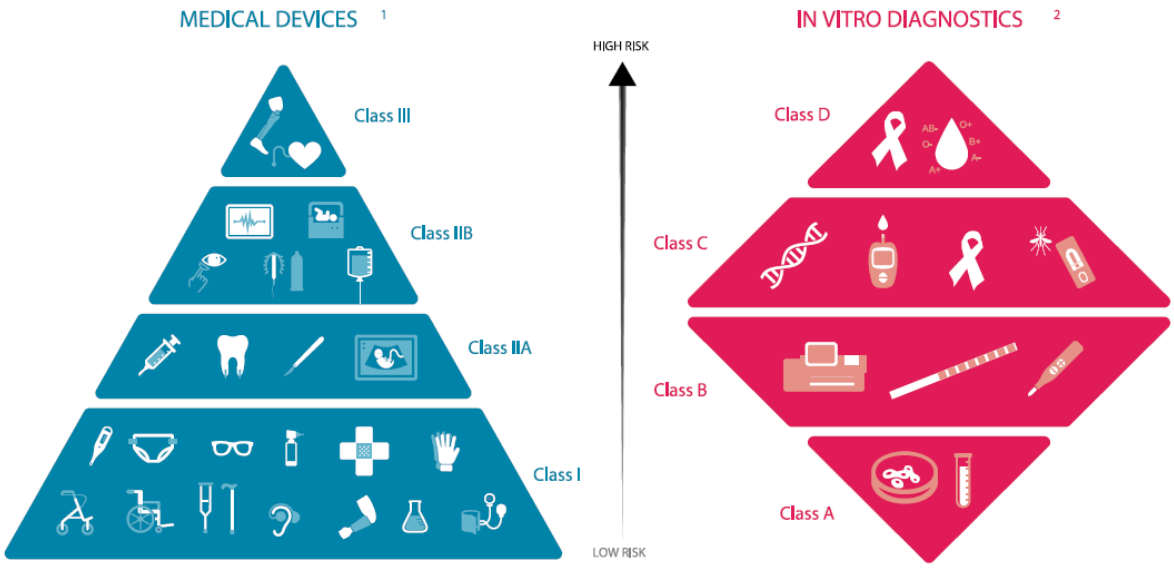

Figure 1: Classification for medical devices and IVD [2]

Classification for IVD

The IVD Directive groups In Vitro Diagnostic Medical Devices into four categories. These categories are also in order of increasing perceived risk.

- Device of **List A**, Annex II of the directive, which includes reagents and products for human immunodeficiency virus I and II, hepatitis B, C and D.
- Device of **List B**, Annex II of the Directive, which, among others, includes reagents and products for rubella, toxoplasmosis and phenylketonuria as well as devices for self-testing for blood sugar.
- Device for **self-testing** (not listed in Annex II): a device intended by the manufacturer to be able to be used by lay persons in a home environment, excluding self-test devices covered in Annex II.
- **Other/General** device: all devices except Annex II and self-testing devices. [12]

2.4 ISO 13485 certification

ISO 13485 specifies requirements for a quality management system where an organization needs to demonstrate its ability to provide medical devices and related services that consistent meet regulatory requirements. The ISO requirements are not only applicable to the manufacturers that launch the medical devices on the market, but also for organizations that are involved in one or more stages of the product life-cycle (including design, development, production, storage and distribution, installation, or servicing of a medical device and design and development or provision of associated activities (e.g. technical support)). Regardless to the size and type of organizations are the requirements of ISO 13485 applicable to all organizations in the supply chain of a medical device. Also, the processes that are applicable to the

organization but not performed by the organization itself, are the responsibility of the organization and are accounted for in the organization's quality management system by monitoring, maintaining, and controlling the processes.

The primary objective of ISO 13485 is to facilitate harmonized medical device regulatory requirements for quality management systems. It includes some requirements for medical devices and excludes some of the requirements of ISO 9001 that are not appropriate. Because of these exclusions, organizations whose quality management systems conform this international standard cannot claim conformity to ISO 9001 unless their QMS conform also to all requirements of ISO 9001. The first version of ISO 13485 and ISO 13488 standards specific to medical devices were published in 1996. The difference between the two medical device industry standards were fundamentally the inclusion of design controls in the ISO 13485 standard where ISO 13488 did not include this. In 2003 (after the ISO 9001 revision), the ISO 13485:2003 was published, which replaced the previous two standards. The prominence of certification increased significantly because many country requirements mirrored the ISO 13485 standard. In 2016 again a revision was published with only some slight changes to close the gaps between the regulatory requirements today and what was expected over the last 10 years. [13] [14]

2.5 CE Marking

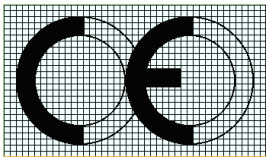

Figure 2: CE mark

A **CE Marking** is the symbol shown in Figure 2. The letters "CE" are the abbreviation of the French phrase "*Conformité Européene*" (European Conformity). CE marking on a product is a manufacturer's declaration that the product complies with the essential requirements of the relevant European health, safety and environmental protection legislations (for MedTech, the three directives described before). The product Directives contains the "essential requirements" and/or "performance levels" and "Harmonized Standards" to which the products must conform. Only a CE Marking on the product indicates to governmental officials that the product may be legally placed on the market in their country and ensures the free movement of the product within the EFTA (European Free Trade Association) and European Union. To obtain CE certification, a conformity assessment should be performed by a notified body. For all devices except Class I (non-sterile, non-measuring) the QMS and a technical file or design dossier must be audited by a notified body. For Class I (non-sterile, non-measuring), CE certificates do not expire. For all other classes, the manufacturer will be

audited each year by a Notified Body to ensure ongoing compliance with the Directives. CE marking certificates are typically valid for 3 years. [15] [16]

3 Why MedTech matters?

Medical technology can save lives, improve health and contribute to sustainable healthcare. By diagnosing health problems or by preventing a disease through modern testing methods, MedTech can literally make the difference between life and death. People can live healthier, more productive or independent through the use of medical devices. Also the healthcare systems can work more efficiently by preventing acute care, allow less invasive and shorter interventions, shorten recovery times or enable care at home. The medical technology sector has a broad impact on healthcare.

3.1 MedTech, flagship of the medical industry

Innovation

The MedTech-sector is one of the flagships of the medical industry. The high level of research and development within the industry and the close co-operation with the users result in a constant flow of innovations. Medical devices typically have a lifecycle of only four to five years before an improved product becomes available. (For implants it is only 12-18 months). The European Patent Office published their 2015 annual report, a summary of the most active technology fields can be found in Table 2 below.

	Technology field	Patent applications 2015	Patent applications 2016
	Medical Technology	12 474	12 263
	Digital Communication	10 762	10 915
	Computer Technology	10 549	10 657
	Electricity/Energy	10 198	10 293
	Transport	7 802	8 402

Table 2: Worldwide patent applications filed at the European Patent Office (EPO) in the most active technology fields during 2015 and 2016 [17]

(Note: The number of patent applications mentioned in Table 2 are the applications filed at the European Patent Office. This does not mean that these applications all come from European companies.)

Medical Technology was once again the field with the highest number of patent applications during 2015, growing by a further 11% compared with 2014. This high number of patent applications expresses the high degree of innovation of the MedTech industry. [18] In 2016, it remains the field with the greatest number of

patent applications but had a slight drop compared to 2015. [19] European companies were overtaking the US companies in the medical technology sector in terms of patent applications filed during 2016. 48% of these applications were filed from European countries and 52% of other countries with the majority of US patent applications followed by Japan. Biotechnology and pharmaceuticals are number nine and ten in the list of top technical fields in patent applications. While over the last decade the number of European patent applications doubled in the field of medical technology, pharmaceuticals and biotechnology patent applications were relatively stagnant. This is shown in the graph below.

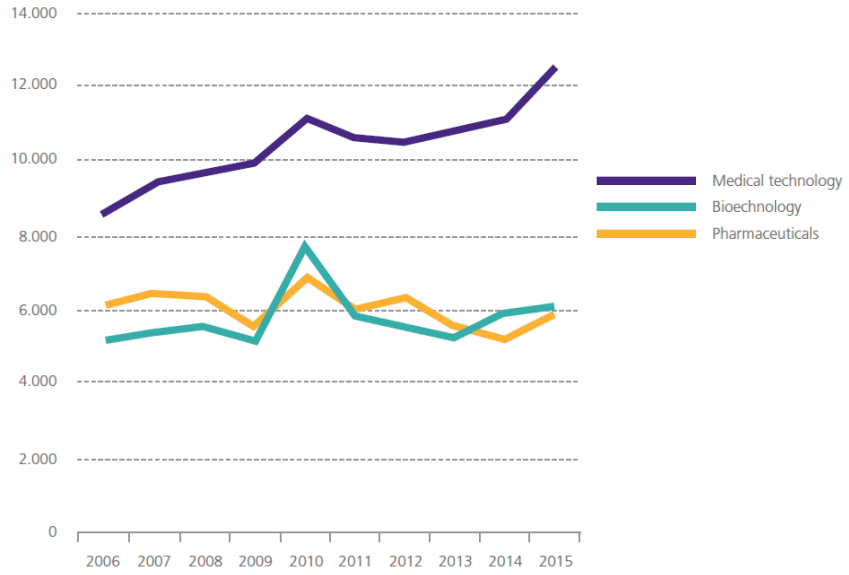

Figure 3: Evolution of European Patent Applications of Medical Technology, Biotechnology and Pharmaceuticals [2]

Market size

Worldwide Medical Technology has a market of approximately 350 billion dollars. [20] USA represents 39% of the market, followed by Europe with 31%. This European medical technology market is estimated roughly €100 billion. The market size of the top 10 European countries based upon the manufacturer prices can be found in Figure 4. [2] [21]

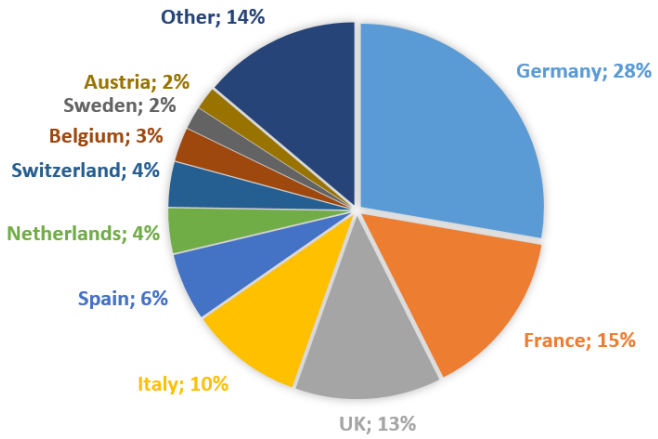

Figure 4: European Medical Device market by country in 2015 [2]

Belgium has only 3% of the European market. The biggest MedTech markets in Europe are Germany, France, the United Kingdom, Italy and Spain. There are almost 25,000 medical technology companies in Europe. The European medical technology market has been growing on average by 4.6% per year over the past 8 years. The graph below shows the European medical device market growth rates.

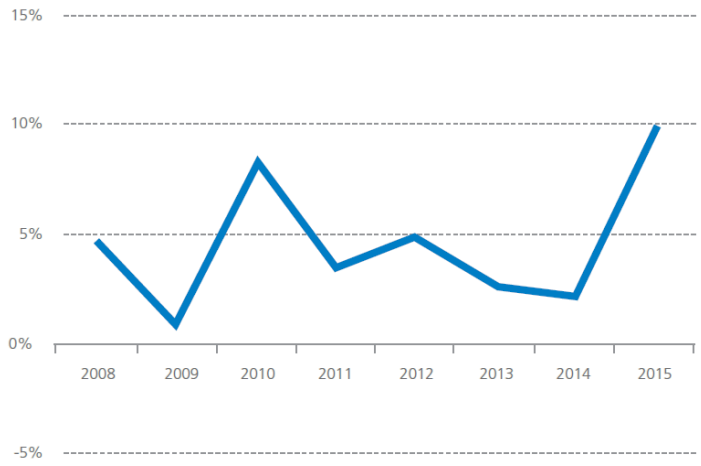

Figure 5: European Medical Device Market Growth Rates, based upon manufacturer prices (2008-2015) [2]

It is clear to see that the demand for medical devices dropped in 2009 due to the economic crisis. The market recovered in 2010, but growth rates decreased in 2011. During 2015, the growth rate again made a big headway to almost 10%. The figures for the past year have not yet been published, but again a positive increase of the growth rate is expected.

Employment

In Europe, there are approximately 26,000 MedTech companies. The importance of the MedTech industry is reflected in the high level of employment. There are approximately 650,000 people employed in the European

MedTech sector, while the European pharma industry employs around 700,000 people. From this we can say that the medical technology industry is an important player in the European economy.

The graph in Figure 6 shows the top ten European countries with the most number of people employed in the medical technology industry per 10,000 habitants.

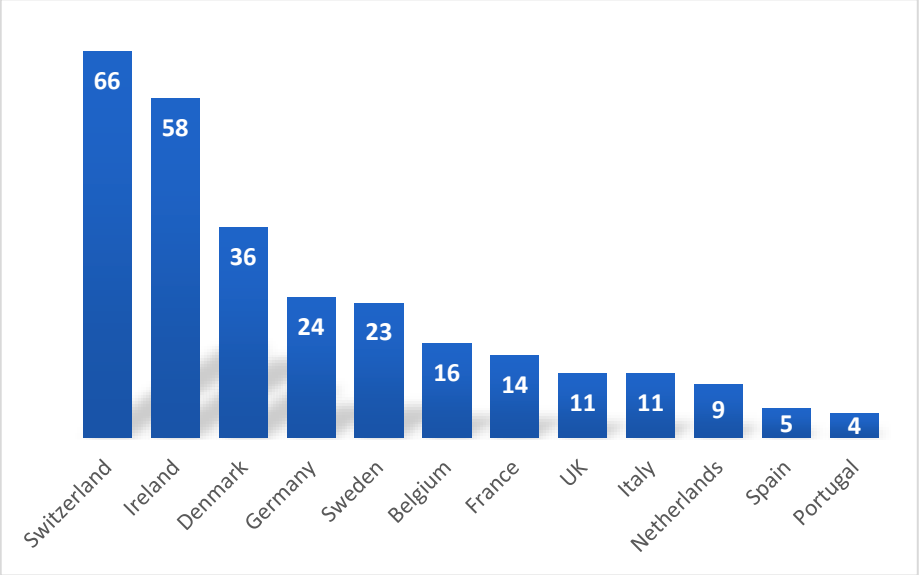

Figure 6: Number of people employed in the medical technology industry per 10,000 inhabitants [2]

Sweden is the largest employer of the European MedTech industry. Curiously, the highest scoring countries in terms of employment do not match the countries with the largest market size, based on the figures MedTech Europe published in 2015.

Trade

The MedTech trade balance for Europe is estimated at 14.1 billion euros in 2015. Compared to 2006, this trade surplus is doubled. Comparing this to the trade balance of 5 billion from the United States, one can say that Europe is very strong in the MedTech world trade. The main trade partners for the European companies are the US (58,9%), China (10,2%) and Japan (6,1%). [2]

3.2 Belgian HealthTech is alive and kicking

In the Belgian start-up landscape, HealthTech is the undisputed leader. According to a recent study of Sirris, 10% of all the technological start-ups and 46% of the scale-ups are in the field of HealthTech. 18% of these start-ups and 25% of the scale-ups are spin-off companies that have grown out of research organizations, this is twice the percentage that other sectors experience. This means that HealthTech entrepreneurship has more links to existing organizations and structures than entrepreneurship in other sectors. The universities or research organizations with the most spin-off are listed in Figure 7.

Position	Spin-off	Share
1	Université catholique de Louvain	22%
2	University of Leuven	18%
3	Ghent University	11%
4	imec	11%
5	University of Antwerp	9%
6	Université libre de Bruxelles	9%
7	Vrije Universiteit Brussel	6%
8	University of Liège	4%
9	Centre Hospitalier Universitaire de Liège	4%

Figure 7: Belgian universities or research organizations with the most spin-offs

In recent years, a lot initiatives and networks that are supporting healthcare entrepreneurship came up (Voka Health Community, MIC Flanders, impulse.brusels, Leuven Mindgate, Agoria Health, MedTech Flanders, Flanders Care etc.). This creates a real crucible of opportunities for entrepreneurs. In the beginning of September 2017, the European Commissions' European Innovation Scoreboard ranked Belgium as a champion of innovation networks. Belgian HealthTech is also doing extremely well in terms of the number of investments. We rank fourth in Europe and if we take population size into account, Belgium is actually in second place. But, if the size of investments are compared, Belgium drops to the sixth place.

Position	Country
1	France
2	UK
3	Sweden
4	Belgium
5	Germany
6	Switzerland
7	Netherlands
8	Ireland
9	Spain
10	Italy

Figure 8: European ranking of number of investments in HealthTech

Position	Country
1	Switzerland
2	UK
3	France
4	Sweden
5	Ireland
6	Belgium
7	Serbia
8	Spain
9	Germany
10	Netherlands

Figure 9: European ranking of size of investments in HealthTech

Brussels, Ghent and Leuven are the places to be for HealthTech in Belgium. 26% of health start-ups are to be found in the capital city, with another 10% in Ghent and 8% in Leuven. By number of scale-ups in 2016, Ghent is in the sixth place internationally.

Position	City
1	Paris
2	Stockholm
3	London
4	Cambridge
5	Lausanne
6	Ghent
7	Oslo
8	Barcelona

Figure 10: Top of the cities with most scale-ups during 2016.

Throughout Europe, the government is the most important investor for start-ups, mainly through public and semi-public investment funds. Entrepreneurship in Belgian HealthTech is alive and kicking, and capable of taking the leap towards international business. There is a whole crowd of interesting health start-ups with the potential of further growth. Realizing this potential requires faster market penetration. [22]

3.3 The fourth industrial revolution

During the First Industrial Revolution which took place in the late 18th century, the use of new energy sources including fuels and motive power (coal, steam engine, petroleum…) was introduced. In addition, they started to use new basic materials as iron and steel. Due to the rapid industrial developments during the beginning of the 20th century (the moving assembly line, mass production…) the Second Industrial Revolution came in. The enormous expansion of railways, electricity and telegraph lines culminated in a new wave of globalization, which also had a significant impact on this second revolution. In the 1970s, a new convergence of electronics, communication and information technology are merged to create a powerful new infrastructure for a Third Industrial Revolution.

According to the German Professor Klaus Schwab, founder and executive chairman of the World Economic Forum, we are currently in the midst of a "Fourth Industrial Revolution" that will radically change the way we work and live. This "Industry 4.0" is building on the Third Industrial Revolution and will bring "fusion of technologies that is blurring the lines between physical, digital and biological spheres". The healthcare sector with as core the MedTech and CareTech industry is transforming and evolving fast thanks to the advent of technologies.

According to Schwab there are three reasons why today's transformations represent not merely a prolongation of the Third Industrial Revolution but it can be considered as a next revolution. The first one is the speed of the current breakthroughs. Industry 4.0 is evolving at an exponential rather than a linear pace compared to earlier revolutions. Moreover, it is disrupting almost every industry in every country which makes

it a revolution with a large scope. Across every industry, businesses are currently adopting new technological innovations as a means of gaining a competitive advantage, and the medical industry is no exception. The third reason is the system impact, the breadth and depth of the changes herald the transformation of entire systems of production, management and governance. “The possibilities of billions of people connected by mobile devices, with unprecedented processing power, storage capacity, and access to knowledge, are unlimited. And these possibilities will be multiplied by emerging technology breakthroughs in fields such as artificial intelligence, robotics, the Internet of Things, autonomous vehicles, 3-D printing, nanotechnology, biotechnology, materials science, energy storage, and quantum computing.”, according to Prof. Schwab.

These new technological possibilities bring for providers of healthcare and medical devices new opportunities to address the challenges they face. For example, 3D printing technologies make it possible to design tailor-made implants and prosthetics for individuals or custom designed hearing aids to the exact geometry of a person’s ear. Customized bionic eyes can help people with profound vision loss by a retinal implant. Technologies like telemedicine, robotics and drones can make it easier to support aging individuals in monitoring or receiving caregiving. Mobile health applications can monitor and provide direct provision of care to patients and helps healthcare being accessible across the world.

Nanotechnology (the ability to manipulate atoms and molecules, has the potential to vastly improve diagnosis and treatment. Technological development is happening at every corner of the MedTech field.

It will be crucial to have a healthy regulatory environment that creates a business ecosystem that supports SMEs and encourages innovation and creativity. The medical industry is positively transforming due to these technological advances. Embracing the technological advances enables challenges to be addressed in ways not previously achievable, ultimately helping patients to live better, healthier and longer lives.

Risks and responsibilities associated with these quick changes will also need to be considered, such as the possibility of hacking medical devices, privacy, confidentiality, financial inequality, aging and overpopulation, transhumanism or bioterrorism. [23] [24] [25] [26] [27]

3.4 Small and Medium Enterprises (SMEs)

It is estimated that small and medium-sized companies (SMEs) make up 95% of the industry, the majority of which employ less than 50 people. Research about medical technology is usually the result of small or micro collaborations between health professionals, academia and SMEs. The rapid MedTech innovations are the results of this particular business and research interaction model. Unfortunately, many SMEs are failing, making many new technologies never see the light of day.

Why Start-ups fail

In 2014, CB insights analysed 101 start-up failure post-mortems to identify the top reasons start-ups fail. The top 20 reasons can be found in Figure 11.

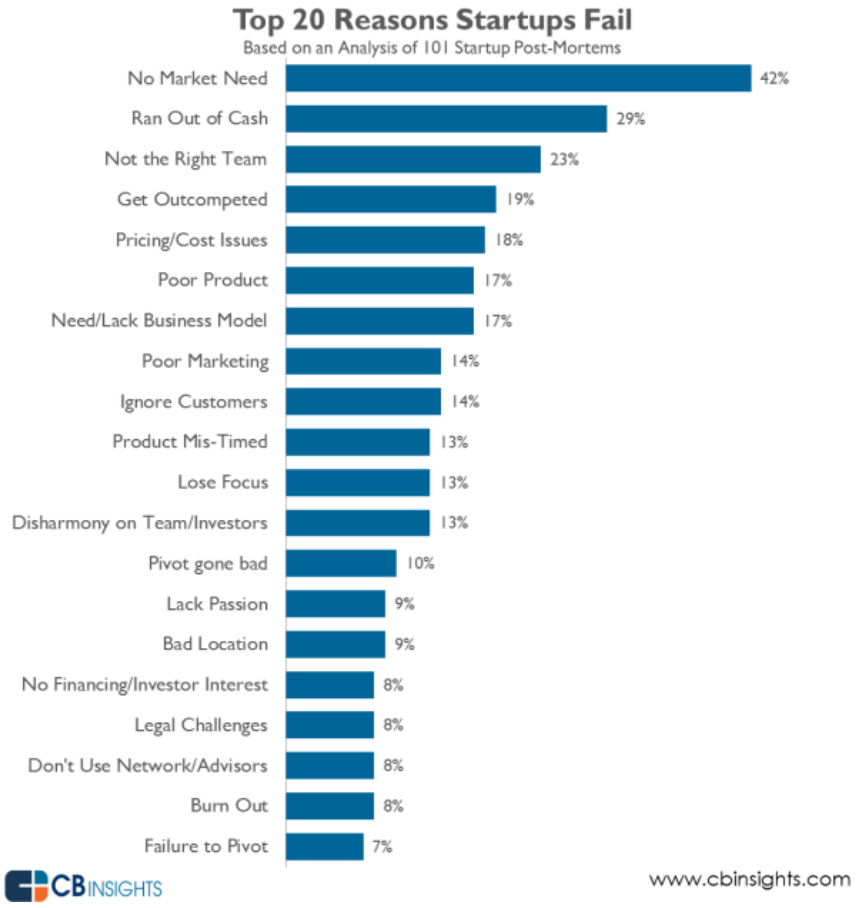

Figure 11: Top 20 reasons start-ups fail according to CB Insights

It is clear to see that market need is unmistakable, the product or service should have a clear, unmet clinical need. Next to this, funding and the composition of a cross functional team is very important to survive as a start-up. This is definitely the case in the field of MedTech. [28]

Valley of Death

Start-ups have difficulties with covering their negative cash flow during the early stages of the product development. The costs for R&D, prototyping and starting up your business are piling up, while there are no revenues from real customers. Most of the time are the up-front development costs for medical devices very high. The start-ups need to attract investors, but these investors want a proven business model before they invest, rather than the riskier research and development efforts. There is less seed capital available for "early stage investments". Many valuable ideas and concepts for new medical devices do not survive the so-called "Valley of Death" (first described by Osawana in 2006). [3] [29]

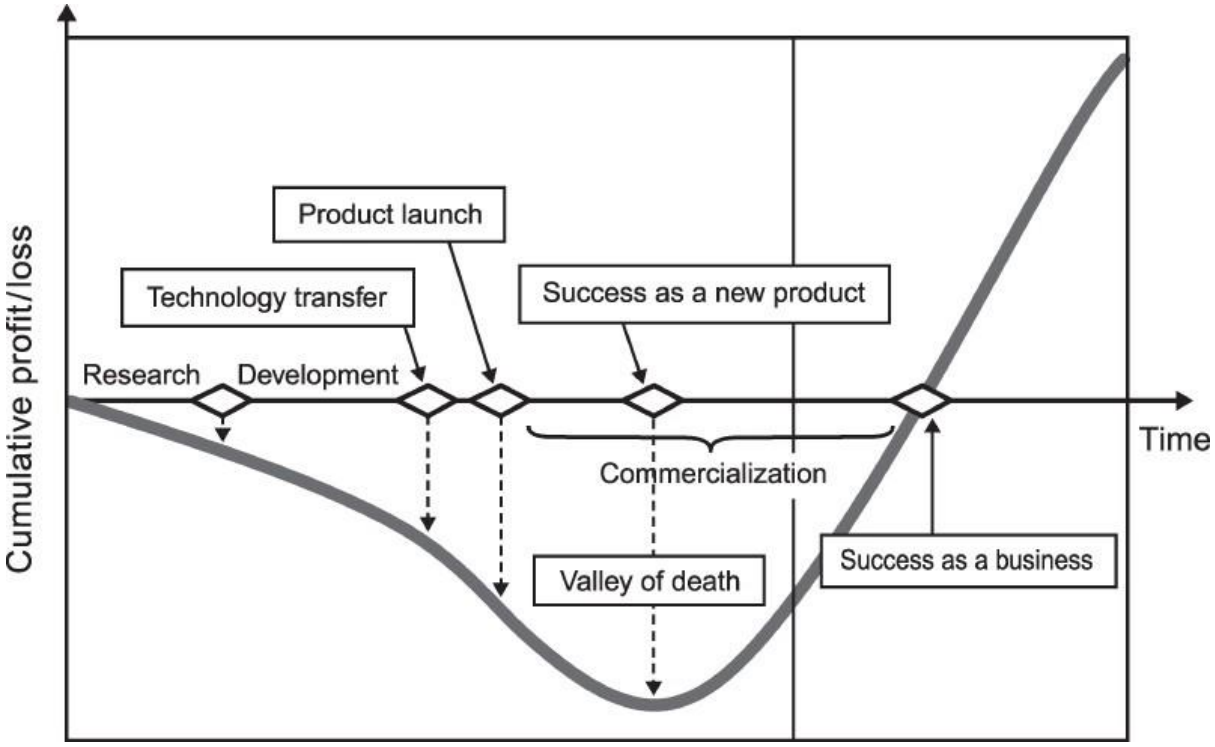

Figure 12: Valley of Death [30]

The life cycle of medical devices today is on average four to five years. During this short period, the investment must be recouped. Next to investors, the research and development can be subsidized. Mostly, these subsidies expire when one has a prototype. To get all the necessary regulatory approvals, it takes a period of two or three years. Meanwhile, the product cannot be launched on the market. It is hard to close the financial gap during this long timespan. Many interesting innovations never reach the patient, because the company is failing in bridging this "Valley of Death".

Towards a better framework for SMEs

The MedTech SMEs should be more encouraged and supported by governments to reduce the cost of healthcare and increase benefit to society.

In 2014, the Class Technical Sciences of the Flemish association KVAB (Koninklijke Vlaamse Academie van België voor Wetenschappen en Kunsten) published a white paper "Health Technology (MedTech), a driver for innovative health care", written by Professor P. Verdonck. An analysis was made on how the Belgian companies and start-ups can play a leading part in the MedTech sector. The absolute necessity of integrated thinking and a permanent dialogue between government, industry and hospitals while putting the patient centre stage, was illustrated. Several recommendations at federal and Flemish level were formulated to encourage the MedTech industry in Flanders, including a better supportive and economic favourable

framework for research and development of medical technologies. There are eight major thresholds for start-up companies in Flanders are:

1. Visibility & internal networking
2. Sharing of know-how and infrastructure
3. Knowledge of eHealth data ecosystems
4. Knowledge of quality systems
5. Reimbursement
6. HR-recruitment
7. Access to venture capital
8. Marketing & Business coaching

This framework can be an incentive for the creation of new MedTech companies. The creation of a unique platform was suggested to bring the companies and researches in the MedTech field together and to let them become familiar with the complex valorisation process of a medical device. The existing information channels and financial resources of the government should also be communicated through this platform. Next to this, eight needed policy lines for start-up SMEs active in Medical Technology are formulated. [3] The European Commission is also taking action to better support SMEs. Europe 2020 is the EU's growth strategy for the current decade with five ambitious objectives to be reached by 2020. They focus positively on strengthening and further developing EU policies that support innovation particularly for small and medium-sized enterprises. [31]

4 The MedTech network

4.1 European regulatory

The European MedTech industry is regulated by three Directives (as described above). National legislation at every EU country needs to implement the chalk lines of the European Directives. The Directives are accompanied with some guidance documents to promote a common approach to the implementation of the procedures as laid down in the Directives. As mentioned, the three Directives are replaced by two new EU regulations on May 5, 2017. Currently, there is a transitional period of 3 years for medical devices and 5 years for In Vitro Diagnostic medical devices.

US regulation

At the United States, the regulations according to medical devices are determined by the federal agency FDA (Food and Drug Administration). The Centre for Devices and Radiological Health (CDRH) is the department of the FDA responsible for the premarket approval of all medical devices. [32] The most medical devices should be "FDA-cleared" or "FDA-Approved" prior to marketing a medical device. Respectively a 510(k) or PMA application needs to be filed (depending on the classification of the medical device). Clearance requests are for medical devices when the submitter of the 510(k) shows that the medical device is "substantially equivalent" to a device that is already legally marketed for the same use. To acquire an approval of a device through PMA application, the submitter must provide reasonable assurance of the device's safety and effectiveness. [33]

4.2 Competent Bodies

Each EEA (European Economic Area) member state specifies some Competent Bodies (CB), also called "Competent Authorities" to enact the directive within its territory. Each CB can specify one or more Notified Bodies (NB), to act as third party accessors of the manufacturer's compliance.

4.3 Notified Bodies

A notified body is an organization designated by an EU country to assess the conformity of certain products (accreditation) before being placed on the market. These bodies carry out tasks related to conformity assessment procedures set out in the applicable legislation, when a third party is required. The European Commission publishes a list of such notified bodies.

Notified bodies are responsible for the conformity assessment. The manufacturer of a medical device can only launch the product on the EU market when it meets all the applicable requirements. The conformity of a

product is assessed before the product can be sold. The assessment includes testing, inspecting and certification after demonstration by the manufacturer that all legislative requirements are met. A Notified body may designate that a medical device conforms to the EU Medical Device Directive. Depending on its intended purpose and risks, a medical device may be classified as Class I, IIa, IIb or III. The higher the classification, the greater the level of assessment required.

CE Marking

With this 'Declaration of Conformity', the manufacturer can label the product with the CE Marking, which is required for distribution and sale in the EU. The EU member state accrediting the notified body will then inform the European Commission that the product complies with set standards. Manufacturers are free to choose any notified body that has been legally designated to carry out the conformity assessment procedure. The European Commission maintains an up-to-date list of bodies notified by EU countries. [34] [35] [36]

4.4 Public Health Authorities

Most medical technologies are paid for by Public Health Authorities, usually within a third-party payer system. The reimbursement decisions are made on different levels in each country (regional authorities or at national level). The amount paid for services might differ even within a country. For the MedTech companies, it is a complex system to navigate through.

Healthcare in Belgium is mainly the responsibility of the federal minister and the "FOD Volksgezondheid en Sociale Zekerheid". Both the Belgian federal government and the Regional governments (Flemish region, Walloon region and German-speaking community) have ministers for public health and a supportive administrative civil service. [37] Next to the regional, provincial and local authorities there is a complex federal structure including the Public Administration for Public Health, Food Chain Safety and environment, MEDDEX (Department for medical expertise), Superior Health Council, Scientific Institute of Public Health [38], Federal Agency for medicine and health products (FAGG or FAMHP) [39] etc.

The Belgian National Institute for Disease and Invalidity Insurance, RIZIV (Rijksinstituut voor Ziekte- en Invaliditeitsverzekering, RIZIV or French: INAMI) is a public institution for social security. This institution decides which products or services gain a reimbursement in Belgium. It is very important for the MedTech companies to understand the local payment and reimbursement systems together with policy environments and healthcare systems. Today, it is difficult for the new medical technologies to find their place in the RIZIV's repayment systems. The budget is calculated according to the expenses of the past years, a new technology is often seen as an additional cost, while it is most of the time difficult to accurately evaluate this. [3] [40]

4.5 Investors

The funding of a start-up is very different for each type of company, but every start-up typically goes through several rounds of funding. The graph in Figure 13 shows a typical start-up funding life cycle. The blue line represents the cashflow of the start-up, while the pink line shows the cumulated investments.

Seed capital stage

In this stage the R&D of the new product or service requires a lot of capital. Most of the time the seed capital introduced by the founders of the company and some friends or family. The start-up attempts to gain subsidies or research support of universities, organizations or government funds. Occasionally a crowd funding campaign is set. At this moment, the phenomenon "valley of death" also comes up.

Early stage

During the early stage, Business Angels invest heavily in the start-up. This is a person who has professional experience and expertise in the sector and makes a small portion of his assets available to a start-up. In return for the investment, the Business Angel will receive a part of the shares of the company.

Growth stages

During the early and later growth stages the company endeavours to grow sales. Mostly the company passed the break-even point already at this stage. This stage contains follow-up financing from angel groups, venture capital or investment funds. A venture capital (VC) is a type of private equity capital in which funding is provided to ventures to support their growth, development and expansion, in exchange for equity. The objective of the VC is to generate a return through the realization of a future liquidation event (sale to strategic player or an Initial Public Offering (IPO)). The VC firms source their funds for investment from high net worth individuals through funds.

Mezzanine financing stage

If the expansion continues, the venture attempts to scale its sales. The companies in these later stages of development generally have fully vetted business models, commercialized their product and already achieved reasonable sales momentum. They are looking for additional financing to exponentially scale or grow the company.

Exit stage

The last of the start-up funding rounds. The exit stage requires a bridge round from VCs and culminates in an Initial Public Offer (IPO) or sale the start-up to a strategic player. [41]

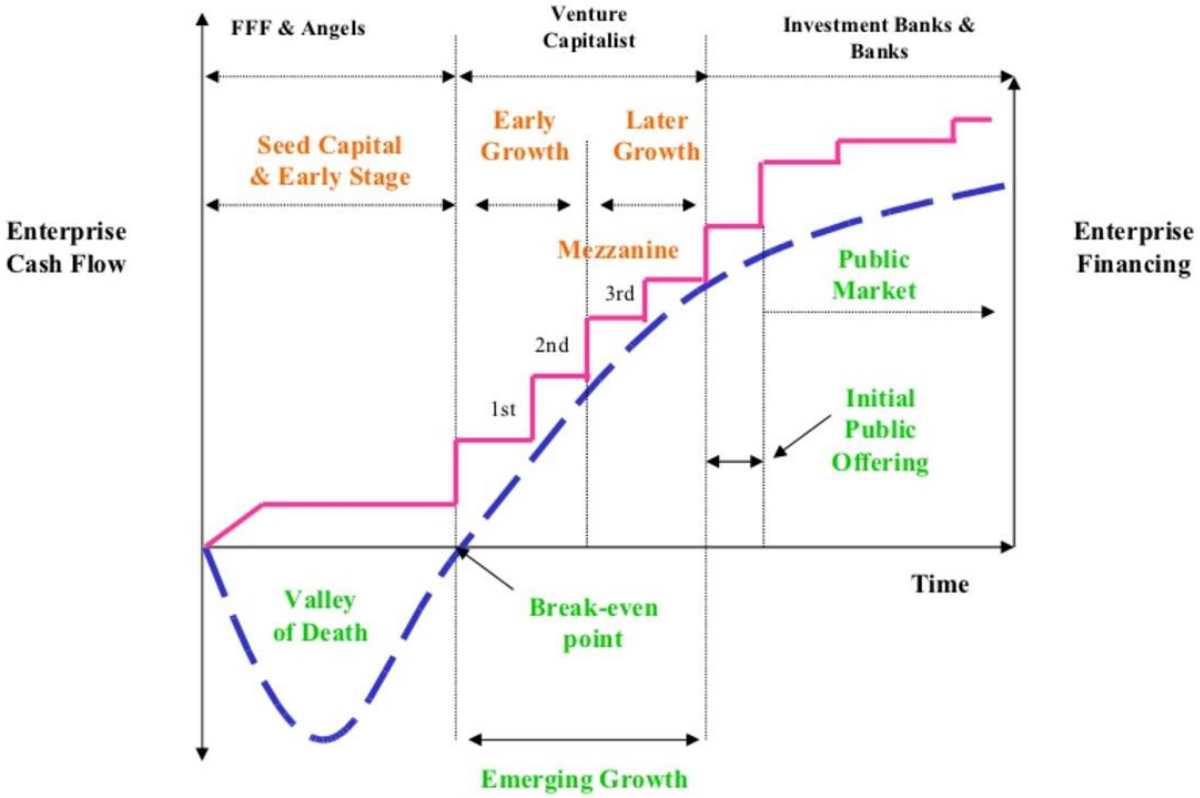

Figure 13: start-up financing cycle [42]

4.6 Manufacturers

The manufacturer is any natural or legal person who is responsible for designing and manufacturing a product with a view to placing it on the Community market "under his own name" (or trademark). Where subcontracting takes place, the manufacturer must retain the overall control for the product and ensure that he receives all the information that is necessary to fulfil his responsibilities according to the 'New Approach Directives'. [43]

4.7 Industry associations

There are several MedTech industry associations at different geographic levels. They all have the mission to make innovative medical technology available to more people and try to make healthcare systems more sustainable. The associations are promoting medical technology's value and the value-based innovations of the industry and do economic research to show the benefits of medical technology. At different initiatives (forums, conferences…) they bring stakeholders together to discuss industry policy, trends, issues and opportunities. The associations also want to help the MedTech industry to meet the growing needs and expectations of the healthcare system.

beMedTech and the National Committee of Biomedical Engineering are partial active in the field of MedTech. Next to these Belgian organisations, there are initiatives on regional level like Voka Health and a lot of companies and research institutes within the field of CareTech. Some institutions as iMinds Health and Flanders' Care are active at both domains. In recent years, several organizations have been created that are also specifically aimed at supporting MedTech.

There are some **LifeTech organizations**, this are non-profit associations which aim to support and to facilitate the development of health and health-care related businesses in their local region. Examples are LifeTech Brussels, LifeTech Limburg, Flanders Smart Hub LifeTech etc.

MedTech Europe is an alliance of European medical technology industry associations founded in 2012. Currently there are the merging of two existing organizations: **EDMA** representing the European in vitro diagnostic industry and **Eucomed** representing the European medical devices industry.

beMedTech is the Belgian federation of the industry of medical technologies. They have a structure based on 5 product groups: implants, medical consumables, medical equipment and systems, in vitro diagnostics and Extra Muros interdisciplinary services and care. These groups are further subdivided into sections to deal with issues specific to a market segment.

MedTech Flanders is a network organization of Flemish medical device companies together with research partners, subcontractors and partner-organizations. This organization is discussed in the next chapter.

Overview of HealthTech stakeholders, source: Sirris

Figure 14: Overview of stakeholders and organizations in the MedTech development field

4.8 Other stakeholders

There are also other important stakeholders. The **patients** should always putted central during the development of medical devices. In Flanders, patients are represented in the sector by organizations like the Flemish Patient Forum. The **caregivers** and **doctors** will use or need to introduce the medical device at the patient. In the regulatory framework there are a lot of consultative bodies who represent the patients, doctors and patients (commissions, joint commissions, committees, board of physicians, advisory boards for coma patients,...). [44]

5 MedTech Flanders

The subject of this master dissertation was commissioned by MedTech Flanders. MedTech Flanders is a network organization of Flemish medical device companies together with research partners, subcontractors and partner-organizations. The mission of MedTech Flanders is to support the development of Medical Technology in Flanders so it would become an important economic activity in our Flemish region. This cluster of MedTech companies and organizations can positively stimulate each other towards an international recognized eco-system. The organization was founded in 2015 with the goal to double the production and export of Flemish Medical Technology within five years.

The core members of MedTech Flanders are companies who are developing medical devices in Flanders, according to the European Medical Device regulation. In addition, there are general members who are developing other medical technology products in Flanders. At present 27 members have joined the network.

Figure 15: Members of MedTech Flanders

Flanders is currently playing a limited role within the MedTech industry. However, there are many top researchers in Flanders who develop advanced medical technology and there are number of renowned Flemish hospitals asking to fit new innovations into their practice. The step between the research and development on the one hand and the commercialization and implementation of the products on the other hand, appears to be very large in practice. The complexity of the health care sector (regulation, privacy laws, etc.) is an additional difficulty. Nevertheless, there is a lot of potential to further develop the MedTech sector in Flanders because of the excellent healthcare system and the talented researchers. MedTech Flanders can provide important incentives to allow the sector to become a mainstay of the Flemish economy. Their strategic plan consists of three pillars. First, they want to support the further growth of existing MedTech SMEs in collaboration with existing organizations and the government. In addition, they want to stimulate new activities or the establishment of new start-ups by bringing together physicians, clinicians, technology experts and entrepreneurs. The third pillar is to facilitate the complex medical product development trajectory, so the new technologies certainly reach the patients.

In practice the MedTech Flanders cluster of medical technology companies can positively stimulate each other and share their knowledge, equipment, facilities and network. By working together, the companies can achieve some economies of scale and they can reach out more easy to additional workers or investors. An umbrella organisation representing a sector may also put more pressure on government discussions. In the end, the focus should be on the patient. New (lifesaving) medical technologies or products should find their way faster to the patient.

II. DETERMINING THE EVALUATION FRAMEWORK WITH APPROPRIATE PARAMETERS

1 Project scope

1.1 Problem description

The goal of the development of medical devices is to provide a better quality of life, better treatments for patients and ultimately save lives. As previously described, medical devices play a crucial role in the prevention, diagnosis, treatment and monitoring of diseases, medical conditions or disabilities. The common drive through all applications of medical technology is the beneficial impact on health, quality of life and society as a whole.

But the development team of a new medical device faces difficult challenges. First of all, they need to navigate through the complicated legislation for medical devices. In addition to complying with regulations (directives, CE-labels…), one must set up a full quality system (ISO 13485 certification). The companies need a strategy about how they will protect their ideas and inventions (Intellectual Property Protection, Patents, keeping the technology black-box…). Clinical trials often make an important part of the product development process; these trials also involve a lot of regulations and strategy thinking. On top, there are many economical complications. Most of the MedTech companies are SMEs. They struggle with the 'Valley of Death', investor-funding, reimbursements by public health authorities and access to government grants.

As a consequence of these thresholds, many good ideas or new technologies do not reach the patient. Developments in medical devices or new technologies need to reach patients, caregivers or hospitals in a faster way. The engineers, researchers and developers need early recognition and understanding of the complex valorisation trajectory to develop and launch a medical device. In addition, the real needs of the patient population (the pull-theory) must be known to evaluate if the medical device fills up a clear unmet clinical need and has an added value for the patient, the healthcare system, the society. Also, the commercialization and implementation of the products are stumbling blocks. MedTech Flanders wants to

stimulate new activities and support start-ups and SMEs in the field of MedTech by facilitating the complex development trajectory for a new medical device.

1.2 Project objective

The purpose of this master dissertation is to develop a simulation model, a tool to support newly established MedTech development teams with the early understanding of the complex development process of a new medical device.

On the one hand the tool should estimate the success rate potential of a start-up with the new product or service they have in mind. With the given knowledge and organizational structure of the start-up, one wants to predict the quantitative success rate of ideation. This tool should include a risk analysis of the product development cycle of a new MedTech product or service. Attention must be given to many criteria like: needs of the patient population, the health-economic complexity of reimbursements, innovation-degree of the product or service, skills covered by the cross functional development team etc. On the other hand, the simulation must help to gain insight and awareness among the product-developers with the feasibility of the technological, economic and regulatory development process. Knowledge, expertise and insights from various experts in the field of MedTech must be passed on to the new developers and researchers. The experience of start-up engineering companies already affiliated with MedTech Flanders must be included in the algorithm.

A simulation with the new simulation model should lead to a quantitative proposal of the success-rate (expressed as a percentage) to go from an idea to a commercialized product or service. The solution model must be sufficiently robust to enable an investigator to gain insight on the basis of simulations into the feasibility of the technological and economic development trajectory of a clinical product.

1.3 Project outline

The evaluation process consists of three major steps. First, there is a newly developed questionnaire presented to the development team. Based on their selected answers, certain weights are elected to the answers in a mathematical algorithm. This simulation algorithm has to generate a total success rate together with a report with strengths, weaknesses and pitfalls of the organization and the concept

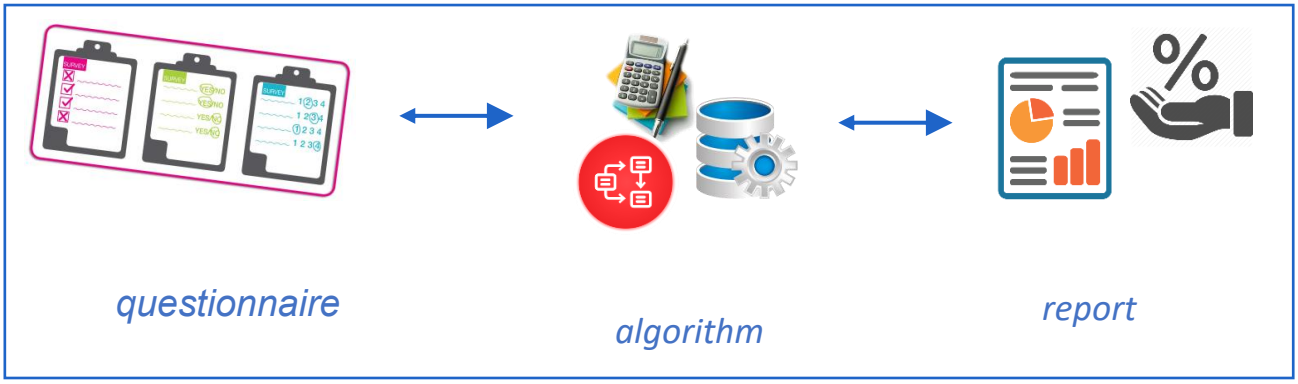

Figure 16: Structure of the evaluation process

1. **Questionnaire**

The evaluation tool should be a simple multiple-choice questionnaire for the end-user. The medical device developers should be able to answer the questions without looking for documents or data. The questions must be to the point but not too complex at the same time. To limit the complexity of the model, only multiple choice questions are considered. Open answer questions are too difficult to identify and quantify when an automated computer algorithm is implemented without the use of artificial intelligence. The questions must be generic in the first version of the tool. The questionnaire can be filled in by development teams from all different types of (active) medical devices; also by software developers, designers of eHealth applications or manufacturers of patient-specific prosthetics. So the tool is also useful for HealthTech applications. But the target group are start-ups in the field of MedTech. These companies must already have a business case in order to properly fill in the survey.

2. **Algorithm**

The algorithm should assign a weight or score to each possible answer. The weight of the chosen answer must be stored. By doing mathematical calculations on all weights linked to the answers, a total success rate must be retrieved. The parameters linked to the questions that obtain a low score must be saved to be able to show the pitfalls of the organization or medical device.

3. **Report**

The total success rate for the start-up with the product or service they putted forward, should be presented in one report. In addition, one can zoom on the scores of the different evaluated parts of the development process. Starting from this report, it will be possible to deduce the strengths, weaknesses and pitfalls of the organization or the medical device.

2 Evaluation framework

2.1 Medical device evaluation from different stakeholder perspectives

The first step in building the tool is finding the right evaluation criteria and parameters. Both the innovation-degree of the new product or service as well the internal organization of the start-up must be examined. At a later stage, these parameters should be queried in questions. It is important to gain insights from the perspective of investors, hospitals, caregivers, patients, public health regulators and other stakeholders. The various actors in the MedTech network pay attention to other determinants when they evaluate new technologies. The stakeholders are seeking value through managing clinical benefit, increased access, improved life-quality and financial implications (cost-effectiveness, revenue, budget impact, financial stability…). There are many ways to investigate value proposition with different types of quality measures.

Patient point of view

When customers evaluate a product or service, they consider implicitly value against the price. What consumers truly value is always difficult to pin down and is psychologically complicated. In the September 2016 issue of 'Harvard Business Review', an article of three Bain & Company costumer strategy partners was published about the elements of the value pyramid of consumer value. They identified 30 "elements of value" that fall into four categories: functional, emotional, life changing and social impact. These 30 fundamental attributes were derived from scores of quantitative and qualitative customer studies. The four categories extend Maslow's "hierarchy of needs". This model is mostly represented in a pyramid with the physiological and safety needs at the bottom and self-actualization and self-transcendence at the top.

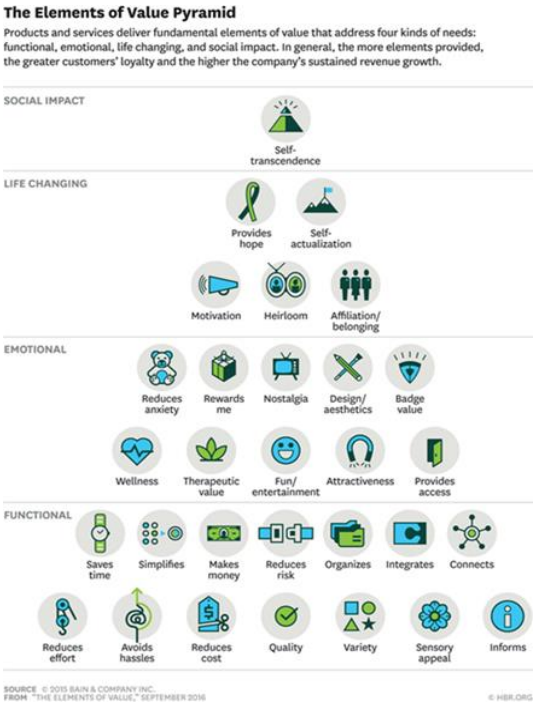

Figure 17: The Elements of Value Pyramid (Bain & Company, 2016)

In general, the more elements provided in a presented product or service, the greater customers' loyalty and the higher the company's sustained revenue growth. It's obviously unrealistic to try to inject all 30 elements into one product or service. Companies must choose their elements strategically. According to the study, companies doing well on multiple elements have more loyal customers and they correlate closely with higher and sustained revenue growth. The elements of value work best when company's leaders recognize them as a growth opportunity and make value a priority with customer-centric design of prototype concepts. For medical devices, a clear unmet clinical need is necessary to differentiate from different other devices. A preliminary market analysis needs to be performed to ensure there is a sufficient market opportunity for the clinical need. Mobilizing resources to meet these needs would certainly avoid further expenses, keep patients satisfied with services and lead to better quality of life. The medical device development teams need to describe what patients, or the population desire to receive from health care services to improve overall health. [45]

Hospital or caregivers point of view

In 2013, Boston Healthcare Associates introduced a model with different evaluation criteria for a new healthcare technology adoption. The purpose was to evaluate new health technologies from the hospital perspective. They proposed to establish Hospital Value Assessment Committees (VAC), including clinicians representing various specialties, nurses and hospital administrators. They need to make an assessment of the new technology based some key review elements (revenue impact, return-on-investment, complication rate, accuracy, safety, OR (operation room) turnaround time, ease of use, price, patient outcome and length of stay). If the technology is deemed appropriate by the VAC, they refine the value proposition. Therefore, they have different value dimensions shown in Figure 18. The value dimensions are clinical impact, economic impact, training and education, performance measurement and documentation, distribution and logistics, patient satisfaction and experience.

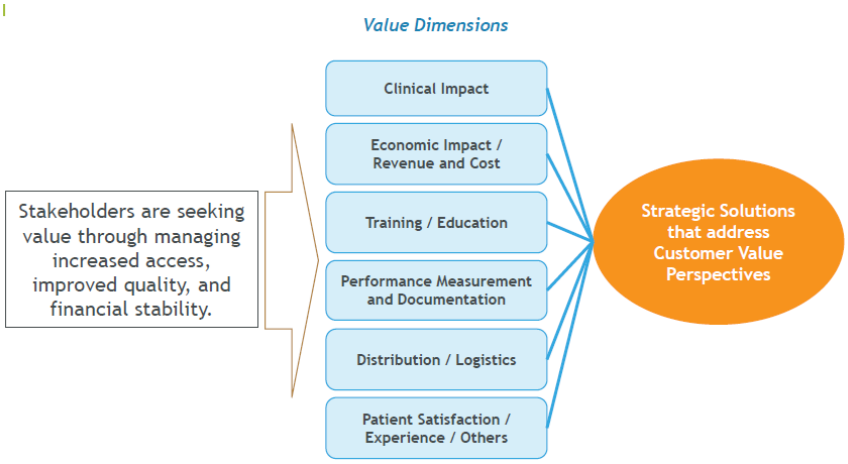

Figure 18: Value proposition with different value dimensions, according to Boston Healthcare Associates (2013)

After implementing the new technology, quality measures should be set to evaluate. There are different measure types possible like access, composite performance, efficiency, patient reported outcome/performance, patient experience, process, cost and resource use or structural implications relevant to the capacity of the healthcare organization. [46] For the evaluation tool this type of VAC evaluations casts light on the problem from just one perspective. Important criteria such as intellectual property protection, regulations, quality systems, marketing tools need to be implemented to look from the viewpoint of the start-up.

Investor point of view

Evidently, investors have a completely different perspective on MedTech developments. Business Angels (BA), Venture Capitalists (VC) and investment funds attach importance to the business case of the new MedTech start-up. From conversations with a few investors (both inside and outside the MedTech field), we learned that most of them have the same approach to evaluate new opportunities. When there is room for new projects in the investment budget, they start the sourcing phase. The offering of the start-up should hold enough potential in a sizable market with a well-defined market pain and international scoop. The eight most important evaluation criteria are listed below.

- **Market potential:** there must be a clear market demand. The payers need to be willing to reimburse by the time the technology hits the market and the clinicians, hospitals or patients are willing to purchase the product. There is no technology push but a market pull by a clear unmet clinical need. The start-up needs to work together with clinicians to better understand the most pressing healthcare challenges from around the globe.
- **Proof of concept:** this is essential to evaluate clinical feasibility before the investment. Having a proof of concept in place also speeds up animal testing and clinical trials.
- **Dramatically decrease of the healthcare costs:** the technologies should be disruptive to the current market and dramatically decrease healthcare costs.
- **Robust Intellectual Property protection:** the prospect's intellectual property protection should be carefully examined or the technology should be advanced enough to beat upcoming competition.
- **Team:** it is important for the investor that the team covers all the required skills and has experience to execute the companies' plan. The team-members need to be flexible enough to change plans when needed. The VC will co-guide the CEO or will insist to scout someone with a management profile within the medical technology industry.

- **Clear regulatory pathway:** by investing in technologies that have a clear pathway to approval from Notified Bodies, the capital efficiency is improved and the start-up is more attractive for a strategic buyer to make an acquisition.
- **Established reimbursement codes:** reimbursement for a product must be ensured before the product goes to market.
- **Exit possibilities:** there must be an attractive exit horizon for the investor. Their target is a high investment return of several multiples. The exit strategy will be identified early on to adequately tailor the development of each company for an acquisition by a strategic buyer or an IPO (Initial Public Offering).

These evaluation criteria of investors are very important to implement in the evaluation tool, because funding is one of the largest difficulties for the start-ups.

Public Health Authorities point of view

In recent years, the health-economic assessment has become important or even mandatory in many countries for providers of new drugs or medical devices. The authorities ask for such an evaluation to be able to better understand the costs and benefits of new technologies. In the most western countries, the biggest payer for these products or services is the public health insurance or a national health system. Value for money is important to spent the government budgets well. A healthier population is more productive and will also consume more and thereby contribute to growth of prosperity. The healthcare systems have a clear challenge to increase their efficiency whilst at the same time ensuring a high quality of care. The way reimbursement policies are developed is not very transparent nor predictable. Many decisions are politically-driven and the criteria are not always well described. This poor transparency means that patients are often unable to gain access to the medical device.

Many public health authorities conduct health-economic evaluations in the shape of comparative analyses of two or more interventions in care, taking into consideration both the costs and the health effects. The PICO-framework is frequently used to describe the new technology. This is a technique used in evidence based practice to frame and answer a clinical or health care related question. [47] The PICO acronym stands for:

- **P - Patient**, problem or population: Description of the group of patients covered.
- **I - Intervention:** Which main intervention, prognostic factor or exposure is considered?
- **C - Comparison, control or comparator**: What is the main alternative to compare with the intervention?
- **O - Outcome:** What will be accomplished, measured, improved or affected? [48]

Next, the **I**ncremental **C**ost-**E**ffective **R**atio (ICER) is calculated with equation (1). This statistic is used to summarise the cost-effectiveness of the new health care technology, defined by the difference in cost between the new intervention and the intervention that is currently reimbursed, divided by the difference in effectiveness of these interventions. [49]

$$\mathrm{ICER} = \frac{C_1 - C_0}{E_1 - E_0} \tag{1}$$

$$with \begin{cases} C_1: \text{cost of the new intervention} \\ C_0: \text{cost of the currently reimbursed intervention} \\ E_1: \text{Effectiveness of the new intervention} \\ E_0: \text{Effectiveness of the currently reimbursed intervention} \end{cases}$$

The costs are usually described in monetary units and the health effects in **Q**uality-**A**djusted **L**ife **Y**ears (QALY). Although one treatment might help someone to live longer, it might also have serious side effects. Another treatment might not help someone to extend their life, but it may improve their quality of life (e.g. reducing pain or disability). QALY is a generic measure of disease burden, including both quality and quantity of life. This makes it possible to compare different treatments. A number of factors are considered when the quality of life in terms of health is measured. They include the level of pain, the mobility of a patient, their general mood etc. QALY is the product of the years a person will live longer with a quality of live rating with values below 0 (worst possible health) to 1 (best possible health). (1 Year of Life x 1 Utility value = 1 QALY). The data of the quality of life is collected through use of surveys such as EQ-5, Time-trade-off, standard gamble or the Visual analogue scale. [50] [51]

One QALY equates to one year in perfect health. If an individual's health is below this maximum, QALYs are accrued at a rate of less than 1 per year. To be dead is associated with 0 QALYs, and in some circumstances it is possible to accrue negative QALYs to reflect health states deemed 'worse than dead'.

It is possible to use the willingness-to-pay as a threshold for the new technology. If the ICER is above this threshold, the technology will be deemed too expensive and thus should not be funded. In Figure 19 a two-dimensional representation is made. The current technology is situated at the origin and the new technology can be situated at the cost-effectiveness plane. Depending on the quadrant where the new technology is situated, a decision on the reimbursement of the new technology can be made. [49]

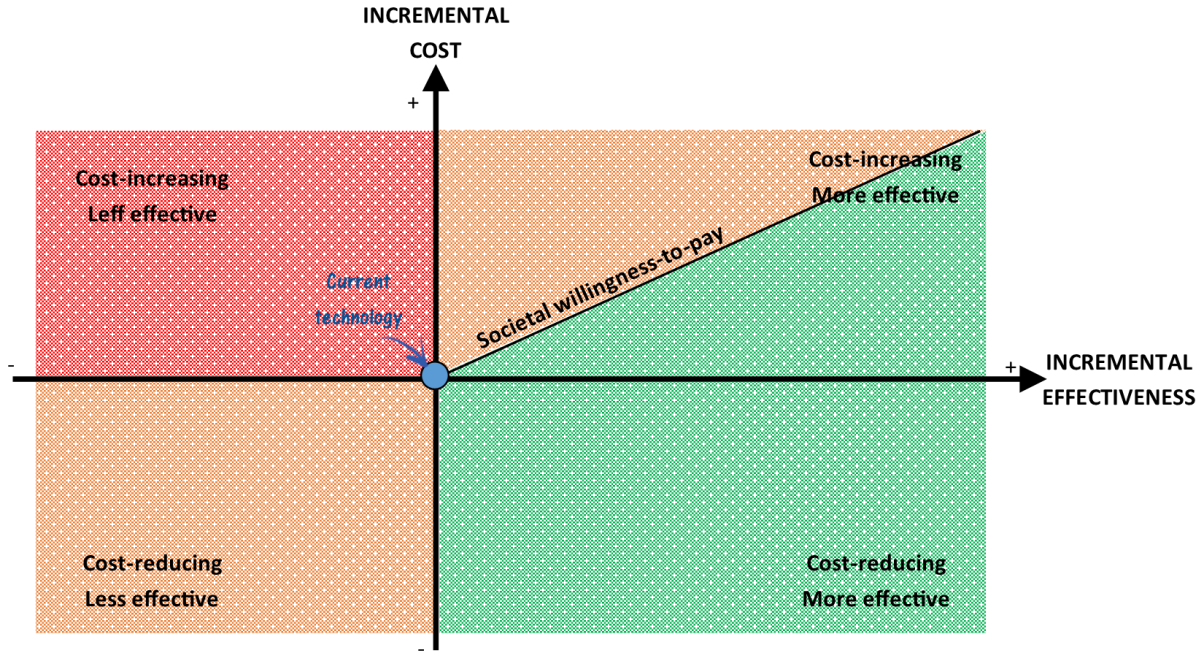

Figure 19: 2-dimensional representation of the ICER analysis

Some controversy has arisen among some healthcare experts about the use of this ratio in pricing and reimbursement decisions. Especially because this comparative analysis is a type of rationing, the use of the ICER-ratio will limit the amount or types of treatments and technologies available to patients and no healthcare system has already implemented explicit an ICER threshold. [52] [53] Next to the cost-effectiveness of the new technology compared to another, the number of patients covered should be considered.

Manufacturers point of view

The manufacturers of medical devices are working their way through the product development process. To evaluate the product or service from a manufacturer view, the different steps in the development trajectory should be overviewed. The innovators want to know which factors at each of the development stages contribute to the success of the new product or service. They want to bring the medical device as fast as possible to the market, without making any mistakes. Several process representations of the medical device development already exist.

1. Waterfall models

The design process is often graphically displayed as a waterfall, mostly with an iterative feedback loop for review, verification and validation steps. The model in Figure 20 shows a waterfall model used in the "Design Control Guidance for Medical Device Manufacturers" published by FDA in 1997 and earlier published by the Medical Device Bureau of Health Canada. [54]

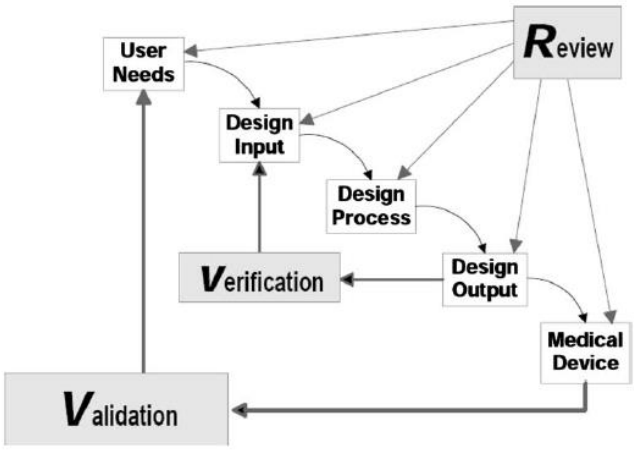

Figure 20: application of design controls to waterfall design process (Medical Devices Bureau, Health Canada)

The interaction of the different design controls is clearly displayed, but some important stages for the companies are not included like the regulatory requirements, commercialization or post-market surveillance.

2. Linear models

There are also linear models. Figure 21 shows the one used by the Medical Engineering and Research Commercialization Initiative (MERCI) of the National University of Singapore. [55]

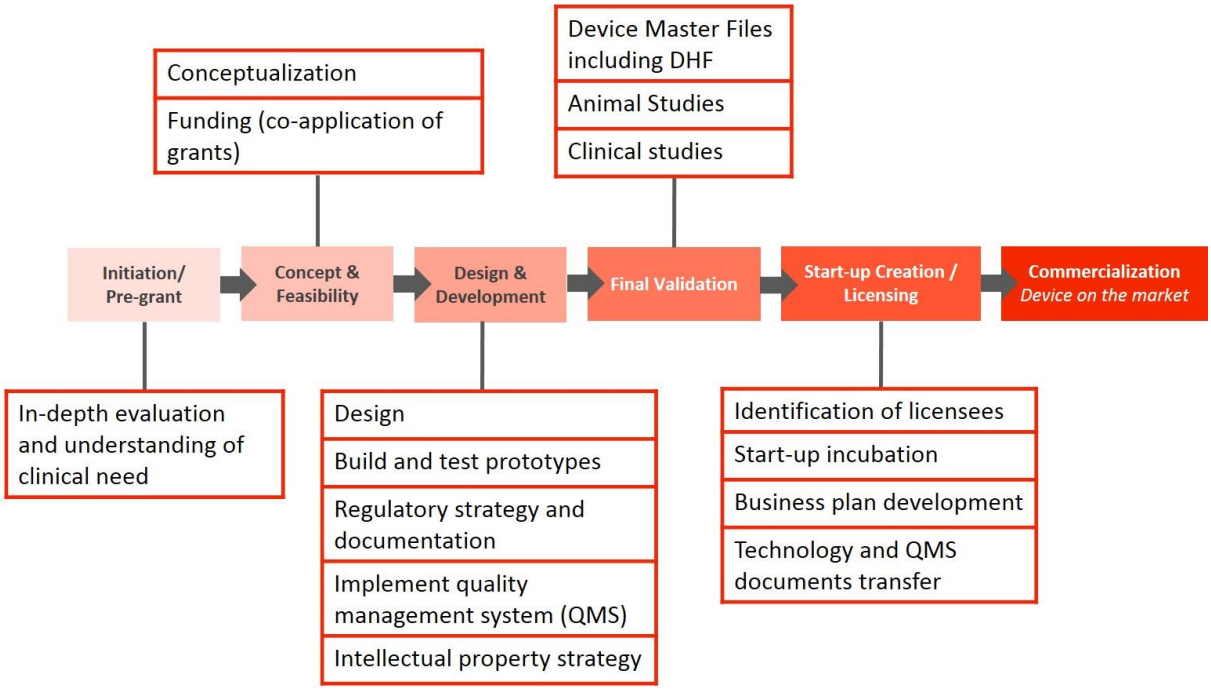

Figure 21: Linear medical device development model of the National University of Singapore [55]

This model includes nearly all the necessary steps for the creation of a start-up company for a new medical device. Post-market surveillance and the iterative nature of the development process are lacking. The FDA also published a linear model for medical device development as shown in Figure 22.

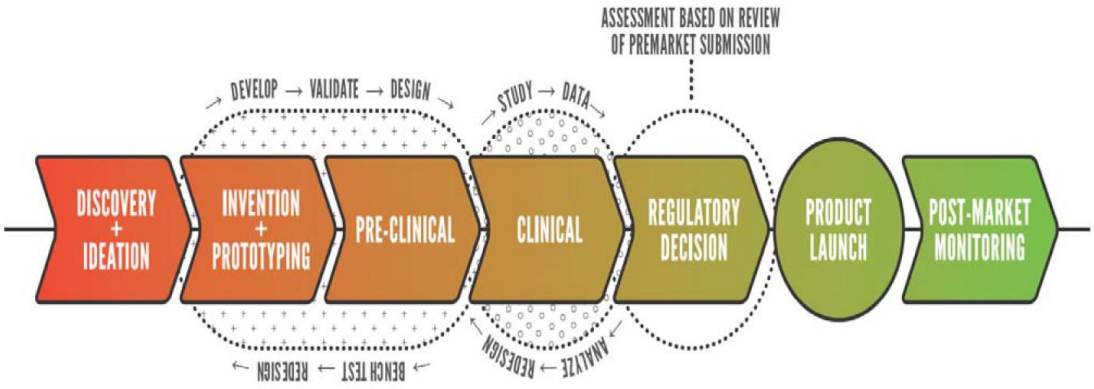

Figure 22: Linear medical device development pathway with the iterative nature of device design and development [56]

This graphic depicts the iterative medical device development pathway. The development process begins when a new idea is discovered. The inventor then brings the idea through the passes of development, validation, design and bench testing, which occur doing the prototyping and pre-clinical phases. In response to these activities, the invention is often redesigned to accommodate deficiencies identified during pre-clinical testing. Once the device has completed the cycles of the pre-clinical phase, it moves to the clinical testing phase where a clinical study is conducted, data is gathered and analysed and the device may again undergo redesign. Once the device has reached its optimal form, the data from the clinical phase are submitted to notified bodies for a regulatory decision. The device undergoes an assessment that is based on the regulatory pathway under which it is submitted. Finally, if the device is cleared or approved, it is then launched and available to be used by or on patients. Once the device is on the market, post-market monitoring occurs and the device is again modified and further innovation takes place until a newer model is ready to navigate through the development process. This FDA-model of the development process is already extensive. Unfortunately, the business side of the start-up (business case, investor involvement…) is missing.

3. Stage-gated models

In 2008, five researchers at the Stanford University Program in Bio design performed a study on the development process of medical devices. [57] They presented a new comprehensive development model that captures all aspects of device development and commercialization from early-concept selection to post market surveillance. The model was constructed on best-practice analysis and in-depth interviews with more than 80 seasoned MedTech development experts. This linear stage-gate model includes five major phases, separated by four decision gates or milestones. Predevelopment activities occur prior to Gate I, development activities occur between Gates I and III and product launch and post market assessment occur after Gate IV.

The gates occur at different times in the development process depending on the type of device. The five major phases include the following:

- (Phase 0: predevelopment activities (focus right clinical need))
- Phase 1/Gate 1: initiation, opportunity and risk analysis
- Phase 2/Gate 2: formulation, concept and feasibility
- Phase 3/Gate 3: design and development, verification and validation
- Phase 4/Gate 4: final validation and product launch preparation
- Phase 5: product launch and postlaunch assessment.

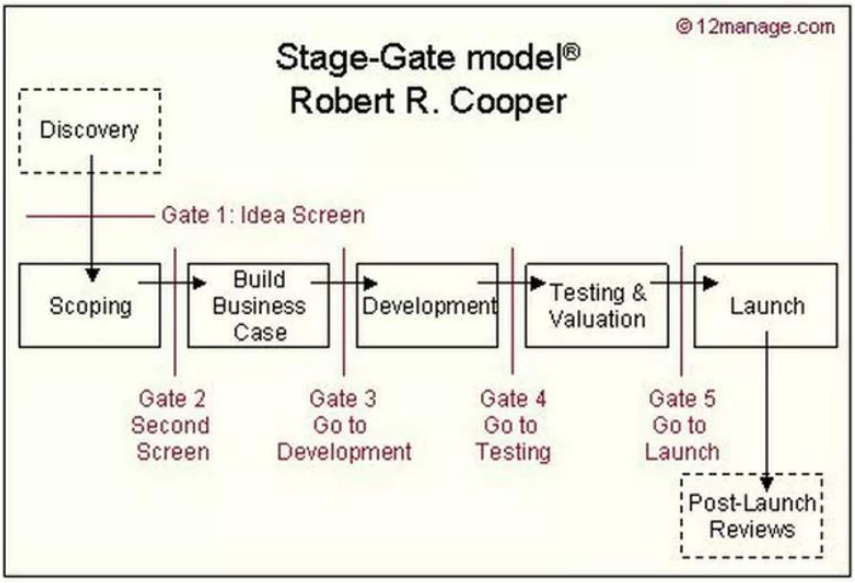

Figure 23: Stage-gate model for the medical device development process [57]

4. Cyclic models

FDA also released a total product life cycle model (Figure 24), where the iterative nature of medical device development is highlighted, together with the importance of incorporating user needs and device experience into next-generation device developments. The iterative process does not always follow the linear idealized model, but rather involves fuzzy boundaries between the different development stages. Some parts of the development project can already be in a more advanced phase, while certain activities of a previous phase need to be repeated at the same time. [54]

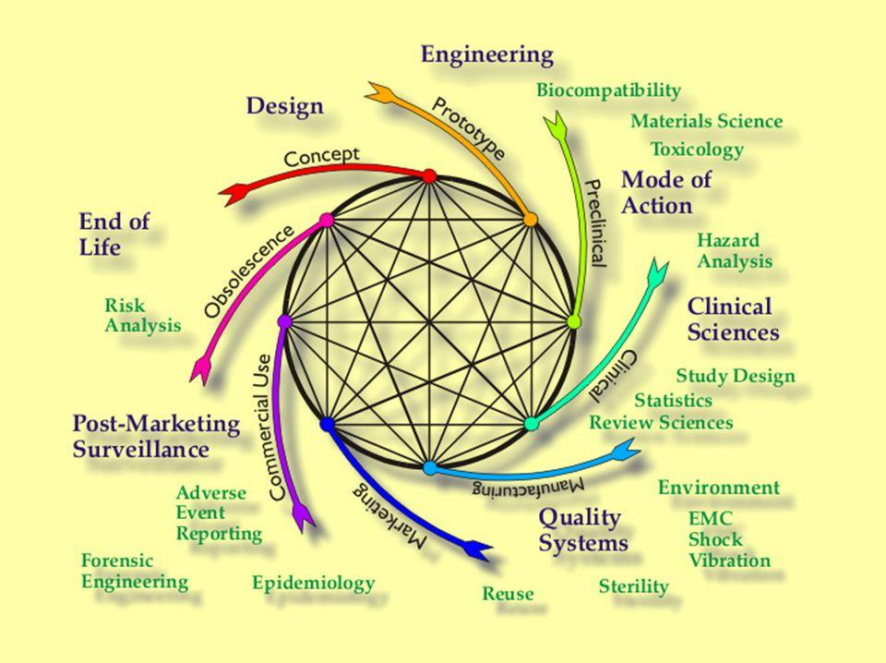

Figure 24: Total product life cycle (FDA, 2005)

2.2 Our new model with 11 evaluation stages

The evaluation tool aims to support newly established medical device development teams and start-ups in the field of MedTech. The purpose is to offer these start-ups a report about the strengths, weaknesses and pitfalls of their product or service and the robustness of their internal organization. In this respect, it might be best if the evaluation algorithm covers the total product life cycle from the manufacturer's point of view. The other point of views described above should be implemented across the different evaluation parameters. Based on in-depth interviews of experts linked to the MedTech Flanders organisation, an evaluation framework was built. During the first round of interviews, the perspective of MedTech experts on the medical device development process was questioned. The experts were asked to share their individual experience about what they considered to be the most critical steps in the development process. Based on the very first interviews, six important evaluation stages of the most important phases during product development and commercialization of a new medical device was made.

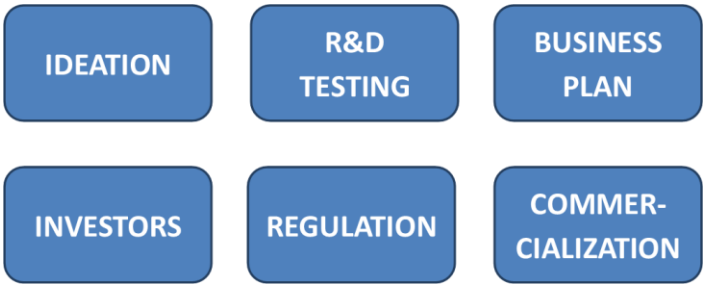

Figure 25: First draft of the MedTech development evaluation stages

It quickly became clear that some important evaluation stages were still missing in this oversimplified approach or had to be further broken down. Critical phases like prototyping, clinical testing and post-market surveillance earned more attention. By reading papers about medical device development [55] [57] [56] (some of them mentioned above) and further interviews with MedTech experts, a larger evaluation model with 11 evaluation stages came up, as shown in Figure 26. It should be emphasized that the evaluation stages are not necessarily chronological as the iterative process of medical device development does not always follow the linear idealized model, but rather involves fuzzy boundaries between development stages. For instance, most activities belonging to the "Quality and Regulatory" evaluation stage already start at the very beginning of the product development process.

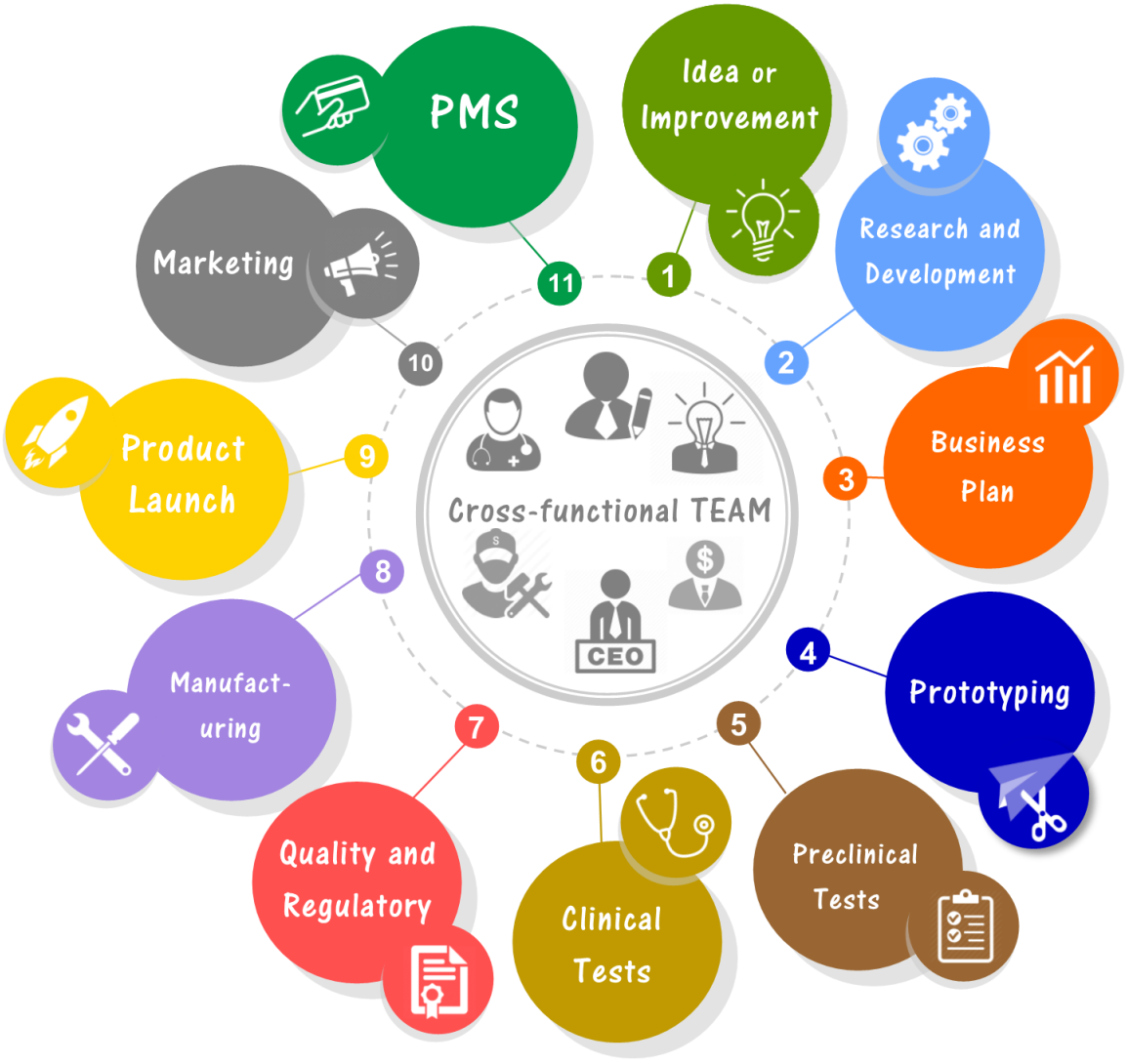

Figure 26: Evaluation framework

The different evaluation stages and their critical parameters are described in detail in the next chapter. A cross-functional engaged team with an experienced CEO should be at the heart of every start-up. Despite the importance, no separate evaluation stage was created for this. The evaluation criteria about the team were

spread across the various other stages. In a second round of interviews, the initial evaluation representation was presented to the MedTech experts, and feedback was obtained. These experts clarified the biggest obstacles and key decision they managed to overcome in various MedTech projects. The evaluation model outlined the different evaluation stages and the parameters, activities or decisions that could be linked to these stages. Based on the feedback, some additions and changes were continuously integrated. The model was discussed in detail with each interviewee to obtain an accurate and comprehensive description of the various activities and decisions. The broad background of the experts and the different types of medical devices they are familiar with, provided interesting insights. The procedure for the development of imaging software compared to the design of a new hearing aid are quite different. For this reason, the evaluation parameters must be very generic to be applicable for each type of medical device.

The evaluation parameters were casted in multiple choice questions. Some extra interviews followed again to verify the listed questions. At a later stage, when the mathematical algorithm was determined, some MedTech experts were asked to complete the evaluation tool for their current MedTech project. This allowed us to test if the different weights linked to the parameters were appropriate and to evaluate the benchmark rules for the final success-rate. Finally, four start-ups that participated in the MedTech Flanders accelerator program of 2017 were asked to complete the tool as a first case-study of the evaluation tool.

3 Idea or Improvement

3.1 Terms & definitions

Term	Definition
Market share	The percentage of a market (defined in terms of either units or revenue) accounted for by a specific entity. [58]
SWOT-analysis	An acronym for strengths, weaknesses, opportunities, and threats and is a structured planning method that evaluates those four elements of an organization, project or business venture. [59]
Seed capital	A form of securities offering in which an investor invests capital in exchange for an equity stake in the company. [60]
Notified bodies	An entity that has been accredited by a Member State to assess whether a product to be placed on the market meets certain preordained standards. [61]

Table 3: Terms and definitions for the idea or improvement stage

3.2 Stage construction

The questions in the first evaluation stage need to assess the idea for a new medical device or improvements for an existing device. It is difficult to judge a new concept or idea, however some parameters can be distinguished that contribute to a final evaluation score of this stage. The degree of i**nnovation** can be directly related to the success of new technologies. There are some key elements to estimate if a product is innovative (in comparison with already existing techniques): the revenue impact, return on investment, complication rate, accuracy, safety, OR (operation room) turnaround time, ease of use, price, patient outcomes and length of stay. [46] When a new medical device is created, inventors and medical device development teams must focus on the right clinical need. Many innovative device or technology developments find their origin in an attempt to cure patients facing inefficient treatment options. Physicians or surgeons are well placed to monitor and evaluate the clinical need. Therefore, the **background environment** of the team is very important because clinical experience is truly an added value during this phase of the medical device development process. **Doctors and caregivers need to be pitched** about the new idea or improvement for an existing device. If the idea is backed up by the fact that there is a **clinical need** for the medical device, this is a bonus. [62] [63]

After identifying the clinical need, a **review of the existing intellectual property** needs to be performed. Development teams usually examine the intellectual property in the field of the medical device they have in mind, to investigate if there are no limitations before further development. It is very important that the developers are aware of what is on the market and how the intellectual property of those existing techniques and products is protected. [63]

In an attempt to find a novel treatment, physicians/surgeons often collaborate with engineers to estimate the manufacturing possibilities. An important factor is whether the technical **expertise & know-how** is mainly in-house or the team must invoke consultants for most of the technical knowledge. As known, team members with experience in the medical and technical sector are almost indispensable for a medical start-up. Moreover, there are also other important skills that need to be covered by the development team of the start-up. Experience with product registration at **notified bodies** is imperative for a medical start-up. If this experience cannot be covered by a team member of the start-up, they should be surrounded with reliable consultants to help with these regulatory affairs. A cross-functional team with various backgrounds and insights is beneficial for the general operation of the company. If the start-up already gained **market share** with previous products within the targeted market, they will have a better market penetration with new products or services. Medical device development and testing is often expensive. In addition, medical device companies have a global market place. Access to **seed capital** from early investors before the development stage is another beneficial aspect for the progress of the development cycle. The seed capital is not only needed for research. Many governmental subsidy channels postulate also the presence of employees on the payroll of the company, so financing by private investors is vital. [63] [3]

A feasibility study needs to verify the technological and economic facets of the proposed clinical validation. This is useful to determine the viability of the idea before proceeding the further development. Correct validations of the medical need, exploring the manufacturing possibilities and estimating the economic impact on health benefits, may help practitioners transition successfully from a theoretical idea to a new cost-effective treatment option. [62] The medical device development process includes a lot hurdles to overcome. It is very important to be aware of the complex valorisation process and rigorous requirements right from the start of the development. A brief **project plan** including a market analysis, a financial review, a risk management plan and a competitive product assessment should be made in the first phase of the development process. The potential regulatory paths need to be examined as well. [57]

A **SWOT-analysis** is often performed at this stage. This analytical framework evaluates the position of a company (Strengths, Weaknesses, Opportunities and Threats) and determines which obstacles must be overcome to achieve the desired results. [64] SWOT analysis was originally built to provide analyses in other

industries, but now it is also a frequently used and well known tool in the healthcare industry. At last, **risk management** is an important component of the first analysis and includes mainly the identification, mitigation and quantification of risks. ISO 14971 defines the international requirements for risk management systems for medical devices, defining best practices throughout the entire life cycle of a device. The main benefits of this ISO guideline consist of the implementation of methods to reduce risks for all stakeholders, the development of devices or services that are proven effective and the streamlined regulatory process that will enable access to targeted markets. [65]

3.3 Parameters & Questions

Parameter	Question
Background environment	Which of the following options describes best your background environment?
Market share	If your start-up or company has already launched MedTech products or services in the same market segment of the new product you have in mind, what is the market share of these earlier launched medical devices?
Innovation	On how much of the following key elements is your product innovative in comparison with already existing techniques?
Demand Research	How arose the idea for the new medical device?
Research for use	Are doctors/patients pitched about the idea and involved in the development of the new medical device?
Expertise & know-how	Do you have expertise and know-how inside the company with this type of medical technology?
Seed capital	How much seed capital from early investors did you have already available before the start of the product development stage?

Notified Bodies	Has someone in your team experience with product registration at notified bodies or are you in contact with a partner/consultant that helps you at regulatory affairs like product registration at notified bodies?
SWOT-analysis of idea/service/product	Did you perform a SWOT-analysis for the new idea or improvement available?
Review of the existing intellectual property	Are there patents on products technologies that are comparable to your product/idea?
Project plan + risk analysis + timeline?	Was there already a project plan made for your product/idea before you started the R&D phase of the medical device development process?

Table 4: Parameters of the idea or improvement stage

4 Research & Development

4.1 Terms & definitions

Term	Definition
Pilot study	A pilot study or pilot experiment is a small scale preliminary study conducted in order to evaluate feasibility, time, cost, adverse events, and effect size (statistical variability) in an attempt to predict an appropriate sample size and improve upon the study design prior to performance of a full-scale research project. [66]
FMEA	Failure mode and effects analysis (FMEA) was one of the first highly structured, systematic techniques for failure analysis. It involves reviewing as many components, assemblies, and subsystems as possible to identify failure modes, and their causes and effects. [67]
BOM	A bill of materials (BOM) is a list of the raw materials, sub-assemblies, intermediate assemblies, sub-components, parts and the quantities of each needed to manufacture an end product. [68]
IP protection	Intellectual Property is protected in law (for example by patents, copyright or trademarks) which enable people to earn recognition or financial benefit from what they invent or create. [69]

Table 5: Terms and definitions of the research & development stage

4.2 Stage construction

Research is considered as the generation of hypotheses or models that are confirmed or falsified by experimental research, producing new knowledge in repeatable and unambiguous fashion. Research is coherent: the outcome fits existing knowledge and is consistent with it. Knowledge is expressed in terms of relationships among events or variables. [70]

After the initial concept design, the research process must be initiated. This research phase requires detailed analysis of the disease state, technical risks, market potential, ethics, research on shortcomings of current available devices or services and health care dynamics. [62] [71] Possessing all the necessary **technical possibilities & infrastructure** can sometimes be an obstacle for start-ups at the beginning of the device

development. The nature of the device or service and the background of the development team are mostly determinative for the availability and the access to infrastructure. It would be remarkable if a team including only graduate students would already have access to all techniques necessary to make a successful medical device. Although, this could be the case if only software (e.g. a mobile health application) is needed to create a product or service.. A company with already a lot of experience within the field of MedTech, is most likely to have all techniques in-house available. This parameter depends mainly on the technical complexity of the new product or service. As mentioned earlier, **ethical issues** can arise because all clinical activities impose high ethical standards of comportment to protect the patients at any time.

During the R&D phase, there must be thought of the verification and validation via **risk analysis**. The medical device should be designed sufficiently safe and effective for routine use by patients. FMEA is a systematic technique to provide a failure analysis. [72]

Experimental research has a systematic and scientific approach. The researcher manipulates one or more variables and controls/measures any change in other variables. [71] There are many possible aspects to include a scientific approach in a research experiment in order to get a more validated outcome. For example the use of sampling groups, which is especially important when multiple conditions need to be compared during the experiment. One additional sample group is used to verify the data, while all other sample groups are used as real test data. Also a pilot study before the elaboration of the real experiment can be an added value for the research experiment. It ensures that the experiment measures the right values and the whole experiment is set up in a correct way.

In order to obtain a qualitative research experiment, not only the outcome must be reliable and statistically significant. The regulatory and the humane framework that support the research aspect is also crucial. This humane facet of the R&D phase refers to two things. On the one hand, it refers to the **cross functional team**, and more specifically the included knowledge of the team. Medical, technical, regulatory, organization and business knowledge are all different facets that needs to be covered by the research team. Not only during this research and development phase is the composition of the team of great importance, it is also important during all other phases. In general, the team composition is a decisive factor during the whole medical device development process.

On the other hand, **feedback from third parties** is an important aspect. Each team believes that their novel idea could provide a solution to an unmet clinical need or that their device or service is better than the devices/services already on the market. Therefore, it is really important that third parties like physicians or engineers provide useful feedback which could lead to new insights.

The regulatory facet is for most start-ups a big hurdle to overcome. From the start of the R&D phase until the post market surveillance stage, regulatory affairs are part of the job. At this second stage, some guidelines concerning regulatory affairs must be followed to preclude major difficulties during later stages. As mentioned in subchapter 2.3 of part 1, medical devices are divided into classes. Each class has his own regulatory pathway that needs to be followed. During the early design phases of the product or service, one must already keep in mind the **different medical device classifications**. Moreover, regulations are related to this classifications. It is an advantage if the medical device development **team takes already all necessary regulations into account** at the start of the designing phase. [71]

Thinking about a way to protect you intellectual property also needs special attention in this phase of the device or service development. One of the key questions a development team must consider is whether or not protect the intellectual property. The outcome of this question is different for each medical device. IP protection does not always mean patenting. When the technology behind the medical device is very innovative and complex, it could be enough to keep the techniques black-box (business secret). It is important that the company has already a vision on IP protection.

As mentioned above, some regulatory affairs postulate a methodological approach, traceable decisions and well documented processes. To meet these requirements, some documentation must be validated. For example, **detailed technical drawings** are necessary to create an overview of the technical requirements (dimensions, tolerances…) and gives more information about the complex manufacturing process. A **cost-effectiveness** analysis in the development phase can provide insights about budgetary affairs. Both documents are not yet mandatory in the R&D phase, but are both excellent instruments to help a developmental team to already take some provided insights into account. Finally, the cross-functional team members can generate a **verification and validation test matrix.** This matrix provides a foundation for validation testing and consists of R&D, test engineering and quality engineering analysis. [57]

4.3 Parameters & Questions

Parameter	Question
Technical possibilities	Are all techniques and know-how available that are necessary for the development of the medical device?
Infrastructure	Which investments are required for product development infrastructure?
Experiments	If you do a research experiment, how many of the following steps do you include in your methodology?
Regulations	Do you already take into account all necessary regulations (CE, ISO,…) during the first development phases of the medical device development process?
Patent information	Did you already consider a strategy to protect the intellectual property during the early development stages?
Cost-effectiveness	Did you perform a cost-effectiveness analysis during the early development stages? (e.g.: a cost breakdown analysis of the different costs linked to the new product development)
Ethical issues	Is there an analysis of the possible ethical implications of the product during the development phase?
Risk Analysis	Did you perform a risk analysis during the early development stages (FMEA, Risk Plan,…) ?
Technical Drawings	Are the technical drawings already made in detail (BOM, tolerances, technical requirements etc.) during the R&D phase?
Verification and Validation test matrix	Is there a verification and validation procedure

	foreseen?
Team	How many of the following skills are covered by your team?
Meddev classification	Did you design the medical device with the different medical devices classifications in mind? (e.g.: Trying to exclude some functions, so you won't fall in a higher class)
Feedback	Do you ask feedback of doctors, engineers, patients,... during the development of the product?

Table 6: Parameters of the research & development stage

5 Business Case

5.1 Terms & definitions

Term	Definition
ROI	The benefit to an investor resulting from an investment of some resource. A high ROI means the investment gains compare favourably to investment cost. As a performance measure, ROI is used to evaluate the efficiency of an investment or to compare the efficiency of a number of different investments. [73]
Proof of concept (POC)	a realization of a certain method or idea in order to demonstrate its feasibility. [74]
Self-funded	is a self-insurance arrangement whereby an employer provides health or disability benefits to employees with its own funds. [75]
RIZIV	(Dutch: Rijksinstituut voor Ziekte- en Invaliditeitsverzekering) – Belgian Gouvernement for Health Insurance. [76]

Table 7: Terms & definitions for the business case stage

5.2 Stage construction

A business plan has to be one of the foundations of the whole product development cycle. Generally, it starts with an executive summary which gives, among other things, an overview of the business concept, background information on the market of the company, a short description of previous products, the business model (how will you make money), financing (which funds have you already raised) and a brief introduction of the management team. [77] Afterwards, more detailed information about the new medical device and process validation should convince investors.

First of all, the **clinical need** can be considered as one of the key review elements of a business plan. There is a difference between providing an adaptation of a technique or product which already exists or inventing a total new technique. In most cases, new and innovative ideas get more attention from investors. Furthermore, market size and market opportunity investigation can be included in the business plan. Another important determinant in device evaluation is whether the device is **exportable** to other countries or markets. Even if a

non-exportable medical device has excellent market opportunities to become a real success, it is a bonus if it is possible to explore other countries.

Having a description of the key personnel, how the intellectual property is protected and how it will be protected in the future, which regulatory pathway will be followed and a detailed analysis of the product itself, are all standard elements in a business plan. Having an engaged team is a very important driver for the progress in the medical device development cycle. Furthermore, an experienced **CEO** is certainly necessary. The CEO should be someone who already went through the entire MedTech development cycle in the past. This knowledge is crucial and will navigate the team through the very complex medical device development pathway. A CEO with experience, is a real benefit for the team and has a big influence on the success rate of the medical device development. [77]

Indispensable for a business plan is the current status of raised funds and the total amount of investments the company needs. A clear financial framework is one of the first elements that probably will persuade an investor. To provide a good insight in the financial part, it is very important that the **healthcare costs are calculated correctly**. At most calculations, all logical or self-evident costs are included, but for example the costs for training physicians, the referral pattern change costs or the cost of extra equipment or medicines are forgotten. Conclusions concerning the cost-efficiency of the new product or service can be different if these hidden costs are implemented in the calculations. The **new product should involve a proven decrease in total healthcare costs**..

Most of the time, a large part of the manufacturing costs are due to the expensive infrastructure. Therefore, **infrastructure sharing** between multiple companies can sometimes be an option to cut the costs.

Beside the decrease in healthcare costs, a calculation of the **return on investment** is another way to convince potential investors. Also a clear market demand, a robust intellectual property protection, a proof of concept, a clear regulatory pathway and a good prototype are aspects that could play part in the decisions of potential investors. After convincing the investors, it is crucial to **ask them for feedback on the business plan**. It is beneficial to understand why they have decided to invest and what the convincing elements were of the business case. Involvement of investors in the company can bring along knowledge and new insights. This can lead to a better investment framework and supports the possibility to attract **investors in the second phase.** In nearly all cases of medical device development, a second investment round is necessary. It is very important to include this option in the business plan, but this entails a possible redistribution of shares. Finally, a risk analysis is necessary for the business. **Risk management** is, like in the previous evaluation stage, a parameter that has to be taking into account. Generally, risk management is even more important in healthcare than in

any other industries, because the risks can jeopardize the patient next to the financial losses. In the field of MedTech, a proper risk management assessment can make the difference between life and death. [78]

Finally, the reimbursement of the medical devices is another key factor in the business plan. In Europe, each member state independently provides the rules for governmental funding & the reimbursement codes of medical devices. [79] In Belgium, developers can apply a request at the RIZIV, so the patients can receive grants or reimbursements for the medical device. The evaluation criteria for the decisions on reimbursement for medical devices, are generally vague formulated. [80] Therefore, it is not the purpose of this dissertation to list all possibilities to receive grants or reimbursement.

5.3 Parameters & Questions

Parameter	Question
Disease state	What are the current options for diagnosis/treatment?
Healthcare costs	Will the new product involve a decrease in total healthcare costs at community perspective?
Calculation of the healthcare costs	How many of the following costs did you include in the cost calculation?
Return On Investment	Can you evince the return on investment to convince potential investors?
Infrastructure sharing	Is infrastructure sharing with other companies possible?
Reimbursement	Do you think grants or reimbursement will be possible? (In Belgium: RIZIV)
Exportable	Is the device exportable (with some modifications)? Is there a possibility to explore other countries?
Investors	Next to ROI, how many of the following parameters do you highlight?
Involvement of investors	Are the investors asked for feedback on the business case?
Risk management plan	Did you include a risk assessment in the business plan?
Second phase investors	Is there a possibility for second phase investors?
CEO	Do you have a CEO that already went through the whole MedTech development cycles?

Table 8: Parameters for the business case stage

6 Prototyping

6.1 Terms & definitions

Term	Definition
E-Health	eHealth is the use of information and communication technologies (ICT) for health. The eHealth unit works with partners at the global, regional and country level to promote and strengthen the use of ICT in health development, from applications in the field to global governance. [81]
Beta launch	The second version in field release. During the beta release, enough of the system should be working to convince the customer that soon the beta application will be a real product. [82]

Table 9: Terms & definitions of the prototyping stage

6.2 Stage construction

By definition, prototyping is an early sample, model, or release of a product built to test a concept or process or to act as a thing to be replicated or learned from. [83] Especially in health care, prototyping makes an indispensable part of the medical device product cycle. In general, prototyping is linked to medical device products and less to medical device services or applications. This is certainly one of the most difficult evaluation stages to be applicable for all types of medical devices. It is hard to find evaluation determinants and to formulate questions in a generic way. Therefore, there are not many questions implemented at this evaluation stage. For almost every question of this stage, it is possible to indicate in the questionnaire that the evaluation parameter is not applicable for medical device. However, considering the impact of prototyping in health care, this stage must be included and rated.

Moreover, there are some prototyping-decisions that are again product specific and therefore not measurable. For example, how many prototypes are necessary to proper evaluate all requirements? It depends on whether the prototype(s) will be used for a pilot study, a preclinical study or a beta launch on a test-market. One should strike a balance between spending more time and money in the prototyping phase or freezing the design. The development teams do not want to paint themselves into a corner if it turns out that they have to make more units than firstly anticipated.

During medical device development, a good practice is to **use real production processes, medical grade materials, real production methods and materials with the same mechanical properties like the final material**

wherever possible. The developers should design the prototype in the same way the product will be designed for manufacturing. [84] Once the regulatory affairs are set in place, a revision of those dossiers due to material and design changes can be difficult and expensive. Another reason to do so, is to make more easily **a proof of concept** with the prototype. This is possible if the prototype is already made the same way as it will be during the manufacturing process. Materials from a Do-It-Yourself store are good for conceptualizing a product and acquire know-how during initial testing. When the development progress goes further, it is good to think strategically and plan how many prototypes will be made, which materials will be used and which production methods are needed. [84] For eHealth prototyping, this evaluation questions aim the software of the application and whether or not one built the application in the same environment as the one intended for the final application.

6.3 Parameters & Questions

Parameter	Question
Production processes	Do you use the same production processes during the prototyping as you will use during the real manufacturing? (In case of E-Health: do you build your application/software in the same environment as the one you will make your final application in?)
Mechanical properties	Do you use materials for the prototypes with the same mechanical properties as the material you will use for the product that will be sold?
Material choice	Did you use medical-grade materials for the prototype?
Proof of concept	Can you use the prototype to make a proof of concept?

Table 10: Parameters of the prototyping stage

7 Quality and Regulatory

7.1 Terms & definitions

Term	Definition
Patent	A patent is a set of exclusive rights granted by a sovereign state to an inventor or assignee for a limited period of time in exchange for detailed public disclosure of an invention. An invention is a solution to a specific technological problem and is a product or a process. [85]
Trademark	A trademark is a recognizable insignia, phrase or other symbol that denotes a specific product or service and legally differentiates it from all other products. [86]

Table 11: Terms & definitions of the quality & regulatory stage

7.2 Stage construction

Several medical device start-ups are putting a lot more time and effort into the regulatory affairs compared to what they initially expected. For new MedTech companies, that never went through the entire development cycle, it seems like an overwhelming task. It is hard devise a strategy for the intellectual property protection. [84] However, intellectual property protection is an absolute must for the start-up for many reasons. **Intellectual property** refers to a group of property rights including patents, copyrights, trademarks, and trade secrets. Other rights are also included, such as trade dress, mask works, unfair competition, and publicity rights. The particular kinds of IP that one cares about will depend on the nature of the company and the marketplace in which the company competes. For medical device–technology companies, this is typically patents, trademarks, and trade secrets. [84]

As specified in part I, the MedTech industry has grown rapidly in recent years, causing an outpaced regulatory framework for medical devices. The European regulators therefore considered that a change was needed and the European Commission published in 2012 two **new proposals for regulations** to replace the existing directives: The MDR & IVDR directives. [10] It is of crucial importance that companies are aware of those new rules and that they check whether the qualifications of their medical devices are confirm the new rules and definitions. It is possible that **additional documents** are necessary before continuing the development process. Those documents were already crucial, and are now gaining even more importance with those new regulations. Based on a clinical evaluation, companies will have to demonstrate that their device has an

acceptable benefit compared to the risk. This evaluation is based on **clinical data** and all relevant information on the performance and safety, when the medical device is used as intended by the manufacturer. The data is retrieved from clinical investigations and peer reviewed clinical literature of either the device in question or similar devices. The clinical data can also be retrieved from the post-market surveillance system. All the data is collected and analysed within the **clinical evaluation report**. This report must be continuously updated throughout the lifetime of the medical device. [10] Manufacturers of implantable devices and devices of Class III, **may in some cases also rely on clinical data of an equivalent device**. This is the case when the device has been designed as a modification of a device that has already been marketed by the same manufacturer. The modified device has been demonstrated by the manufacturer and accepted by the notified body as equivalent to the already marketed device. The clinical evaluation of the modified device needs to demonstrate conformity with the relevant safety and performance requirements. [10] Finally, it is important to consider if an **ISO environment** is necessary (if not already available). Due to the strict regulations, it appears to be a huge effort and cost to arrange an entire ISO environment for medical device manufacturing.

As mentioned in part I, the rules for medical device ordination are based on the risk classification. Products are categorized into **four risk classes** starting from the lowest risk category: classes I, IIa, IIb and III. For each medical device class there is a different regulatory path. Like mentioned, a comparison between the different options is already an important decision during the development team of the medical device. Some development teams try to design their medical device in such a way the device is covered by another MedTech class.

Also the possibilities on reimbursement are again considered in this evaluation stage. There are some **reimbursement factors** which definitely have an influence to raise the odds for governmental financial intervention. First of all, it is important to lobby with the user association at the governmental institute. In Flanders, the RIZIV institution is responsible for the decision on reimbursement. Secondly, the existence of evidence-based data is an advantage to have any chance to get a reimbursement. Conversely, if the company does not have any evidence-based data, it can have a negative effect on the approval. Finally, it is easier to launch a type of medical device in a sector where is not much consumed of this type during the last years. There are also some obstructive factors for reimbursement. For example the budget impact: if the RIZIV thinks that the use of the considered new technology will be too expensive, mostly no reimbursement is ascribed.

7.3 Parameters & Questions

Parameter	Question
Classes	Which of the four classes covers your medical device?
Clinical data	Is it possible to rely on clinical data of an equivalent device?
Clinical evaluation report	How many of the following parts are included in your clinical evaluation report?
Patent	How is the intellectual property protected?
ISO environment	Is an ISO environment necessary?
Reimbursement	Do you think grants or reimbursement will be possible? (In Belgium: RIZIV)
Reimbursement factors	How many of the following factors can you identify with your company? (Multiple answers possible, only fill in if you did not receive any reimbursement yet)
New rules	Are you well informed by the new rules concerning regulation of medical devices?
Additional Data	Do you need to draft extra/new documents due to the new regulation directives?

Table 12: Parameters of the quality & regulatory stage

8 Preclinical tests

8.1 Terms & definitions

Term	Definition
Biocompatibility	a measurement of how compatible a device is with a biological system. The purpose of performing biocompatibility testing is to determine the fitness of a device for human use, and to see whether use of the device can have any potentially harmful physiological effects. [84]
ISO 10993	Series of standards for evaluating the biocompatibility of medical devices. These documents were preceded by the Tripartite agreement and is a part of the international harmonisation of the safe use evaluation of medical devices. [87]

Table 13: Terms & definitions of the preclinical tests stage

8.2 Stage construction

Preclinical tests are an important part of the medical product development cycle. The purpose of performing **biocompatibility** testing is to determine the fitness of a device for human use, and to see whether the use of the device can have any potentially harmful physiological effects. As stated by the International Organization of Standards, "The primary aim of this part of **ISO 10993** is the protection of humans from potential biological risks arising from the use of medical devices". [84] It is of crucial importance that the finished device is tested to ensure that human use of the device would not result in any harmful effects. The main goal of biocompatibility testing is ensuring the general protection of humans. Therefore, animal testing is in most case needed even though one tries to limit these tests and minimize the number of tested animals. With this in mind, it is important to properly document all component materials and existing data from similar devices. Latter can be useful to demonstrate biological safety of separated parts. It goes without saying that this will depend on the use of the device or service, moreover the way it interacts with the body and how long this interaction takes place. **Good Laboratory Practice** (GLP) is required for certain regulatory affairs. In general, it is beneficial to conduct tests for biocompatibility according to GLP in order to have maximum regulatory flexibility. [84]

As a manufacturer, you should gather safety data of every component or raw material used in a medical device. The tests should be conducted as specified by ISO 10993. [84] Furthermore, material screening tests

help to ensure that there is no need to redesign the medical device because of biocompatibility test failures. The turnaround time of all preclinical tests can vary from three weeks to several months. The execution of all tests and the gathering of clinical data is time consuming, but at least equally important is the evaluation of the results. The interpretation and **statistical analysis** provides insight if additional testing is needed or the existing data provides enough information to get an biocompatibility assessment of the device.

Finally, experience with preclinical tests is again a key factor for this evaluation stage. To obtain good results, **the covered skills of the cross-functional development team** are important. It also is essential to take an informed choice on the research lab. A lab with inexperienced personnel with a lack of knowledge to assist the team in the intraoperative facet can be costly. Therefore, it is important to have knowledge about the capabilities and infrastructure of the laboratories.

8.3 Parameters & Questions

Parameter	Question
Biocompatibility	Did you investigate the biocompatibility of your medical device? (e.g.: Analytical chemistry, in-vitro tests, animal models,…)
GLP	Have you conduct biocompatibility tests according to GLP (Good Laboratory Practice) ?
ISO 10993	Have you achieved an ISO 10993 certificate?
Statistical analysis	Did an expert assessor analysed the gathered preclinical test data? (Significance tests, variability, sensitivity analysis,…)
Team	Does someone of your team has experience with preclinical testing?

Table 14: Parameters of the preclinical tests stage

9 Clinical tests

9.1 Terms & definitions

Term	Definition
METC	Medical Ethical Test Committee (Dutch: 'Medisch-ethische toetsings-commissie.') is a body responsible for ensuring that medical experimentation and human research are carried out in an ethical manner in accordance with national and international law. [88]

Table 15: Terms & definitions of the clinical tests stage

9.2 Stage construction

A clinical study involves research with human people, with the purpose of gathering medical knowledge. There are two main types of clinical studies: **clinical trials and observational studies**. In an observational study, investigators gather health outcomes in groups of participants that are not following a research plan or protocol. Participants may receive interventions or procedures as part of their routine medical care, but participants are not assigned to specific interventions by the investigator. [89] In a clinical trial, participants receive specific interventions according to the research plan or protocol created by the investigators. [89] Every clinical trial has a research plan. This research plan describes what will be done during the study, how it will be done and why each part of the study is useful. Each study has its own rules about who can take part. Some studies need volunteers who suffer from a certain disease or are going through a current treatment. Others search specific populations based on gender or age. Rules about who can participate a clinical trial, are called **eligibility criteria**. [90]

First of all, a favourable opinion from the **Ethics Committee** or from a more local ethical test committee (**METC**) must be received in order to start with clinical trials. Their task is to review and approve all clinical trials. An ethics committee is an independent committee of physicians, statisticians and members of the community. [89] Statisticians are included because a **statistical analysis** is executed after gathering all data from the clinical trials. The role of an ethics committee is ensuring that the study is ethical, that it is protecting the rights and wellbeing of all participants and to make sure that the risks are reasonable when compared to the potential benefits. [89] After the approval, a **multi-centre study** proves the concept. By integrating **regular feedback** in the methodical approach of the design process, the concept or prototype can be changed in time if necessary. [91] [90] The protection of the patient is unbearable for a clinical trial. An **informed consent** is a

process used by researchers to provide potential and enrolled participants with information about a clinical study. This information helps people decide whether they want to enrol in the study and continue participating. The informed consent process is intended to protect participants and should provide enough information for a person to understand the risks of, potential benefits of, and alternatives to the study. [90]

Before executing clinical trials, it is recommended to first perform a **pilot study**. This can provide an added value for the clinical trials because it ensures that the right planning, set up and monitored values are picked. Moreover, it provides the chance to adjust some parameters before the real clinical trials are executed. Expertise and know-how of a pilot study is crucial. Clinical experience is an often returning parameter but it truly can fasten the clinical trials.

A recurring problem is the difficulty of executing a generic evaluation concerning clinical trials for all types of medical devices. This stage is less relevant for some medical devices. For example, applications are a category of medical devices for which this stage can be irrelevant. To overcome that companies have to fill in questions that does not apply on their device, this stage can be skipped. A more extensive explanation of skipping this stage and possible consequences, is provided in part III of this master dissertation.

9.3 Parameters & Questions

Parameter	Question
Pilot study	Are pilot studies performed before the real clinical trials?
Permissions METC	Do you have a permission by the ethical commission METC to perform clinical trials?
Informed consent	How many of the following types of informed consent do you provide?
Clinical Trials or observational study?	Which description of clinical trials corresponds best with the one that you will use?
Multi-centre study	Did you perform clinical tests in multiple centres?
Statistical analysis	Are the clinical trial data statistical analysed? (Significance tests, variability, sensitivity analysis,…)
Possibilities feedback to design	What are the possibilities to adjust the product design after the clinical trials?
Team	Who conducts the clinical studies?
Eligibility	Do you have a well described protocol with eligibility criteria, number of participants, schedule on tests etc.?
Ethical committee	Did you received a favourable opinion from Ethics Committee?

Table 16: Terms & definitions of the clinical tests stage

10 Manufacturing

10.1 Terms & definitions

Term	Definition
ISO 13485	Medical devices – quality management systems – requirements for regulatory purposes, is an internationally agreed standard that sets out the requirements for a quality management system specific to the medical devices industry. [92]

Table 17: Terms & definitions of the manufacturing stage

10.2 Stage construction

After research, regulatory hurdles, preclinical tests and clinical trials, all gathered knowledge is bundled in the manufacturing of the product. Before starting the manufacturing, most developers must achieve an **ISO 13485 certificate** This quality standard outlines the requirements for a quality management system, concerning the workplace environment. This standard is set up to be used by organizations involved in the design, production, installation and servicing of medical devices or related services. [92] If a company has **suppliers** that produce a part of their medical device, it is also mandatory to apply ISO 13485. It can be a challenge to assess the level of risk each supplier could potentially add to your process. However, this is a critical exercise. ISO 13485 imposes also the **traceability of all suppliers' materials**. Knowing this, a proper consideration whether or not to invoke external suppliers is very useful. Because once subcontracting is decided, the regulatory effort can increase or decrease, depending on the experience of the subcontractor.

The complex procedure to obtain a **CE-marking** is described before. It is necessary to perform a conformity assessment to get this CE-marking. To guide this assessment in the right direction, someone with some experience in this conformation process is necessary.

One of the most overlooked parts in this development phase, is the **packaging** and product configuration. Next to regulatory requirements on the package, one should think on how to make the product easy to unpack for the end user. If the packaging involves many instruments and implants, which is typically the case in orthopaedic and neurosurgery, it is critical that the flow of a surgery matches the configuration of the instruments and implants. Product configuration and packaging are factors that significantly affect the adoption of your device. On the medical device or packaging, clear **marks and labels** need to be placed to

clarify the correct use of the device. Also a surgical/procedural **technical guide** should be well documented with clear instructions, drawings, pictures or even video-material. [93]

One last important determinant for the manufacturing evaluation stage is the possibility to scale the product to the international market. If the medical device can be sold across borders, there will be new opportunities to generate profit and the company is not anymore dependant of only one market. Nevertheless, this higher flexibility due to the international market includes additional risks (political risks, transfer risks, commercial risks, financial risks…). To export the product to other companies, sometimes only symbolic values, labels or the language of the manuals should be adjusted. Some other products need an adjustment to adapt local conditions (colour, packaging, voltage…). If a lot adjustments to the core of the medical device are necessary to sell the product in other countries, additional costs need to be incurred. [94] [93]

Again, not all parameters about manufacturing are relevant for all medical devices developers. To overcome this, this stage can be skipped in the tool. A more extensive explanation of skipping this stage and possible consequences, is provided in part III of this master dissertation.

10.3 Parameters & Questions

Parameter	Question
Suppliers	Can your suppliers present documents to trace all purchased products, goods and raw materials?
Audit suppliers	Can your suppliers present an ISO-certificate?
Subcontracting	Did you make a proper consideration about subcontracting?
ISO environment	How long will it take to get an ISO 13485 certificate?
CE-labels	Are you (or someone in your team) familiar with registering CE-labels for a 'MedTech' product?
Packaging	Does the packaging fulfil all regulatory requirements?(In case of eHealth or software: the console instead of 'packaging')
Packaging	Is the packaging flow well-designed for the end user? (e.g. follows flow of the surgery)
Internationally adjustments	Which adjustments are necessary before your product can be sold in other countries?
Labelling	Are there clear marks or labels on the device concerning the usage?
Technical guide	How well documented is the surgical/procedural technical guide?

Table 18: Parameters of the manufacturing stage

11 Product launch

11.1 Stage construction

A well-chosen moment for the product launch of a medical device is crucial. The design freeze is a critical decision in the design process, after which no element of the product's design is allowed to be changed anymore. [95] Some companies choose for a late design freeze whereby they extensively tested the medical device. This late design freeze may reduce the likelihood of a subsequent iteration, but also can lead to a substantial delay in bringing the product to the market. If the development team releases the product too early, users may write it off as not good enough and the first impression of the product or service was negative. If they release the product too late, they may have missed a window of opportunity in the market. Finding the right balance between the two alternative can be a major challenge for the development team. [57] This product launch is sometimes called the **momentum.** When the product development team decides to launch the product, one should think about the right positioning strategy for the new medical device. **Product positioning** is one of the most overlooked activities associated with medical device product launches. The basic premise of product positioning is to consolidate the many beneficial facets of the product into a core statement of value that resonate with the end user. There are six basic strategies to accomplish this goal, with the most common one being positioning the product by its attributes or benefits. Others are positioning the new applications of the device or they are focusing on the specific new patient population that can be covered. Sometimes they position their device by being the best of their product by price category or by comparing to competitors. [94]

Next to the positioning, the **pricing** is also important. Different pricing basic pricing strategies are known (market penetration, market skimming, comparable pricing or flanking pricing). [94] The margin of profit can be calculated in various ways. It is very important to think about an **international pricing strategy**, which takes into account the different tax policies in various countries, transportation costs, other competitors etc. [94] [95]Most companies forget to consider the cannibalization-effect. If the company already has a product in the same market segment when a new product is launched, it is possible to have a sales loss on the earlier launched product. This sales loss should also be quantified when they predict the revenues. [94]Finding the right **distribution partners** for the new medical device is an important factor for the marketing success of the new medical device. A distribution partner with a large network of hospitals and caregivers will accelerate the sales of the new product. Also **pre-launch trainings** for physicians, caregivers, patients or other end-users will speed up the market penetration. [93]

11.2 Parameters & Questions

Parameter	Question
Discount margin	Which of the following techniques describes best how the margin of profit is determined?
Pricing	Which of the following pricing strategies corresponds best to your strategy?
Global pricing strategy	Is there an international pricing strategy (including different tax policies, competition, transportation costs …)?
Momentum	Will you take an informed decision when choosing to transfer your product to the product launch phase?
Positioning strategy	What is the main positioning strategy you will use at the product launch?
Pre-launch training for physicians	Did you provide pre-launch training for physicians/patients/end users?
Cannibalization	Did you quantify the sales loss on other owned product concerning the product launch? (e.g.: If Coca-Cola launches their new product 'Coca-Cola Zero', they will also lose some sales at their regular Cola that needs to be quantified next to the extra market-share obtained with the new product.)
Distribution partners	Are you already in contact with third party distributors?

Table 19: Parameters of the product launch stage

12 Marketing

12.1 Terms & definitions

Term	Definition
PEST-analysis	PEST is an acronym for Political, Economic, Social and Technological. This analysis is used to assess these four external factors in relation to your business situation. Basically, a PEST analysis helps you determine how these factors will affect the performance and activities of your business in the long-term. [96]

Table 20: Terms & definitions of the marketing stage

12.2 Stage construction

A start-up should be very flexible in the fast changing MedTech industry. Marketing is an important tool to increase the market share and profitability of the company. It is also a mechanism to develop long-term strategic partnerships on an international level. In the field of MedTech, the international perspective of marketing is important. Different marketing strategies must be rolled out at the various markets. Each country or continent has another political framework. **Pricing and marketing strategies** should be adjusted to the local environments. If the start-up wants to launch their product or service on the international market, a **PEST-analysis** for each market can be useful to identify the international opportunities and threats. [94] This analysis helps to outline the Political, Economic, Socio-Cultural and Technological challenges in the local business environment. The **marketing plan** of the company should be documented and well-considered, including a clear **competition strategy**. In the literature, there are 3 basic strategies defined to compete. With the low-cost leadership strategy, one tries to compete by selling the product at a lower price than a competitor. If the differentiation strategy is used, the company tries to offer a product or service that is more sophisticated than the devices that are already on the market. It is also possible to focus on a very specific application or market-segment (e.g.: patient-specific products), this makes it difficult to let other companies compete. It is essential **to identify the different patient-segments** in the market, in order to set up targeted marketing campaigns. [94] [95]

The marketing budget should be well calculated. Again, there are different ways to do this. The “affordable method” is often used. In this method the company looks which budget they want to spend on marketing purposes. It is also possible to set the budget at a specified percentage of the sales or by defining some

objectives that the company wants to reach. It can be interesting if the marketing team can change the marketing budget based on the actions or promotions of competitors. It is important to **continuously measure the marketing results.**

Promotion tools are the basis for each marketing campaign. This includes advertising tools (logo's, commercials, brochures, posters, corporate movies…) as well sales promotion tools (coupons, gifts, discounts, trade promotions…). It is important to maintain the public relations of the company and to attend fairs, exhibitions, congresses etc. Publications of white papers or articles in scientific magazines can provide a boost for the medical device promotion. CRM and big data technologies to gather customer data can support the start-up in using direct marketing tools to reach their target audience of the marketing campaign. [95]

12.3 Parameters & Questions

Parameter	Question
Pricing variation geographically	Have you thought about a price variation in different areas/countries?
PEST-analysis	Have you made a PEST-analysis (only fill in if you go to the international market.)
Medical education	Are there possibilities/plans to grant medical education, workshops etc. about the product?
Marketing plan	Do you have a documented marketing plan?
Competition strategy	Which strategy describes best the way you want to compete?
Marketing budget	Which method describes best the way you calculate your marketing budget?
Promotion: advertising	Which advertising tools will you make/use?
Managing marketing results	How are the marketing results analysed?
Promotion: Sales promotion	How many of the following sales promotions do you provide?
Promotion: Public Relations	How many of the following public relations tools do you provide?

Promotion: Sales Force	How many of the following tools do you provide for the sales representatives?
Promotion: Direct Marketing	Can you use direct marketing tools (through knowledge of target markets)(e.g.: by customer data collection from previous products, data about interested people at fairs or congresses, you can mail info about your new product to people who will certainly be interested)
Target audience	Did you identify different segments in the market?

Table 21: Parameters of the marketing stage

13 Post-Market Surveillance

13.1 Terms & definitions

Term	Definition
Eudamed	European databank for medical devices. [97]
Vigilance	One aspect of PMS. It refers to incidents and recalls, which can occur with medical devices and in-vitro diagnostic medical devices when they do not perform as intended, in the worst case leading to injury or death. [98]

Table 22: Terms & definitions of the post-market surveillance stage

13.2 Stage construction

Medical device post-market surveillance (PMS) is more than a regulatory requirement, it is a good business practice. After bringing the device on the market, post-market surveillance assists the medical device development team analysing the performance of the device. It also provides continuous feedback to the manufacturer wherefore one can maintain the product quality. This feedback or **traceability** system allows the company to trace the patient. After all, Electronic health records and patient registers can be retrieved. PMS should allow the company to collect and review all those necessary information concerning the medical device and related competitors' devices, once the device is available on the market. [98] Inversely, it is also important to provide **feedback possibilities for all customers**. The European Forum of Notified Bodies Medical Devices has developed a guidance on post-market surveillance systems and has summed up the possible achievements or goals of a PMS system, where the importance of feedback in both ways is emphasized. [98]

- Detection of manufacturing problems
- Improvement of medical device quality
- Verification of risk analysis
- Intelligence of long-term performance
- Intelligence of chronic complications; performance trends
- Intelligence of performance in different user populations and mechanisms the device may be misused
- Feedback on indications for use, instructions for use
- Feedback on training required for users
- Feedback on use with other devices

- Feedback on customer satisfaction and market performance and sustainability
- Identification of incident reports (and field safety corrective action reports)

Monitoring risk is an important facet of the whole PMS process, however it should be noted that this applies to all phases of the device lifecycle. EN ISO defines risk as the combination of the probability of occurrence of harm and the severity of that harm. There are several types of risks that need to be investigated, however functional failure hazards is one of the most important wherefore a **failure analysis** must be developed to minimize the total risk. [98] As known, risk can never be completely eliminated. The mentioned monitoring process which provides feedback through PMS to maintain risk at an acceptable level is unbearable. The **PMS data** can be gathered in many different information sources, including post market clinical follow-up studies, literature reviews, customer complaints, customer surveys, expert user groups, patient registries, user reaction during training programs, trade shows, media, maintenance/service reports, field evaluation, in-house testing, retrieval studies on explants or trade-ins, and failure analysis. Off course, the collected data varies a lot, so a **data review** is from time to time necessary to keep track with the reality. Regulatory bodies require timely, coordinated action and provision of information from the manufacturer in relation to incidents and recalls that are related to the device.

Europe provides some tools to assist companies with new medical devices. At first, the European Commission offers a range of **guidance documents** to assist stakeholders in implementing directives related to medical devices. The MEDDEVs promote a common approach to be followed by companies and notified bodies that are involved in conformity assessment procedures. The guidelines are not legally binding. However, concerning the participation of interested parties and the experts from authorities, it is more or less expected that the guidelines will be followed. In that case, uniform application of relevant directives is ensured. [99] Secondly, a European databank on medical devices called **Eudamed**, is provided. The main purpose of Eudamed is to strengthen market surveillance and transparency in the field of medical devices. This is done by providing national authorities with fast access to information. It also contributes to a uniform application of the directives. [99]

A post-market surveillance systems is also developed because it is a way to maintain a good the consumer satisfaction. This consumer satisfaction can stay at a high level because PMS is able to minimize incidents and product recall processes, which off course is related to the consumer satisfaction. There is no real definition of PMS in the European medical devices directives, but surveillance indicates the active collection of information on medical devices. Again, knowledge and experience of good clinical practice that will follow up the post-market system within **the team** is important. It can lead to an efficient way of implementing and monitoring the post-market surveillance. This leads to activities carried out by the manufacturers. One can conclude that

a well-established PMS system helps to protect the user from risks by monitoring the product performance and identifying areas to improve quality and to reduce costs. [98]

13.3 Parameters & Questions

Parameter	Question
Traceability	Is there a system for traceability?
Guidance Documents	Will you use the guidance documents of the European Commission to implement directives?
PMS data	How many of the following channels do you use to gather PMS data?
Data review	How often will you review and trend the data from the vigilance report?
Customer feedback	Do you have a system to let customers (doctors/patients/...) give feedback on the product?
Failure analysis	Do you have a system for failure analysis? (Reporting database)
Eudamed	Will your new product be registered at Eudamed?
Team	Have you already invested in personnel with a deep knowledge of Good Clinical Practice that will follow up the Post Market System?

Table 23: Parameters of the post-market surveillance stage

III. BUILDING AN EVALUATION TOOL

1 Questions & rating of answers

The origin of all question evaluation parameter for each stage is explained in previous chapters. In this chapter, the focus will lie on the rating of all possible answers, quantifying the total score of evaluation stages and finally on calculating the total success rate for the medical device. As already mentioned, the algorithm assigns a weight or score to each possible answer for a question. These weights are used in a mathematical algorithm in order to generate a total score for each stage and finally a total success rate over all stages is calculated. These weights are decimal numbers between zero and one and can be considered as a 'percentage'. The weights should be conceived as the maximum percentage one can score for the stage, in the case that all the other questions for that stage are perfectly answered. The weight indicates the contribution of the selected answer to the total stage score. Four different weight classes were chosen. So each answer has only four different weight possibilities:

- Class A – 100% (1.00)
- Class B – 95% (0.95)
- Class C – 85% (0.85)
- Class D – 70% (0.70)

A model is chosen where all weights per stage are multiplied to receive a total score for an evaluation stage. A detailed explanation about the calculation and the weight choices can be found in chapter 4 . To provide a good insight in each existing type of questions and how the rating can be explained, next paragraphs briefly explain each type of question and the associated answers. Not all weights related to the answers are mentioned. One keeps most of the weights in a proverbial black box, to avoid that people can fill in the tool with prior knowledge of the weights in order to receive a better total success rate.

1.1 Class A & B answer rating

Question 53 (preclinical tests) – Statistical analysis	
Did an expert assessor analysed the gathered preclinical test data? (Significance tests, variability, sensitivity analysis,…)	
Answer options	**Weight**
Yes	1.00
No	0.95

Table 24: Example question including answer weights of class A & B

The first type of questions include answers with a related weight of class A and B. These questions have a smaller impact on the stage score than all other types of questions. For example, Table 24 shows a question concerning statistical analysis of preclinical test data. This is off course a relevant parameter, but has not the same impact on the success rate of the medical device like some other real stumbling blocks. If the user of the evaluation tool picks the answer option "No", he will still be able to score 95% at maximum for this evaluation stage, if all other questions are answered with a class A answer option.

1.2 Class A & C answer rating

Question 77 (product launch) – Global pricing strategy	
Is there an international pricing strategy (including different tax policies, competition, transportation costs …)?	
Answer options	**Weight**
Yes	1.00
No	0.85

Table 25: Example question including answer weights of class A & C

The second type of questions includes answers with a related weight of class A and C. These questions have a bigger impact on the total score of the stage than the first type, but are nevertheless not that decisive. For example, Table 25 shows a question concerning the global pricing strategy in the product launch phase. In the rating of this development phase, international perspectives are definitely a bonus. Still it is also possible to conduct a sufficient product launch without going to the international market. If the user of the evaluation

tool picks the answer option “No”, he will still be able to score 85% at maximum for this evaluation stage, if all other questions are answered with a class A answer option..

1.3 Class A & D answer rating

Class A & D

Question 24 (research & development) – Feedback	
Do you ask feedback of doctors, engineers, patients,... during the development of the product?	
Answer options	**Weight**
Yes	1.00
No	0.70

Table 26: Example question including answer weights of class A & D

The third type of questions includes answers with a related weight of class A and D. These questions have the biggest impact on total score of the evaluation stage. If this type of questions are negatively replied, the rating of the concerned stage will drop significant. For example, Table 26 shows a question concerning feedback in the research & development phase. Feedback during the first steps of your development process can be seen as an unbearable aspect, which has a big influence on the success of the research & development phase and even more, on the success of the product development cycle as a whole. If the user of the evaluation tool picks the answer option “No”, he will still be able to score 70% at maximum for this evaluation stage, if all other questions are answered with a class A answer option.

1.4 Mix of classes

Question 10 (idea or improvement) – Review of the existing intellectual property	
Are there patents on products or technologies that are very similar to your product/idea?	
Answer options	**Weight**
Yes	0.85
No	1
I don't know	0.7

Table 27: Example question including answer weights of more than two different classes

The fourth type of questions include answers of more than two different classes. Table 27 shows question 10 concerning the review of existing intellectual property in the idea or improvement stage. Weights of class A, C and D are assigned to possible answers. Logically, it is beneficial for the rating of a certain idea if there nowadays are no existing patents on product technologies that are very similar to this product or idea. Therefore, this answer option has class A. If there is already a patent on a similar product or technology and one is aware of it, this is crucial for the success of the medical device product launch. A weight of 0.85 is assigned to this answer. At last, if the team does not know if there is a patent on a similar existing technology, this can cause real problems. A patent on a similar existing technology or product is crucial and also has a big influence on the different paths that can be followed to continue the product development. This leads to an answer of class D.

1.5 Multiple answers type 1

Question 14 (research & development) – Experiments
If you do a research experiment, how many of the following steps do you include in your methodology?
Answer options
Make a clear definition of the research problem
Write down the design of the experiment
Use different sampling groups to do an experiment
Do a pilot study before you undergo the real measurement-experiment
Brief written analysis and conclusion
Make a standardized report
Statistical analysis and significance tests

Table 28: Example question where multiple answers can be chosen – type 1

In the first four type of questions, only one answer can be denoted. Hence the tool also included two types of questions where denoting multiple answers is possible. It is important to notice that for every question where multiple answers are possible, all answers have the same contribution to the score. However, it is not possible for questions with multiple answers to relate every answer to a certain class or weight. That is why a new rating for multiple answers is developed, with two types of rating. For both, the relative number of answers denoted is the key factor which is related to a score of class A, B, C or D. The difference of the two types lies in the rating, whereby the first type is rated more strict than the second type. This means that for the same

relative number of answers, type 1 gets in general a lower score than type 2. The rating of this type of questions can be found in Table 29.

Relative number of answers denoted	Weight
0% - 49%	0.7
50% - 69%	0.85
70% - 84%	0.95
85% - 100%	1.00

Table 29: Weight allocation for the first type of questions with multiple answers possible

For the first type, an example is given in Table 28. This question is about research experiments and the included steps in the methodology of the company. If the company includes less than four steps in their methodology, a score of 0.7 is received. If 6 or 7 steps are included, a score of 1.00 is assigned to this question.

1.6 Multiple answers type 2

Question 89 (marketing) – Promotion: advertising
Which advertising tools will you make/use?
Answer options
Clear logos and symbols
Printing ads
Motion pictures, commercials
Display signs, purchase displays
Brochures, booklets
Posters, leaflets
Billboards
Packaging-outer, inserts
Product movie, corporate movie

Table 30: Example question where multiple answers can be chosen – type 2

As already stated before, the second type of questions where multiple answers are possible, is judged less strict than question of type 1. Table 31 gives an overview of the relative number of answers denoted and related weights. No score of class D is included. Table 30 shows question 89 concerning the promotion of the product and the included advertising tools. If less than five steps are denoted, a score of 0.85 is given. Above six denoted answers, the company receives a score of 1.00 for this particular question.

Relative number of answers denoted	Weight
0% - 49%	0.85
50% - 69%	0.95
70% - 100%	1.00

Table 31: Weight allocation for the second type of questions with multiple answers possible

2 Four different product or service scenarios

The purpose of the evaluation tool is to find indicators for evaluation stages, designate the pitfalls of the development process and calculate an overall success rate for all types of medical devices (products or services). This states that the tool has to be generic and applicable for all types of medical devices, which is difficult due to the diversity of the products and services. Medical device development teams usually have different long term objectives. Some of them only want to prototype a very good idea, others want to build a solid company. Also the number of iterations in the development cycle can be different. Some companies want to go to the market as soon as possible as they launch the new product or service and develop a second version based on customer feedback. Other companies want to be very confident of their product before they go to the market. These companies invest a lot of money and time in prototyping, biomechanical tests and clinical trials. One immediately feels that there is a big difference between the two extremes in terms of investments in time and money. Based on these considerations, four different product/service scenarios are formulated and shown in Figure 27.

- **Scenario 1: Sell IP:** Develop, design and prototype some product or technology. The technology will be intellectual protected with the intention to sell the intellectual property to another company.
- **Scenario 2: Early licensing:** Going fast through the development cycle of the product or service with the intention to go very fast to the product launch. Next generations of products will be launched based on feedback of the users.
- **Scenario 3: Late licensing:** Paying close attention to the prototyping and testing phases before the product is launched. The company is going slower through the development cycle because they want to be confident about their product before they launch it.
- **Scenario 4: Autonomous company:** Paying close attention to all the phases in the development cycle and putting a lot of energy in the organization of a solid company next to the product development.

Depending on the product or service scenario, every evaluation stage gets a specific quotation allocated on how much it contributes to the final success rate score. The quotation for each stage corresponds with the quotation factor in the weighted arithmetic mean for the calculation of the total success rate. For example, in product/service scenario 2 the quotation factor of the idea or improvement stage is three while the quotation factor of the prototyping stage is only one. This means that the total score for the evaluation stage of the idea or improvement phase contributes three times more to the overall success

rate than the prototyping stage. All quotations can be found in Table 32. A detailed explanation about the calculation of the total success rating can be found in chapter 4 . All quotation are based on gathered knowledge and expert opinions.

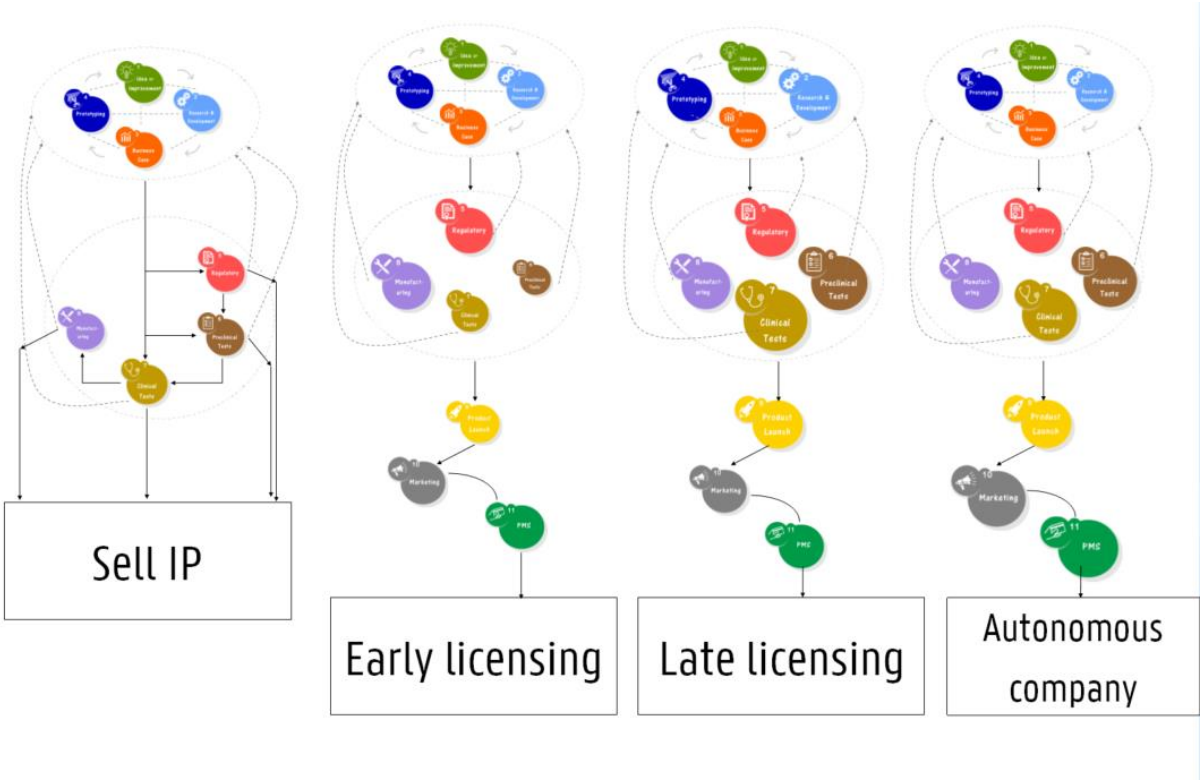

Figure 27: Four different product or service scenarios

Stages	Product/Service scenario 1	Product/Service scenario 2	Product/Service scenario 3	Product/Service scenario 4
Idea or improvement	★★★	★★★	★★★	★★★
Research & Development	★★★	★★	★★★	★★★
Business Case	★★★	★★★	★★★	★★★
Prototyping	★	★	★★★	★★★
Quality & Regulatory	★★★	★★★	★★★	★★★
Preclinical tests	★★★	★★	★★★	★★★
Clinical tests	★★★	★★	★★★	★★★
Manufacturing	★	★★★	★★★	★★★
Product Launch	★	★★	★★	★★★
Marketing	★	★★	★★	★★★
Post Market Surveillance	★	★★	★★	★★★

Table 32: Quotation rules for every stages per product/service scenario

3 Three evaluation moments

The evaluation tool is created for newly established start-up companies, who will launch a product or service in the medical technology sector. Not every product development cycle of a start-up has the same duration. On average, the life cycle of a medical device is four to five years. But for example, implants and smartphone applications or wearables have a shorter life cycle. Depending on the moment the questionnaire is filled in during the development process, the team behind the start-up will have encountered a lot more or less knowledge. An average pattern traversed by most product development teams can be found in Figure 28.

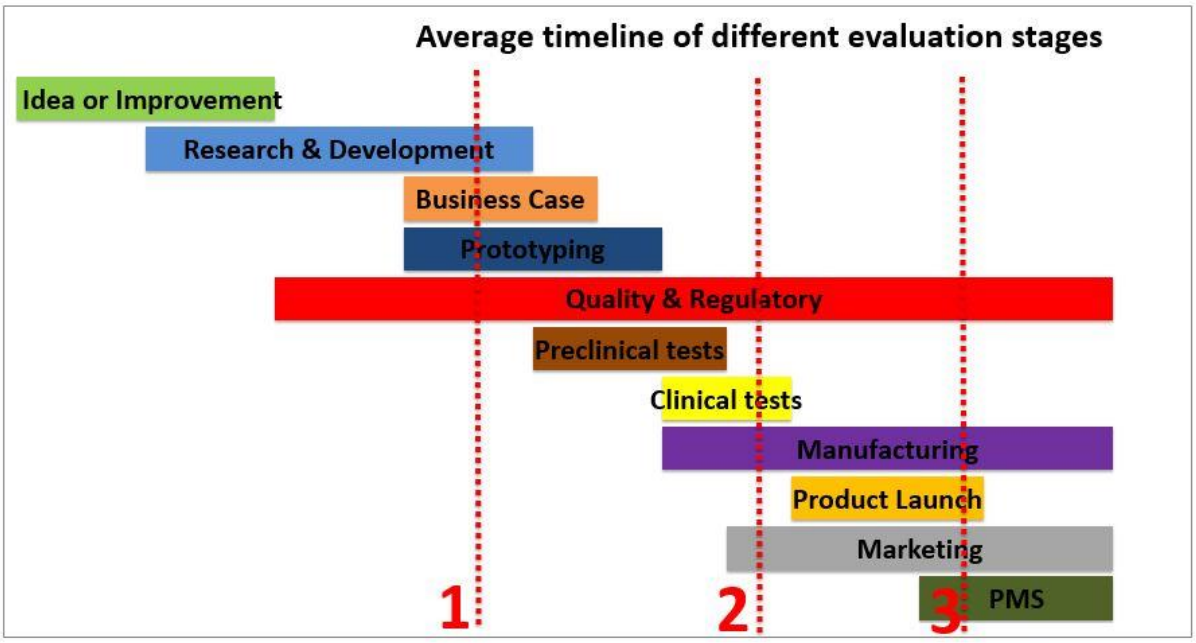

Figure 28: Three predefined evaluation moments for filling in the tool

3.1 Evaluation moments

As mentioned, not every company will have gathered the same knowledge on the moment they fill in the questionnaire of the tool. Therefore, three evaluation moments were predefined at this tool. The users are asked to choose one of the evaluation moments that describes best their current situation. Depending on this moment, not all the questions will partake in the algorithm to calculate the success rate. Some questions are not yet relevant for some development teams, including them would give an irrelevant outcome for the total score of an evaluation stage and moreover for the total success rate. Notice that every question is visible and must be filled in by everybody, only the weight does not contribute to the final stage score. The tool shows all questions to all start-ups in order to make them aware of which parameters they must take into account during the medical device development. Afterwards, this is gathered knowledge for everybody that filled in

the questionnaire. Table 33 and Table 34 show two examples of questions that not contribute for the total success rate for all the evaluation moments.

Question 80 (Product Launch) - Pre-launch training for physicians
Did you provide pre-launch training for physicians/patients/end users?

Table 33: Question that is not taken into account in evaluation moment 1

Table 33 shows a question for which the answer contributes to the total stage score only for evaluation moments 2 and 3. This is based on the fact that at evaluation moment 1, it is not crucial to know if a pre-launch training for physicians, patients or end users will be organized. Table 34 shows a question that only contributes in evaluation moment 3. Again, the relation between the questions and evaluation moments are not revealed in this master's dissertation. One keeps this in a proverbial black box. The decision on which questions or parameters are linked to each evaluation moment are the result of gathering opinions of experts concerning our evaluation framework with the related questions, answers, evaluation moments and product or service scenarios.

Question 91 (Marketing) – Promotion: Sales promotion
How many of the following sales promotions do you provide?

Table 34: Question that is not taken into account in evaluation moment 1 and 2

3.2 Stage skip

After presenting the evaluation framework to different MedTech experts, a last variable was added to our algorithm. An important aspect of our tool is that under all circumstances, the tool or the related outcome may not discourage people who fill it in. In order to overcome the scourge that people get an unpleasant feeling of getting a lot of questions that they do not know yet, some stages can be skipped in the tool. The companies can choose to skip some stages. If they don't fill it in, the stage score is put at zero and has off course no contribution on the total success rate. So either filling in those stages or not, will have no influence on the total success rate. This feature is available for 3 stages: preclinical tests, manufacturing and marketing. Those are the stages that in general include most questions, where a development team has no insight on how they will deal with this at the beginning of the development process.

4 Total success rate calculation

4.1 Weight choice and benchmarking

After linking the weights to each answer of all the question, a total score can be calculated for an evaluation stage and moreover generate a total success rate. The purpose is developing an understandable model which provides justified outcomes for each stages, a realistic comparison between the stages and a substantiated success rate for each company. Since the entrepreneurship of developing a new product or service is admirable and must be supported, in any case the outcome of this tool may not discourage people from continuing with their project.

The development of a product or service is a challenging task with a lot of hurdles that deserve special attention. There are some major parameters in this challenge, which have a big influence on the outcome. For example, the feedback of doctors, engineers, patients,... during the research and development of the product is an example of a key determinant that has a big influence at this stage. If feedback is not provided, there is no longer a high rating possible for the research and development stage, even if all other question are positively answered.

The model must provide the possibility for each question to set a limit at the total evaluation stage rating. Therefore, a model is chosen whereby the weights of all questions per stage are multiplied to calculate a total stage score. From this point of view, four answers classes are arbitrarily chosen. The choice for values 1, 0.95, 0.85, and 0.7 is on the one hand based on gathered knowledge of the product development cycle. The difference between the weights 0.7 and 0.95 is an estimated quantification of the difference between major parameters which must have a big influence on the stage rating and parameters which are important but not crucial. On the other hand, the values are based on the effects of weights in a model. With this knowledge, five guidelines are established whereon the final algorithm is based:

1. Under all circumstances, the total evaluation stage score must be quantified between 0 and 1.
2. The outcome of the tool may not discourage the entrepreneurs. Even though it must have an awareness character.
3. If one third of the questions is answered with an answer of class D and all other questions are answered with an answer of class A, the total stage score should be approximately 50%.
4. If two third of the questions is answered with an answer of class C and all other questions are answered with an answer of class A, the total stage score should be approximately 50%.

5. Stages need to be benchmarked in order to have the possibility to compare all eleven stages among themselves.

Based on those five guidelines, a model for the calculation of the evaluation stage scores and a final success rate is designed. Until now, a simple multiplication of all answer related weights gives us a preliminary stage score. Since not all stages include the same amount of questions, those scores should be adjusted to a certain benchmark. In our example, the benchmark is actually a number of questions to where a preliminary stages score is reduced to. However, first a formula is designed taking into account guideline 1 and 2 and also provides the possibility to include a benchmark factor f. To make sure that the stage score is between 0 and 1, the power function is chosen as ground model.

$$s_{\mathrm{i}} = \left(\prod_{\mathrm{k}=0}^{\mathrm{K_i}} \mathrm{w_{ik}} \right)^{\frac{\mathrm{F}}{\mathrm{K_i}}} \tag{2}$$

$$with: \begin{cases} s_i = Total\ score\ of\ stage\ i \\ \mathrm{K_i} = Total\ number\ of\ questions\ of\ stage\ i \\ w_{ik} = Weight\ of\ the\ k^{th}\ answer\ of\ stage\ i \\ F = Benchmark\ factor \end{cases}$$

To define the benchmark, guideline 3 and 4 are considered. A combination of guideline 3 and equation (2) gives us two restrictions that leads us to a proper value for benchmark factor F. Guideline 3 implies a total stage score of S_i= 0.5 , since this is the approximated stage score that one pursues. It also implies a score where one third of the questions is answered with an answer of class D and all other questions are answered with an answer of class A. For example, if there are 9 questions, 3 of them get a weight of 0.70 and all other a weight of 1.00, which leads to a stage score of 0.343 or 0.70 to the power of 3. So if our benchmark factor is 9 questions, it give a stage score of 0.343 which lies not even close to the requested 0.50. To find the right benchmark factor, one fills in the simple example where there are 3 questions and one of them has a weight of 0.7 and the other two a weight of 1.00 :

$$s_{\mathrm{i}} = \left(\prod_{\mathrm{k}=0}^{\mathrm{K_i}} \mathrm{w_{ik}} \right)^{\frac{\mathrm{F}}{\mathrm{K_i}}} \tag{2}$$

$$with: \begin{cases} s_i = 0.5 \\ K_i = 3 \\ \prod_{\mathrm{k}=0}^{\mathrm{K_i}} \mathrm{w_{ik}} = 0.7 \end{cases}$$

After this, the logarithm with base 0.7 is taken at both sides to find equation (3). The same calculations can be made to find equation (4), by using guideline 2.

$$\begin{cases} F = 3.\log_{0.7}(0.50) = 5.83 & (3) \\ F = 3.\log_{0.85^2}(0.50) = \frac{3}{2}.\log_{0.85}(0.50) = 6.40 & (4) \end{cases}$$

$$\Rightarrow F \approx 6$$

Two proposals for benchmark factors are found, since two restrictions are stated in the guidelines. To fix a reasonable value where both guidelines are neglected, the benchmark factor of six is chosen. It is not necessary to pick an integer, but it gives the benchmark factor a more clear definition. Due to the benchmark factor, every total stage score will now be converted to a stage score as if there were six questions in this stage. This is a clear definition which provides a good insight in the meaning and purpose of benchmarking.

4.2 Total success rate

For the calculation of the total success rate of a product or service, one should take into account the total score for each evaluation stage, the multiple evaluation moments and the different product or service scenarios. As explained in chapter 3 , some of the questions are not incorporated if the tool is filled in in evaluation moment 1 or 2. For this reason, a binary variable y_{ik} is added to equation (2) which is 1 if the question k is taken into account in stage i and zero otherwise. In chapter 2 , all possible product/service scenarios are explained and all related quotation rules are presented in Table 32. A variable B_i is added to equation (2) which represent the weight that is given per product/service scenario in stage i. Finally, a binary variable x_i is added to decide whether a whole stage i is skipped or not. As explained in subchapter 3.2 , this is only possible for three predefined stages. A final algorithm with an outcome that represents the total success rate of a medical product or service, is given in equation (5):

$$\text{Total success rate} = \frac{\sum_i^I x_i \sum_i^I b_i \sum_i^I \sum_k^{K_i} y_{ik} \left(\prod_{k=0}^{K_i} w_{ik}\right)^{\frac{6}{K_i}}}{\sum_i^I x_i \sum_i^I b_i \sum_i^I \sum_k^{K_i} y_{ik}} \quad i = 1 \dots I; k = 1 \dots K_i \qquad (5)$$

with:

$$\begin{cases} x_i = \begin{cases} 1 & \text{if stage i is included} \\ 0 & \text{otherwise} \end{cases} \\ y_{ik} = \begin{cases} 1 & \text{if the } k^{th} \text{question of stage i is included} \\ 0 & \text{otherwise} \end{cases} \\ b_i = \text{product or service scenario weight of stage i} \\ K_i = \text{total number of questions of stage i} \\ w_{ik} = \text{weight of } k^{th} \text{question of stage i} \end{cases}$$

5 MedTech Compass

5.1 Software

After developing a questionnaire and a related algorithm to find stages scores and a total success rate, an accessible software tool must be created. The company 'Survey Anyplace' [100] give us access to their platforms to build an online tool. The evaluation tool is named **'MedTech Compass'**. It took several weeks to implement the full questionnaire and the corresponding weights in an online tool. The web application provides the possibility to fill in each questions by a simple mouse click. Afterwards all outcome data is generated and implemented in an Excel file. This file provides a full report which can be send to the company by email.

Figure 29: Start screen of MedTech Compass

Figure 29 depicted the start screen of the MedTech Compass tool, the full online tool can be found on the link below or by scanning the provided QR-code in Figure 30.

Link: http://su.vc/medtech_compass

QR-code:

Figure 30: QR-code MedTech Compass

5.2 Generated report

After a company filled in the online evaluation tool, a report is generated in Excel were all relevant outcomes are discussed and presented. First of all, a test for consistency is provided. To test whether the questionnaire was filled in consistently, one question is repeated several times in the tool. If this question gets the same answer each time, this box is checked as presented in Figure 31.

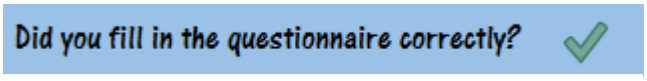

Figure 31: Test for consistency in MedTech Compass

If the box is not checked, this can be an indicator that the user did not consistently filled in the tool. Further investigation is required to validate the evaluation. Another indicator that can be used, is the duration of filling in the questionnaire. The average duration of the tool is around 20 minutes, if the questionnaire is filled at once.

Secondly indicators are depicted for each total score of the evaluation stages. A score of zero at an evaluation stage implies this stage is not included in the calculation of the total success rate. Scores of zero are only possible if the end user indicated that this stage has no significant contribution for the total success rate and those questions are skipped in the online tool. In the example shown in Figure 33, one can see that the

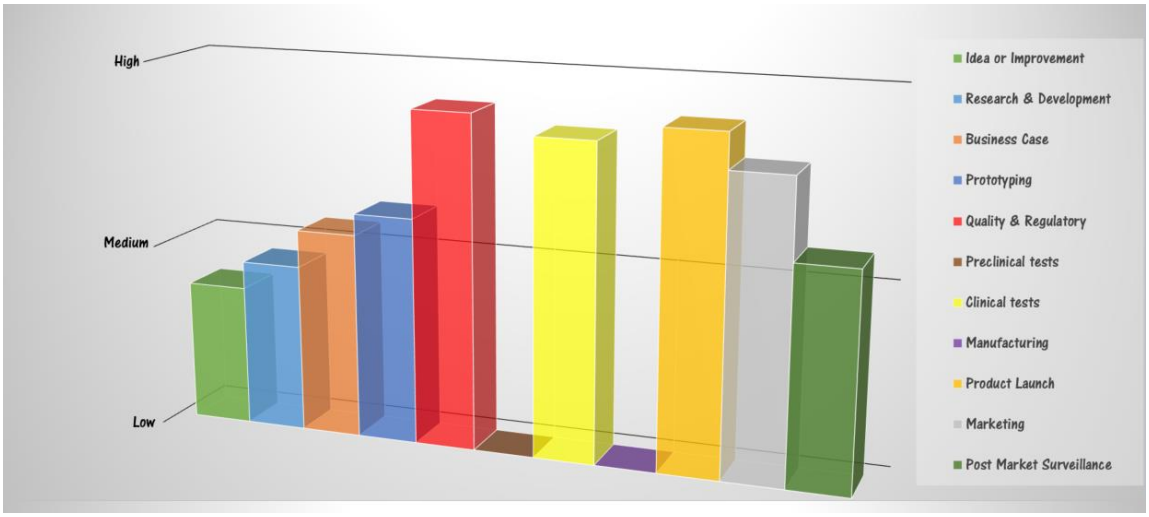

Figure 33: Indicators for all evaluation stages

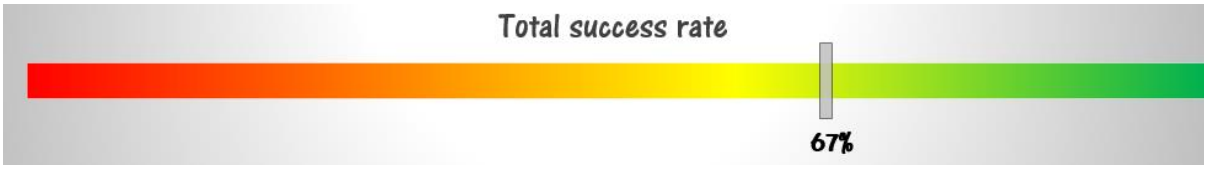

Figure 32: Total success rate

company scores best on the quality & regulatory, product launch and clinical test stage. The total success rate is the weighted result of all the total scores of the different stages, depending on the importance of a stage in the selected product or service scenario. The total success rate for the example is 67%, like shown in Figure 32. An indication of the score for the various evaluation stages is also shown in Figure 34. The multiple product/service scenarios were described above and have an influence on the total success rate, as one can see the variation in the different success rates.

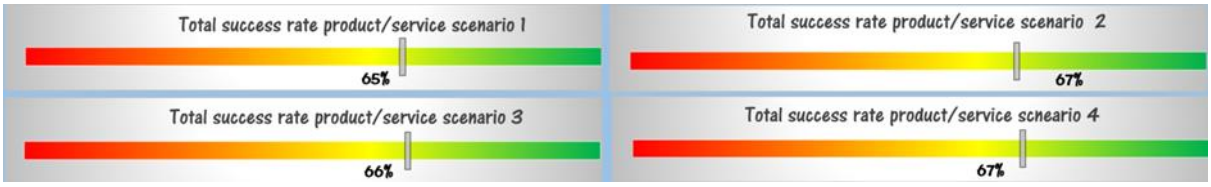

Figure 34: Total success rate for all product/service scenarios

Next, the two evaluation stages with the lowest score are searched. Of these stages, four parameters that require urgent attention are displayed as shown in Figure 35.

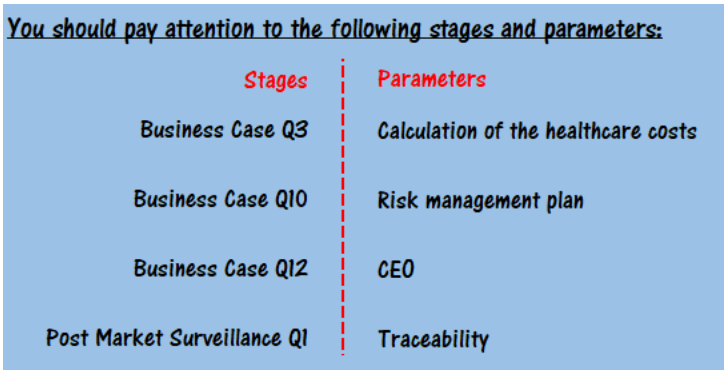

Figure 35: Four lowest scoring parameters related to the two lowest scoring evaluation stages

Finally, the scores of the different evaluation stages are compared to the score they would achieve if they indicated a different evaluation moment in the product development cycle. Figure 36 shows the different evaluation moments and related stages scores.

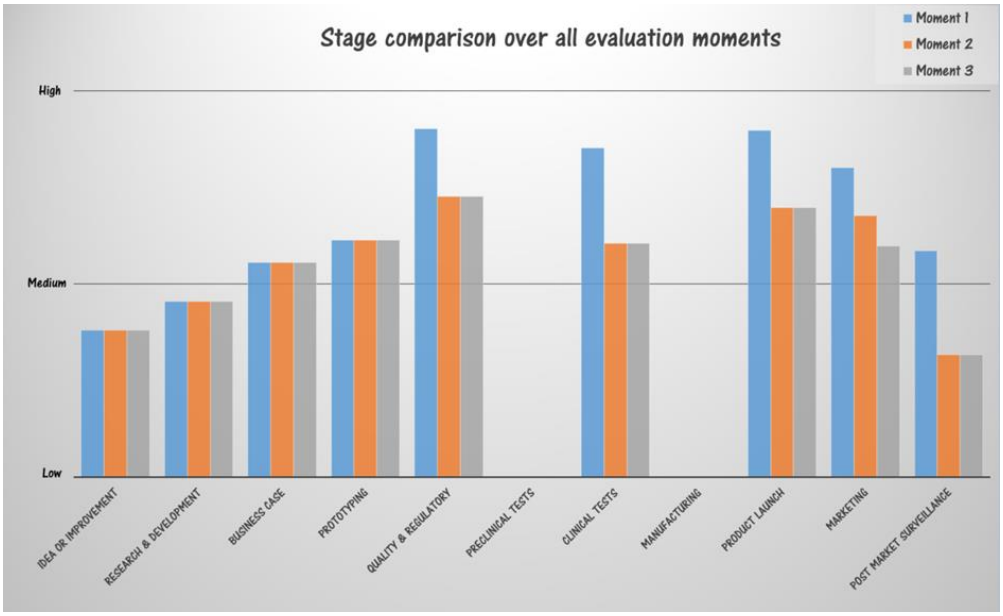

Figure 36: Stage indicator comparison over all evaluation moments

IV. THREE CASE STUDIES

1 Case study 1: Evaluating existing companies of the MedTech Flanders network as a benchmark

The evaluation questionnaire was implemented in the online platform and subsequently the mathematical algorithm was finished. Some of the interviewed MedTech experts were revisited to give their opinion on all weights, scores and quotation rules that are linked to the questions and evaluation stages. Afterwards, three of the MedTech experts who were interviewed during the compilation of the questionnaire, were asked to complete the online tool. These experts did not see the final weights or quotation rules before they filled in the evaluation tool, to get an unbiased success rate determination of their company. They completed the MedTech Compass regarding their experience with the main medical device project in which they are involved. These are projects where the expert is the co-founder or CEO of the MedTech start-up or company. These companies already earned their spurs within the Flemish MedTech industry. Therefore, one expect them to score more than 75% for the success rate of MedTech Compass. To not mention a company by name, the different cases are described as company A, B & C.

Company A

The first company has more than 15 years of experience with the development of implants. It started with one revolutionary product in the sector. By now, they have been gone through the whole medical device development cycle of multiple products. They invested in specialized manufacturing machines, put a lot of effort in quality management and have close contacts with innovative surgeons. Next to the development of their own products, they can also be a subcontracting partner for other companies. Due to the fact that this company has already grown out of the start-up phase, a high success rate on the evaluation tool was expected.

The evaluation algorithm generated a total success rate of 82% for company A. Of course, the quotation rules for the third evaluation moment were applied and the company chose the fourth product/service scenario. If the quotation rules for the first or second evaluation moment had been used, the company would have achieved a success rate of 88% and 82%.

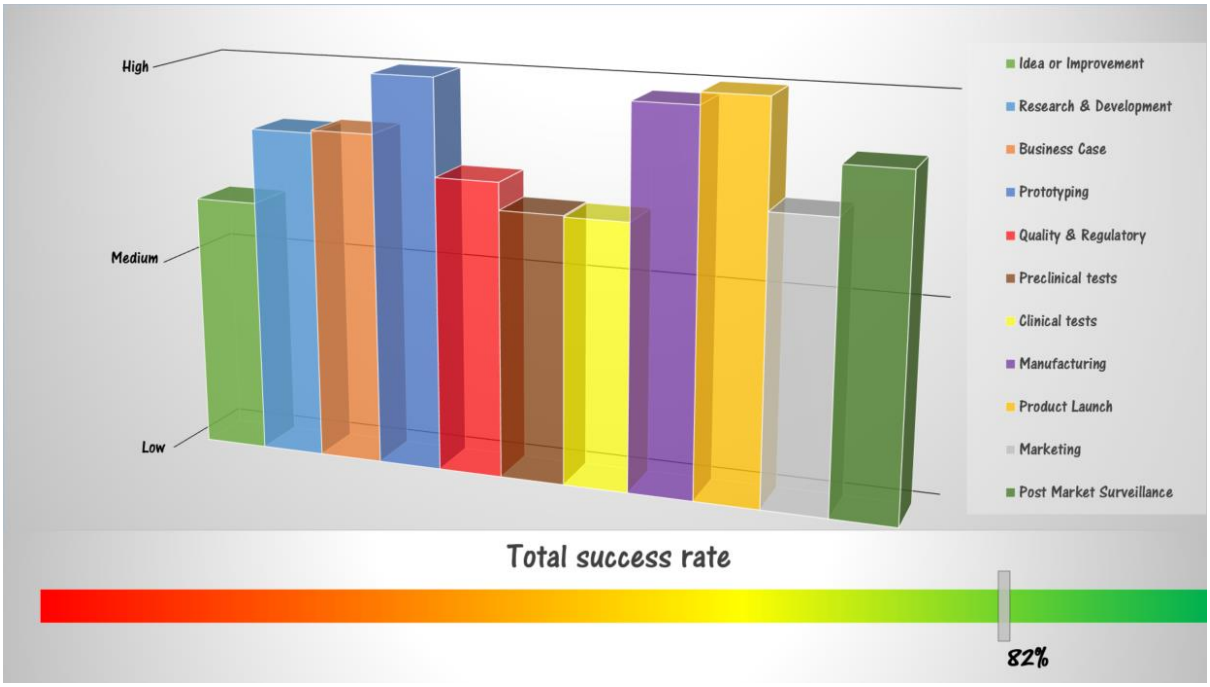

Figure 37: Indicators of the different evaluation stages and total success rate of company A

Despite the strict quotation rules for evaluation moment 3 were used, the indicators of the prototyping, manufacturing and product launch stages were very high. The indicators for the preclinical and clinical tests are scoring slightly lower, these are the stages where special attention is needed. The first indicator of the evaluation stage 'idea or improvement' is relatively low, because it was chosen not to patent the products.

The feedback of the expert included that the questions were relevant and very perceptive. Some comments on questions and evaluation criteria were incorporated into the evaluation tool.

Company B

The second company is active in the field of preclinical imaging. After 5 years extensive research at a Belgian university, a spin-off company with a cross-functional engaged team was founded. Currently they are launching their products on the market. The spin-off quickly raised the necessary funds to launch their product and the ambitious team has a lot of knowledge about medical device development.

The start-up is currently in between the proposed evaluation moments 1 and 2. When they filled in the MedTech Compass tool, evaluation moment 1 was chosen. With the quotation rules of this evaluation moment, the start-up had a success rate of 82%. If the quotation rules of the second or third evaluation moment would have been used, a success rate of 73% or 72% would be obtained.

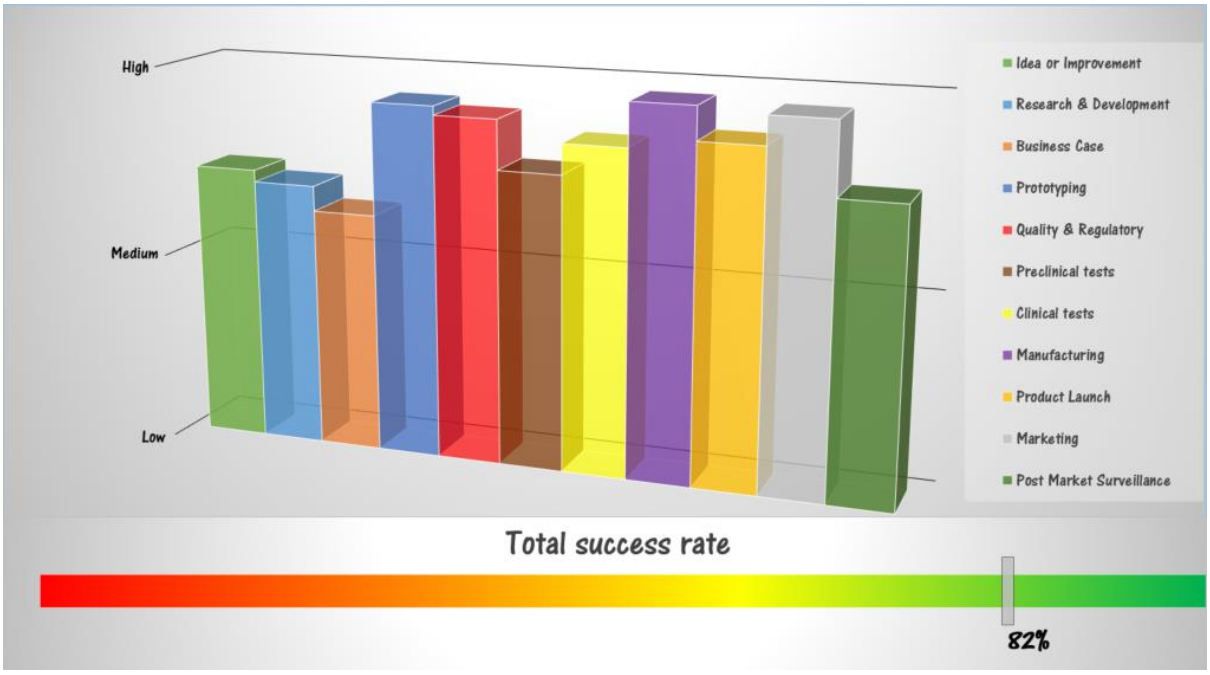

Figure 38: Indicators of the different evaluation stages and total success rate of company B

The evaluation report was presented to the person who completed the tool. He confirmed that the indicators for the various evaluation stages represented the real strengths and weaknesses of the company. The indicator for the business case was the lowest for this company. Although, the company was able to raise the necessary funds relatively quickly. The questions from this evaluation stage need to be revised. However, this also has partly to do with the fact that investors are not only fixated on the business plan. They attach great importance to the unmet clinical need, the proof of concept, the cross-functional engaged team behind the company etc. These determinants are considered in other evaluation stages.

The final conclusion of this case study was that some evaluation criteria of the latest development phases were still too far away in time to be able to give clear answers. Some other experts also confirmed this. For this reason, it became possible to skip some evaluation stages of MedTech Compass.

Company C

The third company is active in the field of product design of surgical tools and instruments. The start-up exists for more than five years but is still in the R&D and testing phase. They placed themselves closest to the first evaluation moment while completing MedTech Compass. Since it was already possible to skip some of the latest evaluation stages, this company chose to do this for the preclinical testing, manufacturing and marketing stage. These evaluation stages are not included in the calculation of the total success rate. The start-up scored a total success rate of 83% with the quotation rules of the first evaluation moment. If the quotation rules of the second or third evaluation moment were used, they would obtain in both cases 75%.

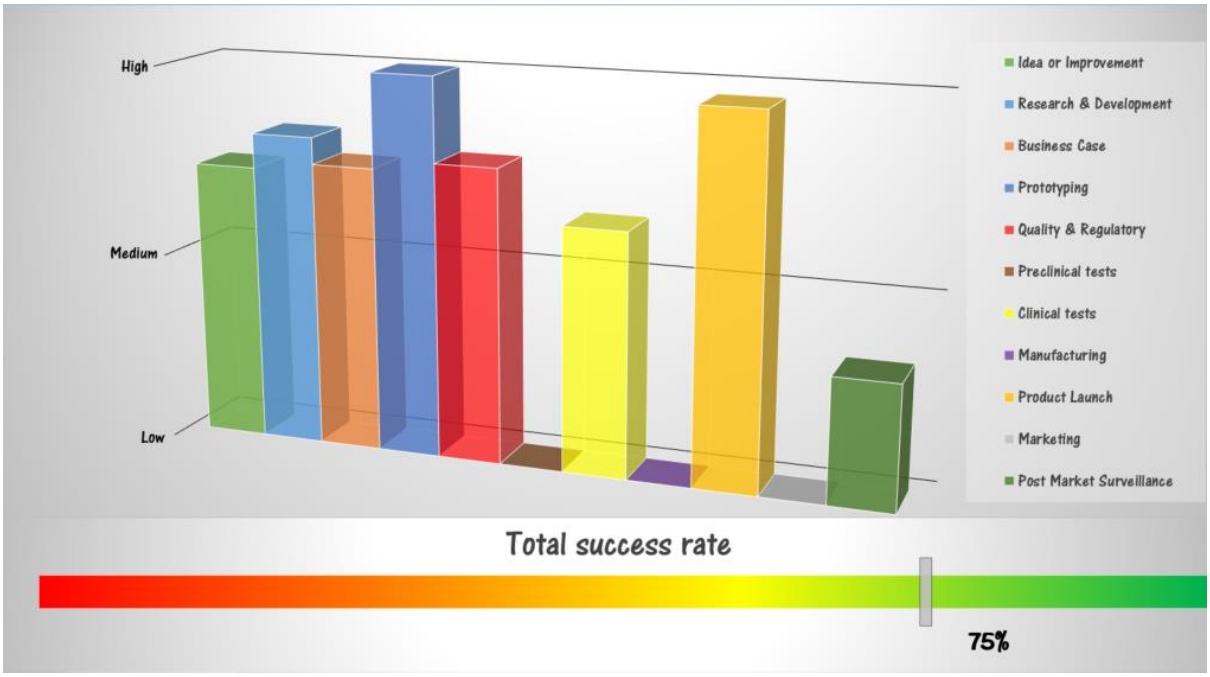

Figure 39: Indicators of the different evaluation stages and total success rate of company C

The overall success rate is again quite high, despite this company is the least far in the development cycle of their product compared to the two previous ones. This obviously has to do with the fact that the scores of three evaluation stages were not included in the mathematical algorithm. The results of this company should therefore not be compared with the previous ones. If company C also had to complete the three other evaluation stages, the total success rate might have been lower. The feedback of the company included that the evaluation tool is a good representation of the medical device development cycle, but they found the questionnaire a bit too long.

Based on these three case studies at existing companies in the MedTech industry and the feedback of other experts, the tool was completed to its final form. The questions, weights and quotation rules were revised by experts. Based on the results of this first case study, one could conclude that the benchmarking rules were well-chosen. MedTech Compass was now ready for its true baptism of fire with the MedTech accelerator participants.

2 Case study 2: Evaluating start-ups participating the MedTech Flanders accelerator program

Figure 40: MedTech accelerator logo

During the first semester of 2017, the first edition of the MedTech accelerator took place. MedTech Flanders wants to boost medical entrepreneurship in Flanders. The MedTech accelerator is an initiative of MedTech Flanders powered by Verhaert Masters in Innovation. Twice a year, companies with breakthrough medical ideas and technology will get the opportunity to make use of profound methodology, expert coaching, facilities and financing support for their business or product idea. Four start-ups in the Field of MedTech were selected to participate.

Figure 41: MedTech accelerator program

2.1 Four start-ups with game changing ideas

The following four start-ups participated the first MedTech accelerator. These start-ups are a good case study to test the evaluation tool.

ANTELOPE DX

Antelope DX is a new spin-off company of Ghent University aiming at bringing a novel lab-on-chip platform to the market. This diagnostics platform allows both consumers and medical practitioners to have on-the-spot access to key health parameters. The antelope technology brings the performance of a clinical lab to a low-

cost device that communicates with a smartphone. The consumer can perform a test at home while his/her medical practitioner can check the results securely via the cloud. This novel detection technology only requires a drop of body fluid to assure picomolar protein detection. The technology builds on patented silicon photonics biosensors developed at Ghent University during the past decade.

Figure 42: Logo Antelope DX

CADskills

CADskills is active in medical image processing, design and manufacturing of patient specific implants, surgical guides and anatomical models. They help evolve reconstructive surgery by combining conventional production techniques with new material combinations (titanium, PMMA, ceramics, polyamide…) and additive manufacturing to deliver patient-specific and physician-specific implant solutions.

Figure 43: Logo CADskills

MoveUp

MoveUp is a coach app that allows recovery after knee surgery at patients own terms. Training videos let the patients follow a rehab program that is automatically adjusted to their actual physical activity and reported pain level. Using wearable technologies and a tablet app, the patient and responsible caregivers receive a personalized report on movement and activities, painkillers intake, reported pain level and progress in the rehab program. The services have been developed within a large hospital in Ghent by orthopaedic surgeons, physiotherapists and engineers. MoveUp improves health management at different levels. For patients, this means a better recovery and a healthier lifestyle thanks to preventive measures. For medical stakeholders, this means a more efficient health management throughout the patient's journey.

Figure 44: Logo MoveUP

VIPUN

VIPUN is a spin-off company of KU Leuven. The goal of VIPUN is to increase survival rates and reduce length of stay of intensive care unit patients. The VIPUN gastric monitoring system offers accurate and continuous monitoring of gastric function. The novel VIPUN nasogastric catheter stimulates gastric well-being and acceptance of medical nutrition. Their ambition is to became a game-changer in the management of critically ill patients.

Figure 45: Logo VIPUN

The four start-ups participating the MedTech accelerator are developing different types of medical devices. VIPUN develops a "classic" medical device, while CADskills designs patient-specific devices. MoveUp is creating a software application linked to a wearable and Antelope DX is develops an In Vitro Diagnostic medical device. The diverse spectrum of different types of medical devices is well represented in this case study.

2.2 Evaluation of the MedTech accelerator participants

All four participants of the MedTech accelerator were invited to complete MedTech Compass. However the start-up Antelope DX quitted halfway through the questionnaire. They are developing an In Vitro Diagnostic device, while the questionnaire is more focused towards "classic" medical devices. The regulatory aspects and questions about clinical trials were too far from what they are currently undergoing. Therefore, one of the suggestions for further research is to delve into the IVD-spectrum of medical devices. The evaluations of the other start-ups are described below. Again, the results are randomly named with start-up A, B and C.

Start-up A

The first start-up indicated they are currently following the fourth product/service scenario of becoming an autonomous MedTech company, but an early exit by selling the patent to another company is also possible (first product/service scenario). The start-up is evaluated with the quotation rules of the first evaluation moment. The results of the evaluation tool can be found in Figure 46 and Figure 47. They obtain a score of 69% for the total success rate. The rate is the same for each of the possible product/service scenarios, which

reflects the fact they take most decisions as general as possible, to not exclude a potential exit or product launch strategy.

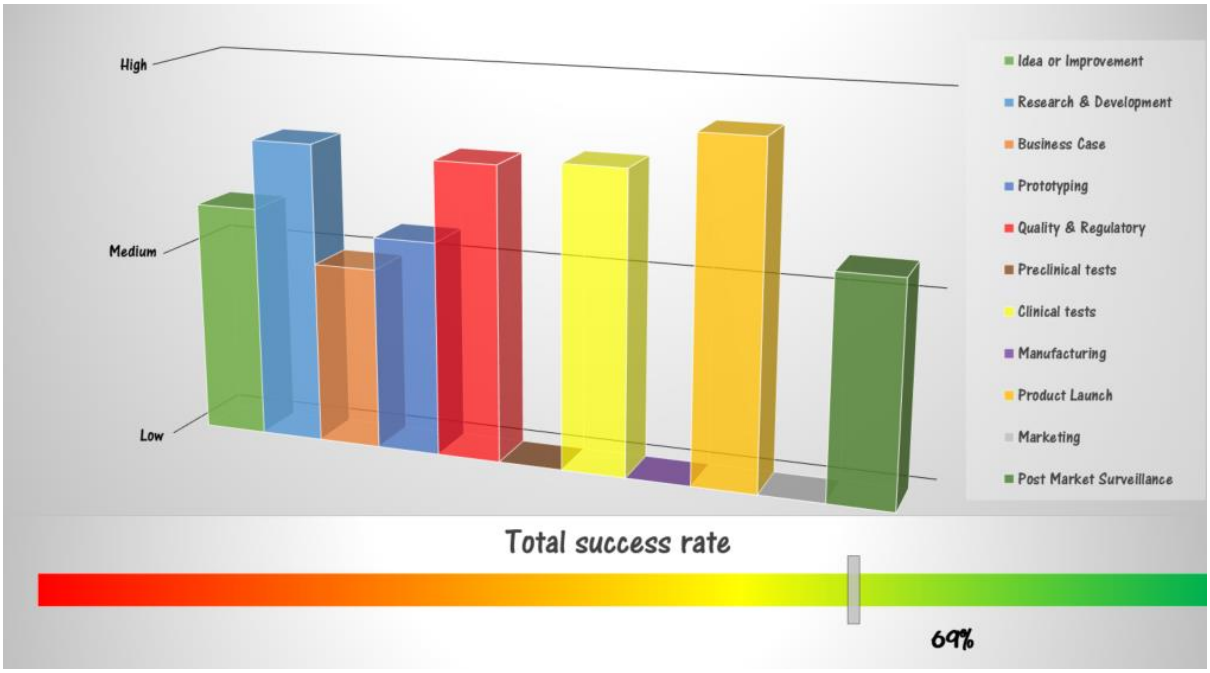

Figure 46: Results of the evaluation tool for start-up A

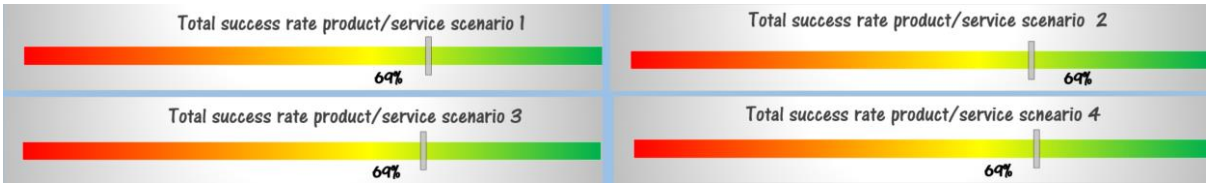

Figure 47: Total success rate for all different product/service scenarios for start-up A

The indicator of the evaluation stage 'business case' is the lowest. The four parameters they should pay attention to are all from the 'business case' stage.

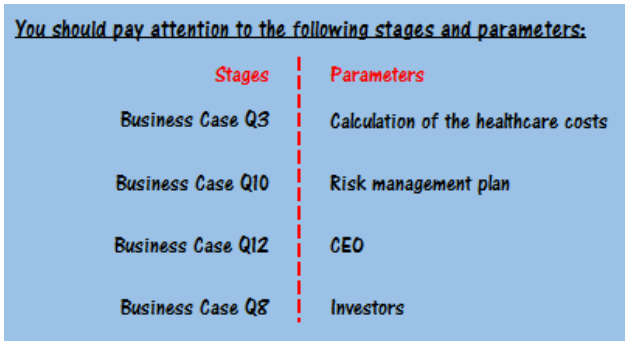

Figure 48: Pitfalls indicated at the evaluation report for start-up A

Start-up B

The second start-up is currently putting a lot of effort to set up a wide distribution network. The third or fourth product/service scenario should be chosen. At the evaluation tool, they indicated the fourth product/service scenario. Because they are already producing their medical devices and sell it to customers, they indicated the third evaluation moment as the one closest to their current situation at the development cycle.

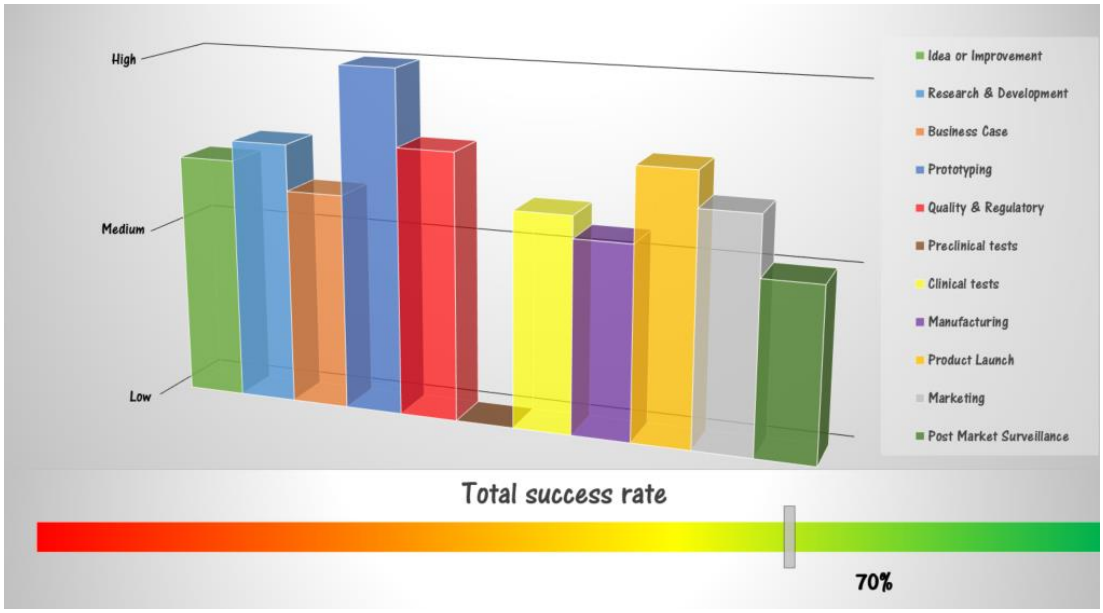

Figure 49: Results of the evaluation tool for start-up B

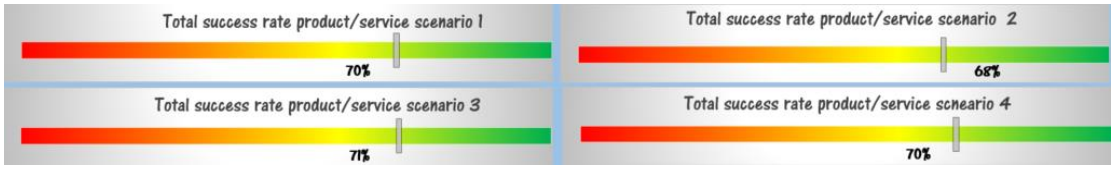

Figure 50: Total success rate for all different product/service scenarios for start-up B

For the third evaluation moment, the start-up obtained a total success rate of 70%, as displayed in Figure 49. If the quotation criteria of the first or second evaluation moment would be used, the success rate would be 82% or 72%. The success rates of the third and fourth product/service scenario always get the best score, irrespectively the evaluating moment. The parameters they should attention to are shown in Figure 51.

You should pay attention to the following stages and parameters:

Stages	Parameters
Post Market Surveillance Q3	PMS data
Post Market Surveillance Q6	Failure analysis
Manufacturing Q4	ISO environment
Manufacturing Q5	CE-labels

Figure 51: Pitfalls indicated at the evaluation report for start-up B

Start-up C

The third start-up is currently putting a lot of effort in bringing a first version of their product to a limited test-market and want to distribute the medical device themselves. They are already working on the first steps of their marketing campaign. Therefore, the third or fourth product/service scenario should be chosen. At the evaluation tool, they indicated the fourth product/service scenario. They indicated the second evaluation moment as the one closest to their current situation at the development cycle. The results of the evaluation can be found in Figure 52 and Figure 53.

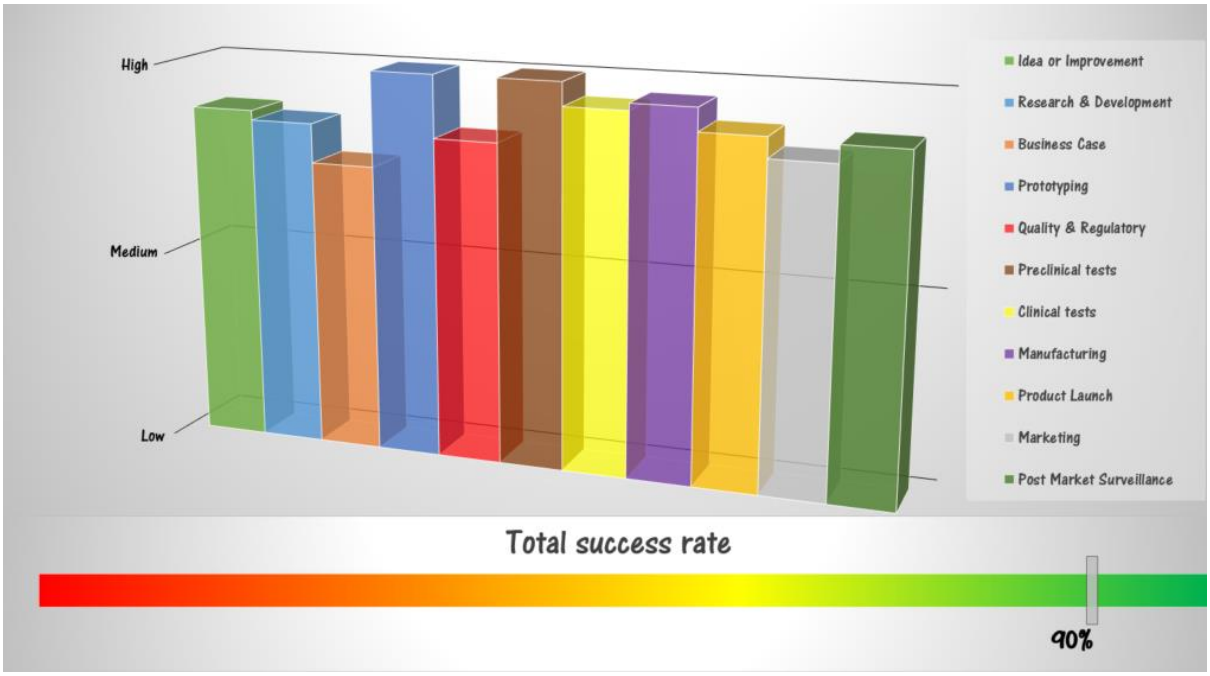

Figure 52: Results of the evaluation tool for start-up C

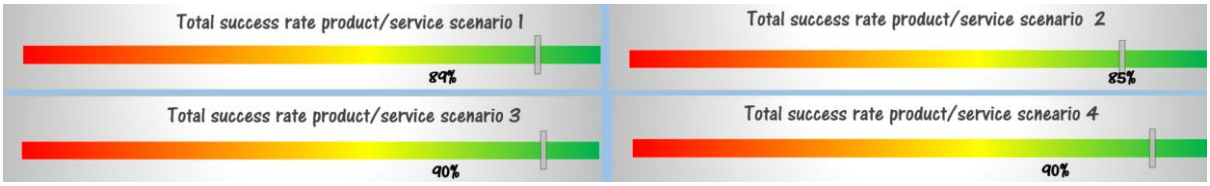

Figure 53: Total success rate for all different product/service scenarios for start-up C

For the second evaluation moment, the start-up obtained a very high total success rate of 90%. If the quotation criteria of the first or third evaluation moment would be used, the success rate would be 94% or 89%. The success rates of the third and fourth product/service scenario always get the best score, irrespectively the evaluating moment. The parameters they should pay attention to are shown in Figure 54.

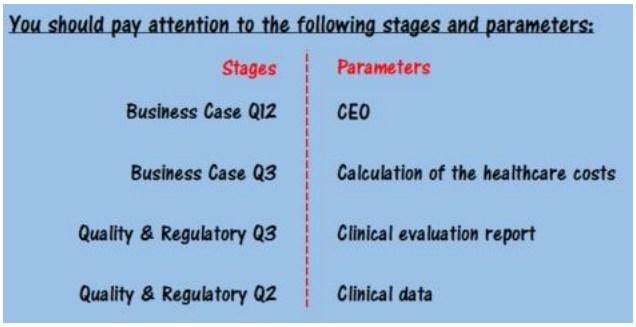

Figure 54: Pitfalls indicated at the evaluation report for start-up C

The coaches of the MedTech accelerator program are shown the results of the different start-ups. Although the start-ups are difficult to compare, due to the different types of medical devices they are developing, the coaches made up a list of which start-ups should score the best on the evaluation tool. This list corresponded to the real order of success rates generated by the MedTech Compass algorithm. The coaches also looked at the indicators of the various evaluation stages, and these indicators were as expected for each of the companies.

Of course, it is difficult to statistically prove the effectiveness of the evaluation tool based on a small case study of three companies. Nevertheless, the positive result of the case study gives an outline on the effectiveness of the success rate determination of the evaluation tool. Furthermore, one must conclude that the tool is not able to quantify the success rate of an In Vitro Diagnostic medical device. At first sight, the tool seems to work relatively well for the other types of medical devices mentioned in this case study.(customized or patient specific devices, software or applications and “classic” medical devices).

3 Case study 3: Evaluating a start-up in the incubation phase

As a final test, the evaluation tool was provided to an engineer who has plans to set up a medical device start-up in the near future. In fact, MedTech compass targets start-ups who can already submit a business case. An engineer or healthcare professional who is in the first phase of the ideation, does not yet have enough knowledge, information and insights about how the development process of the new medical device will look. Nevertheless, it is interesting to present the questionnaire to a person or team in such a situation. The evaluation tool also has an educational facet that gives the development team new insights and awareness on the very complex valorisation process of a new medical device. In this case, the evaluation score calculated by the mathematical algorithm will be not significant. However, the generated report can provide an insight into the various weaknesses and strengths that the development team should keep in mind.

The engineer of this medical device project has a Master degree in Biomedical Engineering & Microtechnology and is currently a medicine student in cardiac surgery. He has already start-up experience as co-founder of a 3D-printing company and did already research on ankle joint prosthesis and artificial irises. Now, he has an innovative idea to create a cardio-vascular assist device.

Despite the fact that this project is still in an incubation phase, the evaluation scores for the different evaluation stages are quite high. Of course, the first evaluation moment was considered and the evaluation stages preclinical testing, manufacturing and marketing were omitted in the evaluation, considering these are unpredictable in this pre-development phase of the medical device. The total success rate is 74% and the evaluation indicators for the different evaluation stages can be found in Figure 55 and Figure 56.

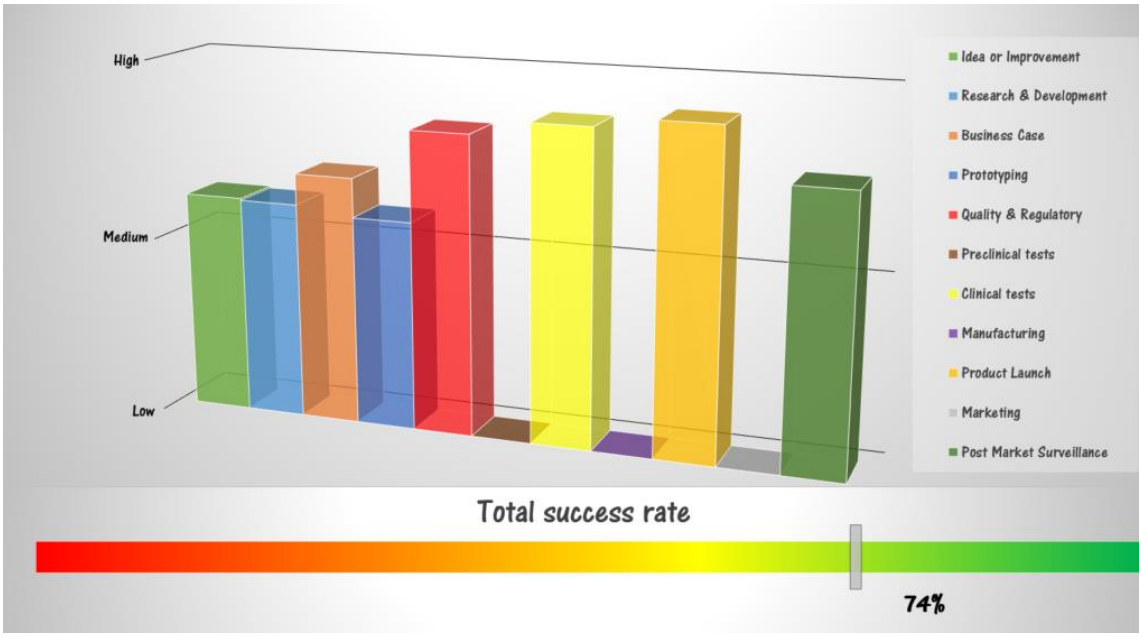

Figure 55: Evaluation stage indicators for the cardio-vascular assisting device project at incubation phase

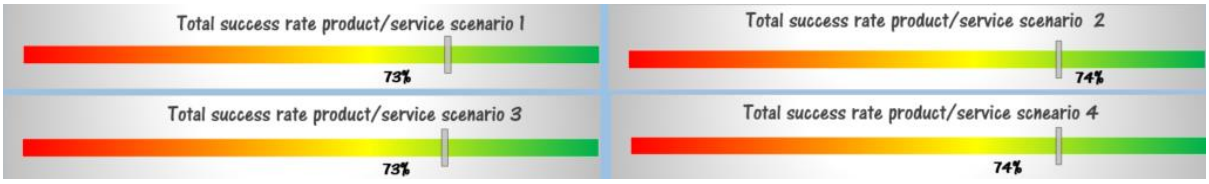

Figure 56: Total success rate for all scenarios for the cardio-vascular assisting device project at incubation phase

The high evaluation scores prove that the engineer has very strong insights in the valorisation trajectory of medical devices in general, despite the fact that he has filled in many questions at his discretion. The strong background of this person has undoubtedly a positive effect on the success rate. The scores of the evaluation stages aimed at the first phases of the development process are relatively low. This indicates it will be important to reflect the R&D phase and the actual design of the medical device. The four parameters that require attention (Figure 57) confirm this, as they are part of the R&D and prototyping stage.

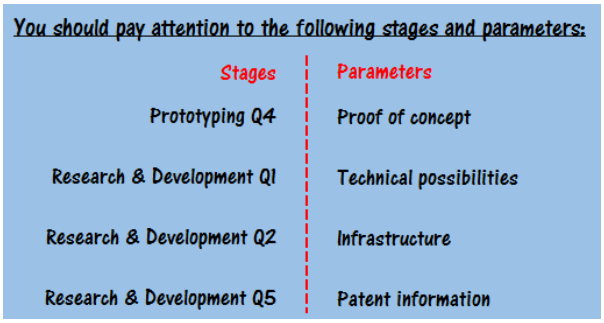

Figure 57: Parameters that require attention of the cardio-vascular assisting device project at incubation phase

The stage comparison over all evaluation moments in Figure 58, shows that the high success rate is due to the high scores on the evaluation stages like regulatory, clinical tests, product launch and post market surveillance. If the project was evaluated with the more strict quotation rules of evaluation moment 2 or 3, the success rate would respectively be 67% or 66%. This reaffirms the importance of incorporating the different evaluation moments.

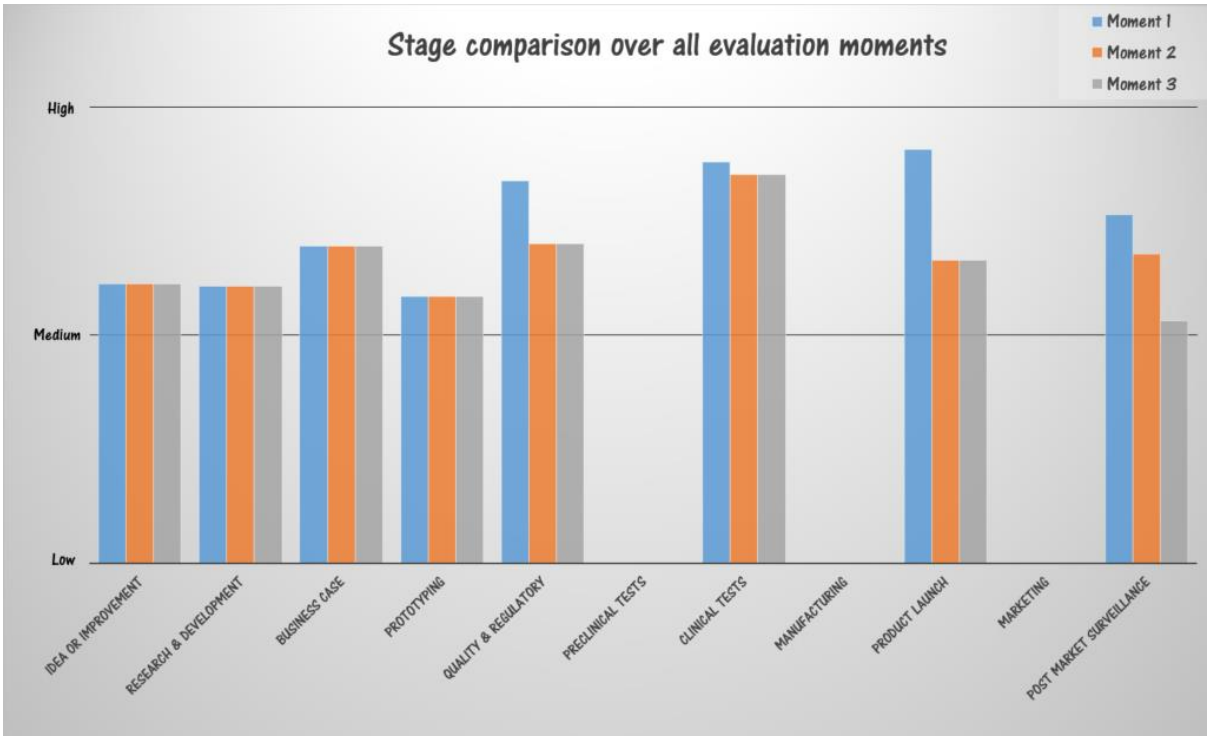

Figure 58: Stage evaluation comparison over all evaluation moments for the cardio-vascular assisting device project at incubation phase

After completing the MedTech Compass evaluation tool, this was the comment of the engineer:

> *The tool really shows what is expected of me during the development of a medical device and is therefore very useful. There were many aspects in the questionnaire where I wasn't aware of. I completed the survey to the best of my abilities, but as I'm still in the "idea" phase, I did not yet thought about all the aspects mentioned. I have mostly answered the questions like "how I would handle it", to at least get some viable evaluation score. Could I get a copy of the questionnaire? These criteria could help me a lot to set up my business.*

V. FUTURE RESEARCH AND CONCLUSIONS

1 Summary

The goal of this master dissertation was to develop a simulation model to support newly established MedTech development teams with the early understanding of the complex valorisation process of a new medical device. The purpose was to estimate the success rate potential of a start-up with a new product or service. The simulation tool assists the user to gain insight and awareness among the product developers with the feasibility of the technological, economic and regulatory development process. The experience of start-up engineering companies already affiliated with the design of medical devices should be passed on to the new developers and researchers.

In part 1, the importance of health technology and medical devices for the patient and community as a whole was emphasized. The development process for a new medical device is very complex to navigate through for a newly established development team. Many innovative technologies never reach the patient. Definitions of the different types of 'health technologies' and 'medical devices' are clarified along with the quality and regulatory framework for medical devices. The economic hurdles for start-ups are described together with the 'valley of death' they need to overcome.

In part 2, first a short overview of the problem statement together with the project objective was given in the first chapter. The evaluation process of the simulation model consists of three major steps. First, the newly developed questionnaire is presented to the development team. Based on the selected answer, a weight is allocated in a mathematical algorithm. The evaluation algorithm has to generate a total success rate together with a report with strengths, weaknesses and pitfalls of the organisation and medical device concept. The second chapter described medical device evaluation from different stakeholder perspectives. An evaluation framework was built from the manufacturer's point of view. The final simulation model consists of 11 evaluation stages as shown in Figure 26. After several interviews with MedTech experts and a lot of literature review, the different evaluation parameters of each stage were determined. For each parameter a question was formulated.

In part 3, the composition of the evaluation tool was explained. The different types of questions together with the answer rating, product or service scenarios and quotation rules were explained. Next to this, three different evaluation moments to fill in the tool were captured. Also the possibilities to skip an evaluation stage were explained together with the benchmarking rules to even out the stages with a lot questions compared to the ones with only a few questions.

During a next round of interviews, the different parameters, questions, weights, evaluation moments and quotation rules were presented to several experts in the field of MedTech. Based on the feedback and suggestions, the questionnaire and mathematical algorithm was continuously updated.

In part 4, a threefold case study was performed. First some established companies of the MedTech Flanders network filled in the evaluation tool. The CEOs or co-founders of the companies did not see the final weights and quotation rules before they filled in the evaluation tool, to get an unbiased success rate determination of their company. It was expected that these companies should score more than 75% for the success rate of MedTech Compass. All three of them had a success rate of more than 80%. They development teams confirmed that the indicators for the various stages represent the real strengths and weaknesses of the company, which proved the effectiveness of all parameters and quotation rules of the evaluation tool.

Based on these three case studies at existing companies in the MedTech industry and the feedback of other experts, the tool was completed to its final form. Next, all four participating start-ups of the MedTech Accelerator were invited to complete the evaluation tool. These start-ups had very diverse types of medical devices (customized/patient-specific, In vitro Diagnostic, smartphone application etc.). The start-up working on the In Vitro Diagnostic medical device quitted the questionnaire halfway. Some of the evaluation criteria were too far from what they are currently undergoing. During further research, a questionnaire for IVD medical devices should be qualified. The reports of the other start-ups were examined. The coaches of the MedTech accelerator program confirmed that the success rates and indicator of the different evaluation stages corresponded to what they expected. This positive result of the case-study gives an outline on the effectiveness of the success rate determination of the evaluation tool. One must conclude that the tool is not fitted for IVD medical devices, but seems to work relatively well for the other types of medical devices of this case-study.

Finally, the tool was handed to an engineer who is at the incubation phase for a new medical device start-up. Notwithstanding the mathematical calculation of the success-rate had no significance, the questionnaire gained insights for the researcher on the complex valorisation trajectory to develop a new medical device.

2 Discussion and future research

2.1 Refinement of the evaluation tool

The new evaluation tool developed during this master's dissertation should serve as a basis for further research. The questionnaires, weights and quotation rules are compiled based on literature and interviews with more than twenty Flemish MedTech experts. Medical technology is a fast growing industry. This simulation model will need to be continuously updated to accommodate the fast changing technologic progresses.

Due to the limited timeframe wherein this master's dissertation had to be completed, only a limited number of experts were interviewed to give their opinion on the critical evaluation parameters for a medical device start-up. During subsequent research, more stakeholders could be interviewed to implement their experience and insights in the simulation model. In addition, it may be interesting to interview development teams of failed start-ups. Information of start-up failure interviews with founders and investors can give a clear view on the hurdles and obstacles of medical device development. More evaluation parameters or answering possibilities can be found with these additional interviews. Over time, the number of weight classes linked to the possible answers can be expanded and become more accurate. Currently, there is a lot of research done on innovation- and service management models. These new insights can be an added value for our simulation model.

Based on the threefold case-study, the report generated by the evaluation algorithm appears to be representative to assess the strengths and weaknesses of a MedTech start-up. To establish the correctness of the success rate determination, a larger statistical analysis is needed. Because success is hard to measure, it is difficult to quantify if a calculated success rate gives a realistic view on the true success rate potential of a company. It will only be possible to judge the accuracy of the current evaluations after five to ten years. Because the success rate determination is a qualitative study, there is a paucity of reliable guidance on estimating the necessary sample size. Methods like the constant comparative method of qualitative analysis will be needed to evaluate the statistical correctness of the evaluation algorithm. [101]. The data of start-ups that completed MedTech compass should contribute to the analysis of next start-ups. The evaluation tool should be able to grow into a self-learning algorithm.

The evaluation parameters of the simulation model try to quantify the success rate of different development stages for a new medical device. These parameters were kept as generic as possible, so the evaluation algorithm would be applicable for most types of medical devices. As a result, it is difficult to quantify whether

the medical device actually relieved the clinical need with the right solution-fit. With a questionnaire, it is hard to check whether the job-to-be-done has been covered with the medical device developed by the start-up. Further research will be required to find parameters to quantify this solution fit.

Finally, the computer implementation of the evaluation tool can be further optimized. Currently, the mathematical algorithm has been processed in an excel spreadsheet and the questionnaire is built on the online platform of 'Survey Anyplace'. The results of the questionnaire are formatted in a CSV-file. The results are manually loaded into the spreadsheet to calculate the success rate and generate the report. First of all, a visual basic script can be coded to automatically load the results into the algorithm. In the long term, a full web application can be developed to immediately return the results in an online tool.

2.2 Extension of the evaluation tool

In addition to further elaborating the evaluation tool, it is possible to apply the evaluation algorithm to different questionnaires for more specific types of medical devices. Next to this, other types of HealthTech can be evaluated in a new tool based on the MedTech Compass evaluation algorithm.

Software and eHealth applications

During the interviews with various MedTech professionals, it became clear that there is a large variety of medical devices. Initially, the evaluation tool was built up with physical medical devices in mind (catheters, hearing aids, scanners,...). After discussions with software developers of mobile health applications and imaging software, it became clear that some evaluation parameters were not directly applicable to their medical device. A separate questionnaire with slightly different evaluation parameters could be made according to those devices. The evaluation algorithm can be applied without difficulty to such a new questionnaire.

Patient-specific medical devices

New innovative technologies make it possible to manufacture patient-specific medical devices. The personalised medical device is designed and produced especially for one patient. For example, innovative 3D printing technology makes it possible to shape composite materials or even titanium into patient-specific products (catheters, facial implants, prosthetics...). These custom made devices should be manufactured in accordance with a healthcare professional's written prescription for the sole use of a particular patient and are not adapted from mass produced items.

There are some differences in the development process of personalised medical devices compared to "classic" medical devices. The design is limited to patient specific information, CE-marking is not obligatory,

manufacturing does not contain “mass-production” and there are other perspectives on clinical trials, marketing and pricing. A more specific evaluation model for this products or services urges to properly calculate the success rate.

In Vitro Diagnostic

The evaluation tool is focused on “classic” medical devices. For In Vitro Diagnostic medical devices, other regulations are applicable. Also the clinical trials that need to be performed for In Vitro Diagnostic are most of the time different compared to the active medical devices. During the threefold case study, it became clear that the questionnaire should be adjusted to be applicable for In Vitro Diagnostic medical devices.

Drug-device combinations and other borderline products

Several important differences exist between the development processes of medical devices and pharmaceuticals. The regulatory requirements between medicinal products and medical devices are also inherently different. Thus, it is important to make a clear differentiation. Devices are more heterogeneous with wide differences in mode of operation and used technology. This heterogeneity leads to a wide variety of preclinical testing types, manufacturing infrastructure and regulations (e.g.. imaging software versus prosthetics). Drugs activate a chemical reaction on or within the human body, while devices usually have more physical effects. In this way, devices are mostly technology/engineering based physical objects, while drugs are chemistry-based compounds. Device tend to require more user interaction than drugs. Most pharmaceuticals are discovered during a laboratory-based research process while the devices are developed with involvement of physicians and patients. New drugs are subjected to other quality and regulatory requirements compared to a new medical device (quality system requirements, CE-labels…) that influence the duration and complexity of the development process. Also the capital-requirements are vastly different for the development process of medical devices compared to pharmaceuticals.

There are also combination products, which increasingly blur the distinctions between medical devices and pharmaceuticals. The drug-device combinations begin to play an increasingly important role in health care innovation. Such as the drug-eluting stents as well as other combination products with biomaterials or cells.

On the regulatory side, in the USA has FDA responded to the increasing number of combination products with the creation of its Office of Combination Products (OCP) in 2002. [57] The OCP has the coordinating responsibility of assessing combination products throughout their product lifecycles. The European Commission launched an extra MEDDEV guidance document [102] in 2007 on borderline products, drug-delivery products and medical devices incorporating an ancillary medicinal substance or an ancillary human blood derivative. [102] On May 5, 2017, the new regulations on medical devices were published in the Official

Journal of the European Union. In the new regulation (EU) 2017/745 is mentioned: “Products which combine a medicinal product or substance and a medical device are regulated either under this Regulation or under Directive 2001/83/EC of the European Parliament and of the Council.”

Combination products bring some additional challenges on the product development pathway. The development process of combination products is more complex than the “classic” medical device development process. Some additional evaluation parameters should be implemented across the different evaluation stages to be able to judge about this products with the existing evaluation tool.

CareTech and HealthTech

In addition to roll out to medical device software and mobile apps, the evaluation tool can be modified to evaluate CareTech or other HealthTech domains. The evaluation algorithm can be used with another questionnaire as top layer.

3 Conclusion

In recent years, the medical device development process has become increasingly complex. As a consequence of these thresholds, many good ideas or new technologies do not reach the patient. In general, developments in medical devices or new technologies need to reach patients, caregivers and hospitals in a more faster or efficient way. The purpose of this master’s dissertation was to support these newly established MedTech development teams with the early understanding of the complex development process of a new medical device, by developing a new evaluation tool.

The goal of this master’s dissertation is achieved; a new evaluation framework is developed and successfully tested on various companies and concepts in the field of MedTech. The evaluation tool, called MedTech Compass, is presented to the development team as a user-friendly questionnaire with multiple choice questions. Based on the selected answers, weights are allocated into an new evaluation algorithm which generates a report with the strengths, weaknesses and pitfalls of the organization and concept, together with a total success rate (percentage). The simulation report together with the questionnaire itself, gains insight and awareness among the product-developers with the feasibility of the technological, economic and regulatory development process.

The evaluation framework is composed based upon a lot of experience of various experts in the field of MedTech. Due to the generic approach during the composition of the algorithm, the possibility for further refinement and extension of the tool is afforded.

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APPENDIX

Question 1 – Background environment

Which of the following options describes best your background environment?

Answer options

Student
Healthcare professional (Doctor, physician, engineer,…)
Start-up
Spin-off company related to an university
Company with product/technology development experience, but not in MedTech
Company with MedTech experience (>2 MedTech products already launched)

Question 2 – Market share

If your start-up or company has already launched MedTech products or services in the same market segment of the new product you have in mind, what is the market share of these earlier launched medical devices?

Answer options

We have no market share gained with recent products
Our company has less than 15% market share
Our company has between 15% and 50% market share
Our company has between 50% and 75% market share
Our company has a monopoly on those products

Question 3 – Innovation

On how much of the following key elements is your product innovative in comparison with already existing techniques?

Answer options (Multi)

Complication rate
Accuracy
Safety
Operation Room turnaround
Ease of use
Price

Length of Stay

Question 4 – Demand Research

How arose the idea for the new medical device?

Answer options

The product is developed because a new invention or a new technology came available
The product is developed because of a unmet clinical need

Question 5– Research for use

Are doctors pitched about the idea and involved in the development of the new medical device?

Answer options

Yes
No

Question 6 – Expertise & know-how

Do you have expertise and know-how inside the company with this type of medical technology?

Answer options

Mainly in-house knowledge
Mainly consulting knowledge
No pitching of the idea

Question 7 – Seed capital

How much seed capital from early investors did you already had before the start of the product development stage?

Answer options

< € 10.000
€ 10.000 - € 50.000
€ 50.000 - € 250.000
€ 250.000 - € 500.000
>€ 500.000

Question 8 – Notified Bodies

Has someone in your team experience with product registration at notified bodies or are you in contact with a partner/consultant that helps you at regulatory affairs like product registration at notified bodies?

Answer options

Yes
No
I've never heard about notified bodies

Question 9 – SWOT Analysis

Did you perform a SWOT-analysis for the new idea or improvement?

Answer options

Yes
No
I've never heard about a SWOT-analysis

Question 10 – Review of the existing intellectual property

Are there patents on products technologies that are very similar to your product/idea?

Answer options

yes
no
I don't know

Question 11 – Project plan + risk analysis + timeline?

Was there already a project plan made for your product/idea before you started the R&D phase of the medical device development process?

Answer options

yes, project plan including risk analysis and timeline
yes, project plan including risk analysis
yes, project plan including timeline
yes, project plan
no

Question 12 – Technical possibilities

Are all technologies available that are necessary for the development of the medical device?

Answer options

All techniques are in-house available
All techniques exist, but they are not all in-house available
Some existing techniques must be further adjusted before development of the product
Some of the techniques are not yet available

Question 13 – Infrastructure

Which investments are required concerning product development infrastructure?

Answer options

All necessary infrastructure is already in-house available
You have access to public or rented infrastructure (innovation centre, university labs,…)
Some necessary infrastructure must be purchased (< 50% of all required infrastructure)
All necessary infrastructure must be purchased

Question 14 – Experiments

If you do a research experiment, how many of the following steps do you include in your methodology?

Answer options (Multi)

Make a clear definition of the research problem
Write down the design of the experiment
Use different sampling groups to do an experiment
Do a pilot study before you undergo the real measurement-experiment
Brief written analysis and conclusion
Make a standardized report
Statistical analysis and significance tests

Question 15 – Regulations

Do you already take into account all necessary regulations (CE, ISO,…) during the first development phases of the medical device development process?

Answer options

I can evince that all regulations are strictly followed
I think that most of the regulations are followed
No

Question 16 – Intellectual property information

Did you already consider a way to protect the intellectual property during the early development stages?

Answer options

Yes
No

Question 17 – Cost-effectiveness

Did you perform a cost-effectiveness analysis during the early development stages? (e.g.: a cost breakdown analysis of the different costs linked to the new product development)

Answer options

Yes
No

Question 18 – Ethical issues

Did you thought during the development process about possible ethical implications of the product?

Answer options

Yes
No

Question 19 – Risk Analysis

Did you perform a risk analysis during the early development stages (FMEA, Risk Plan,…) ?

Answer options

Yes
No

Question 20 – Technical Drawings

Are the technical drawings already made in detail (BOM, tolerances, technical requirements etc.) in the R&D phase?

Answer options

Yes
No
Technical drawings are not applicable for our product (if you make software, apps,...)

Question 21 – Verification and Validation test matrix

Is there a verification and validation procedure foreseen?

Answer options

Yes
No
I've never heard about verification or validation

Question 22 – Team

How many of the following skills are covered by your team?

Answer options (Multi)

Medical knowledge
Technical knowledge
Regulatory knowledge
Organizational knowledge
Business knowledge
Coordination between all facets

Question 23 – Meddev classification

Did you design the medical device with the different medical devices classifications in mind? (e.g.: Trying to exclude some functions, so you won't fall in a higher class)

Answer options

Yes
No
Does not apply for our product/service. It would be the same class anyway

Question 24 – Feedback

Do you ask feedback of doctors, engineers, patients,... during the development of the product?

Answer options

Yes
No

Question 25 – Disease state

What are the current options for diagnosis/treatment?

Answer options

The technique that we want to provide also exists at products of competitors
We optimized the technique which already exists.
We provide an alternative upon a technique which already exists
There is no treatment for this problem yet, we have a total new technique

Question 26 – Healthcare costs

Will the new product involve a decrease in total healthcare costs at community perspective?

Answer options

Yes, we have proven already this decrease in healthcare costs
We think that our product will have a decrease in healthcare costs
We don't know it yet
We don't think that it will have a decrease in healthcare costs

Question 27 – Calculation of healthcare costs

How many of the following costs did you include in the cost calculation?

Answer options (Multi)

Training costs
Referral pattern change costs
Cost of changing in physician specialist providing the therapy
Cost of extra equipment or medicines

Question 28 – Return On Investment

Can you evince the return on investment to convince potential investors?

Answer options

Yes
No

Question 29 – Infrastructure sharing

Is infrastructure sharing with other companies possible?

Answer options

Yes
No
Infrastructure sharing will not be useful due to the nature of the manufacturing process

Question 30 – Reimbursement

Do you think grants or reimbursement will be possible? (In Belgium: RIZIV)

Answer options

Yes
No

Question 31 – Exportable

Is the device exportable (with some modifications)? Is there a possibility to explore other countries?

Answer options

Yes
No

Question 32 – Investors

Next to ROI, how many of the following parameters do you highlight?

Answer options (Multi)

Decrease in healthcare costs
Clear market demand
Robust intellectual property protection
Proof of concept (clinical feasibility)
Clear regulatory pathway (FDA approval)
Prototype
Established reimbursement codes

Question 33 – Involvement of investors

Are the investors asked for feedback on the business case?

Answer options

Yes
No

Question 34 – Risk management plan

Did you include a risk assessment in the business plan?

Answer options

Yes
No

Question 35 – Second phase investors

Is there a possibility for second phase investors?

Answer options

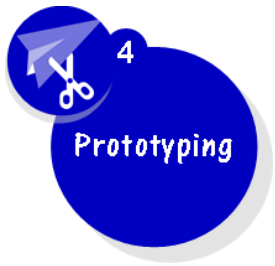
Yes
No

Question 36 – CEO

Do you have a CEO that already went through the whole MedTech development cycles?

Answer options

Yes
No



Question 37 – Production processes

Do you use the same production processes during the prototyping as you will use during the real manufacturing? (In case of E-Health: do you build your application/software in the same environment as the one you will make your final application in?)

Answer options

Yes
No
Does not apply

Question 38 – Mechanical properties

Do you use materials for the prototypes with the same mechanical properties as the material you will use for the product that will be sold?

Answer options

Yes
No
Does not apply for our product/technology

Question 39 – Material choice

Did you use medical-grade materials for the prototype?

Answer options

Yes
No
Does not apply for our product/technology

Question 40 – Proof of concept

Can you use the prototype to make a proof of concept?

Answer options

Yes
No

Question 41 – Classes

Which of the four classes covers your medical device?

Answer options

I (Is/Im)
IIa
IIb
III
I don't know
I'm developing an In Vitro Diagnostic medical device

Question 42 – Class III additional question

Is it possible to rely on clinical data of an equivalent device?

Answer options

Yes
No

Question 43 – Clinical evaluation report

How many of the following parts are included in your clinical evaluation report?

Answer options (Multi)

Data which is up to date
clinical investigations
peer reviewed clinical literature of either device in question or similar devices
clinical data coming from the post-market surveillance system

Question 44 – Intellectual property

How is the intellectual property protected?

Answer options

Our intellectual property is internationally protected by a patent

Our intellectual property is at some nations protected by a patent
No IP, we try to keep the technology black box

Question 45 – ISO environment

Is an ISO environment necessary?

Answer options

Yes
No
I don't know

Question 46 – Reimbursement

Do you think grants or reimbursement will be possible? (In Belgium: RIZIV)

Answer options

Yes
No

Question 47 – Reimbursement factors

How many of the following factors can you identify with your company? (Multiple answers possible, only fill in if you did not receive any reimbursement yet)

Answer options (Multi)

We have lobbied to recommend our product to partners of the RIZIV
We have evidence based data concerning our product
During the last years, there is already a big part of the RIZIV budget spend to the market segment of your medical device

Question 48 – New rules

Are you well informed by the new rules concerning regulation of medical devices?

Answer options

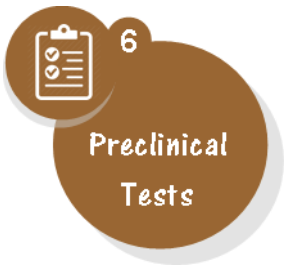
Yes, i am well informed of the recently launched regulation on medical devices which is called MDR
No

Question 49 – Additional Data

Do you need to draft extra/new documents due to the new regulation directives?

Answer options

Yes
No



Question 50 – Biocompatibility

Did you investigate the biocompatibility of your medical device? (e.g.: Analytical chemistry, in-vitro tests, animal models,...)

Answer options

Yes
No
Does not apply for my product/technology

Question 51 – GLP

Have you conduct biocompatibility tests according to GLP (Good Laboratory Practice) ?

Answer options

Yes
No
I've never heard about GLP
Biocompatibility testing does not apply for my product/technology

Question 52 – ISO 10993

Have you achieved an ISO 10993 certificate?

Answer options

Yes
Not yet
I have never heard about this.
Biocompatibility testing does not apply for my product/technology

Question 53 – Statistical analysis

Did an expert assessor analysed the gathered preclinical test data? (Significance tests, variability, sensitivity analysis,...)

Answer options

Yes
No

Question 54 – Team

Is there experience with preclinical labs and tests available within your team?

Answer options

Yes
No

Question 55 – Pilot study

Are pilot studies performed before the real clinical trials?

Yes
No

Question 56 – Permissions METC

Do you have a permission by the ethical commission METC to perform clinical trials?

Answer options

Yes
No
I've never heard about METC
Does not apply for my product/technology

Question 57 – Informed consent

How many of the following types of informed consent do you provide?

Answer options (Multi)

Informed consent document to sign
Recruitment process
Verbal instructions
Question-and-answer sessions
Measure participant understanding
Other

Question 58 – Clinical Trials or observational study

Which description of clinical trials corresponds best with the one that you will use?

Answer options

Compare a new medical approach to an existing one
Compare a new medical approach to a placebo that contains no intervention
Compare interventions that are already available to each other

Participants receive interventions or procedures as part of their routine medical care
I don't know

Question 59 – Multi-centre study

Did you perform clinical tests in multiple centres?

Answer options

yes
no

Question 60 – Statistical analysis

Are the clinical trial data statistical analysed? (Significance tests, variability, sensitivity analysis,…)

Answer options

Yes
No
Does not apply

Question 61 – Possibilities feedback to design

What are the possibilities to adjust the product design after the clinical trials?

Answer options

If necessary, we can go through the whole development phase again
We can only adjust a few aspects

Question 62 – Team

Who conducts the clinical studies?

Answer options

Our own research team
Our own research team together with a physician
Our own research team with some medical cross-functional team members (doctor, nurses, social workers,…)
Our own research team together with an academic medical centre
Other

Question 63 – Eligibility

Do you have a well described protocol with eligibility criteria, number of participants, schedule on tests etc.?

Answer options

Yes
I think it fulfil the most important criteria
No
I don't know

Question 64 – Ethical committee

Did you receive a favourable opinion from Ethics Committee?

Answer options

Yes
No

Question 65 – Suppliers

Can your suppliers present documents to trace all purchased products, goods and raw materials?

Answer options

Yes, all of them
No
Does not apply for my product/technology

Question 66 – Audit suppliers

Can your suppliers present an ISO-certificate?

Answer options

Yes, all of them
No, some of them need an audit
Does not apply for my product/technology

Question 67 – Subcontracting

Did you make a proper consideration about subcontracting?

Answer options

We made a brief consideration (cost-benefit analysis) about subcontracting
We have not thought about subcontracting
It is not possible to find subcontractors for (parts of) our product

Question 68 – ISO environment

How long will it take to get an ISO 13485 certificate?

Answer options

< 3 months
< 6 months
< 1 year

< 2 year
> 2 year
We don't need an ISO-certificate
The workplace is already ISO-certificated.

Question 69 – CE-labels

Are you (or someone in your team) familiar with registering CE-labels for a MedTech product?

Answer options

Yes
No

Question 70 – Packaging

Does the packaging fulfil all regulatory requirements?(In case of eHealth or software: the console instead of 'packaging')

Answer options

Yes, I'm sure
I think all regulatory requirements are fulfilled
I don't know / We haven't designed the packaging of the product

Question 71 – Packaging

Is the packaging flow well-designed for the end user? (e.g. follows flow of the surgery)

Answer options

Yes
No
Does not apply/We haven't designed the packaging of the product

Question 72 – Internationally adjustments

Which adjustments are necessary before your product can be sold in other countries?

Answer options

Adjustment of the core: product is region specific.
Adjustment of services: adaption of the product to local conditions (packaging, colour, voltage,…)
Adjustment of symbolic values: only labelling, language on buttons and language of manuals differ
Does not apply

Question 73 – Labelling

Are there clear marks or labels on the device concerning the usage?

Answer options

Yes
No

Question 74 – Technical guide

How well documented is the surgical/procedural technical guide?

Answer options

Well described how-to steps
Steps are illustrated (2D or 3D)
3D models/simulations are digitally foreseen
Video
Other
We didn't compose a technical guide

Question 75 – Discount margin

Which of the following techniques describes best how the margin of profit is determined?

Answer options

Cost-based (based on the costs you have)
Value-based (based on the value of the product)
Competition based (based on the competitors their prices)
I don't know

Question 76 – Pricing

Which of the following pricing strategies corresponds best to your strategy?

Answer options

Market-penetration strategy
market-skimming strategy
Comparable pricing strategy
Flanking strategy
None of the above strategies
I don't know

Question 77 – Global pricing strategy

Is there an international pricing strategy (including different tax policies, competition, transportation costs …)?

Answer options

Yes
No

Question 78 – Momentum

Will you take an informed decision when choosing to transfer your product to the product launch phase?

Answer options

Yes
No

Question 79 – Positioning strategy

What is the main positioning strategy you will use at the product launch?

Answer options

Emphasize one or multiple benefits of the new technology
Emphasize a new uses or applications
Emphasize the approach of new target groups
Emphasize your product can replace a whole product category
Emphasize that you are better than the other competitor
Emphasize that your product/service has a value for money
I don't know

Question 80 – Pre-launch training for physicians

Did you provide pre-launch training for physicians/patients/end users?

Answer options

Yes
No
Does not apply for your product/technology

Question 81 – Cannibalization

Did you quantify the sales loss on other owned product concerning the product launch? (e.g.: If Coca-Cola launches their new product 'Coca-Cola Zero', they will also lose some sales at their regular Cola that needs to be quantified next to the extra market-share obtained with the new product.)

Answer options

Yes
No
We don't have other products in this product category

Question 82 – Distribution partners

Are you already in contact with third party distributors?

Answer options

Yes

No

Question 83 – Pricing variation geographically

Have you thought about a price variation in different areas/countries?

Answer options

Yes
No
Does not apply for our product/technology

Question 84 – PEST-analysis

Have you made a PEST-analysis (only fill in if you go to the international market.)

Answer options

Yes
No
I've never heard about PEST-analysis
Does not apply for our product/technology

Question 85 – Medical education

Are there possibilities/plans to grant medical education, workshops etc. about the product?

Answer options

Yes
No

Question 86 – Marketing plan

Do you have a documented marketing plan?

Answer options

Yes
No

Question 87 – Competition strategy

Which strategy describes best the way you want to compete?

Answer options

Low-cost Leadership strategy (sell at lower price than competitor)
Differentiation strategy (offering a product or service that is more sophisticated)
Focus strategy (specialized equipment or patient-specific in a segment other companies cannot compete)
I don't know

Question 88 – Marketing budget

How do you calculate your marketing budget?

Answer options

Affordable method (promotion budget is set on the amount you think you can afford as company)
Percentage-of-sales method: budget is set at a specified percentage of sales
Competitive-parity method: budget is set, lowered and raised based on the actions of competitors
Objective-and-tasks method: budget is set by defining specific objectives, tasks and to achieve them
I don't know

Question 89 – Promotion: advertising

Which advertising tools will you make/use?

Answer options (Multi)

Clear logos and symbols
Printing ads
Motion pictures, commercials
Display signs, purchase displays
Brochures, booklets
Posters, leaflets
Billboards
Packaging-outer, inserts
Product movie, corporate movie

Question 90 – Managing marketing results

How are the marketing results analysed?

Answer options

We examine annual results when we do a financial analysis
We define measurable marketing benchmarks (sales growth, market share, new customers,…)
We give feedback to the marketing plan according our CRM (dissatisfied customers, relative service quality,…)
I don't know

Question 91 – Promotion: Sales promotion

How many of the following sales promotions you provide?

Answer options (Multi)

Trade promotion (giving retailers special discounts or gifts)
Consumer promotion (discount)
Entertainment, contest, games, lotteries
Premiums, gifts
Coupons, rebates
Low-interest financing
Trade-in allowances
Continuity programs
Tie-ins

Question 92 – Promotion: Public Relations

How many of the following public relations tools you use?

Answer options (Multi)

Press kits
Fairs, trade shows, exhibits,…
Speeches at schools, congresses,…
Events, seminars
Annual reports
Charitable donations
Sponsorships
Community relations
Lobbying
Identity media, company magazine
Impression features (business cards, uniforms, car-promotion)

White papers, research publications
Publications in scientific magazines,...

Question 93 – Promotion: Sales Force

How many of the following tools you provide for the sales representatives?

Answer options (Multi)

Animations
1-pager about safety
1-pager summarizing clinical data findings
Anatomical model, Tissue Model,...
Customer satisfaction summary
Smartphone app (calculator,...)
Hospital testimonials showing cost savings
White paper
Interactive data model
Invitations for education events
PowerPoint/Slide deck
Overview of published articles/white papers/...

Question 94 – Promotion: Direct Marketing

Can you use direct marketing tools (through knowledge of target markets)(e.g.: by customer data collection from previous products, data about interested people at fairs or congresses, you can mail info about your new product to people who will certainly be interested)

Answer options

Yes
No
I didn't think about this

Question 95 – Target audience

Did you identify different segments in the market?

Answer options

We approach the market as a single segment
We divide the market in different segments
I don't know

Question 96 – Traceability

Is there a system for traceability?

Answer options

We can trace the patient: electronic health records, patient registers (linked to serial number)
Patient or customer can trace us: There is a only a Serial Number on the product, product can be traced if there are complications

Question 97 – Guidance Documents

Will you use the guidance documents of the European Commission to implement directives?

Answer options

yes
no
I've never heard about these guidance documents

Question 98 – PMS data

How many of the following channels you use to gather PMS data?

Answer options

Literature reviews
Post market clinical follow-up studies
patient registries
customer complaints
customer surveys
expert user groups
user reaction during training programs
media
trade shows
maintenance/service reports
field evaluation
retrieval studies on explants or trade-ins

in-house testing
failure analysis

Question 99 – Data review

How often will you review and trend the data from the vigilance report?

Answer options

On annually basis we plan a management review meeting as required by ISO 13485
On quarterly/monthly basis we plan a management review meeting
Depending on the quantity of received feedback, we will decide on reviewing
Depending on the seriousness of the received feedback, we will determine if we act immediately or not
I don't know

Question 100 – Customer feedback

Do you have a system to let customers (doctors/patients/…) give feedback on the product?

Answer options

yes
no

Question 101 – Failure analysis

Do you have a system for failure analysis? (Reporting database)

Answer options

yes
no

Question 102 – Eudamed

Will your new product be registered at Eudamed?

Answer options

Yes
No
I have never heard of Eudamed

Question 103 – Team

Have you already invest in personnel with a deep knowledge of Good Clinical Practice that will follow up the Post Market System?

Answer options

yes
no

MEDTECH COMPASS

Guidance document to analyse the results

This document is an accompanying document to proper analyse the spreadsheet results given by the Medtech Compass tool.

MedTech Flanders is a network organization of Flemish medical device companies together with research partners, subcontractors and partner-organizations.

Our mission is to support the further development of Medical Technology to become an important economic activity in the Flemish region. We want to create a cluster of MedTech companies and organizations who positively stimulate each other towards an international recognized eco-system.

MedTech Compass is a tool to support newly established MedTech development teams with the early understanding of the complex development process of a new medical device.

On the one hand we try to estimate the success rate potential of a start-up with the new product or service they have in mind. With the given knowledge and organizational structure of the start-up, we want to predict the quantitative success rate of ideation. This tool should be a risk analysis of the product development cycle of a new MedTech product or service. On the other hand we want to gain insight and awareness among the product-developers with the feasibility of the technological, economic and regulatory development process.

This tool is built as a simple multiple-choice questionnaire for the end-user. Based on the selected answers, certain weights are elected. These weights were formulated into a mathematical algorithm. The algorithm should generate a total success rate together with a report with strengths, weaknesses and pitfalls of the organization.

questionnaire *algorithm* *percentage report*

11 evaluation stages

The evaluation tool consists of 11 different evaluation stages. These stages are based on 11 key facets in the product development cycle of a new medical device. These components may not be strictly regarded as stages in the development process. It are eleven components which are linked to each other and do not chronologically occur but can be re-iterated.

At each evaluation stage, different parameters are taken into account. A brief overview of the important factors can be found below.

1. Idea or improvement
   - Degree of innovation
   - SWOT-analysis
   - Existing technology?
   - Patient pull or push?
   - Seed capital
   - Research of use
   - Intellectual property
   - Project plan
   - …
2. Research and development
   - Infrastructure
   - Regulations
   - Risk analysis
   - Verification and validation
   - Feedback on design
   - …
3. Business Case
   - Healthcare costs
   - Return on investment
   - Convincing investors
   - Risk management plan
   - …
4. Prototyping
   - Proof of concept
   - Mechanical/material/…
5. Quality and Regulatory
   - Meddev classification
   - Intellectual property
   - Reimbursement
   - …
6. Preclinical testing
   - Biocompatibility testing
   - Statistical analysis
   - …
7. Clinical tests
   - Ethical issues
   - Informed consent
   - Clinical trials protocols
   - …
8. Manufacturing
   - ISO/CE
   - Subcontracting
   - International compatibility
   - Labelling/marking/…
   - …
9. Product Launch
   - Pricing strategies
   - Training
   - Distribution
   - …
10. Marketing
    - Competition strategy
    - Marketing plans
    - Public Relations
    - Sales forces
    - …
11. Post Market Surveillance
    - Traceability
    - Customer Feedback
    - Failure analysis
    - …

The questionnaire

The questionnaire is a composition of multiple-choice questions for each of the stages. The different answers to the questions are linked to a particular weight. These weights are decimal number between zero and one and can be considered as a 'percentage'. These weights should be taken as the maximum percentage one can score for the stage, in the case that all the other questions for that stage are perfectly answered.

To keep it organized, only four different 'classes' of weights were chosen.

A: 100% (1.00) B: 95% (0.95) C: 85% (0.85) D: 70% (0.70)

Here's an example of the manufacturing stage.

Q: ISO environment: How long do you think it will take to get your workplace ISO 13485-certificated?

Answer	Class	Weight
<3 months	D	0.70
<6 months	D	0.70
<1 year	D	0.70
<2 year	C	0.85
>2 year	A	1
We don't need an ISO certification	Does not Apply	DNA
The workplace is already ISO-certificated	A	1

Depending on the chosen answer, a weight will be selected. The weights linked to the answers are determined by importance of the question and value of the selected answer. The weights of all the questions for a stage are multiplied to become a score for the particular stage. In the example above, if one states that the ISO-certification of the workplace can be done within less than 6 months (class D answer), it's deemed they can only score 70% on the manufacturing stage, if all the other questions of this stage are answered with a class A answer.

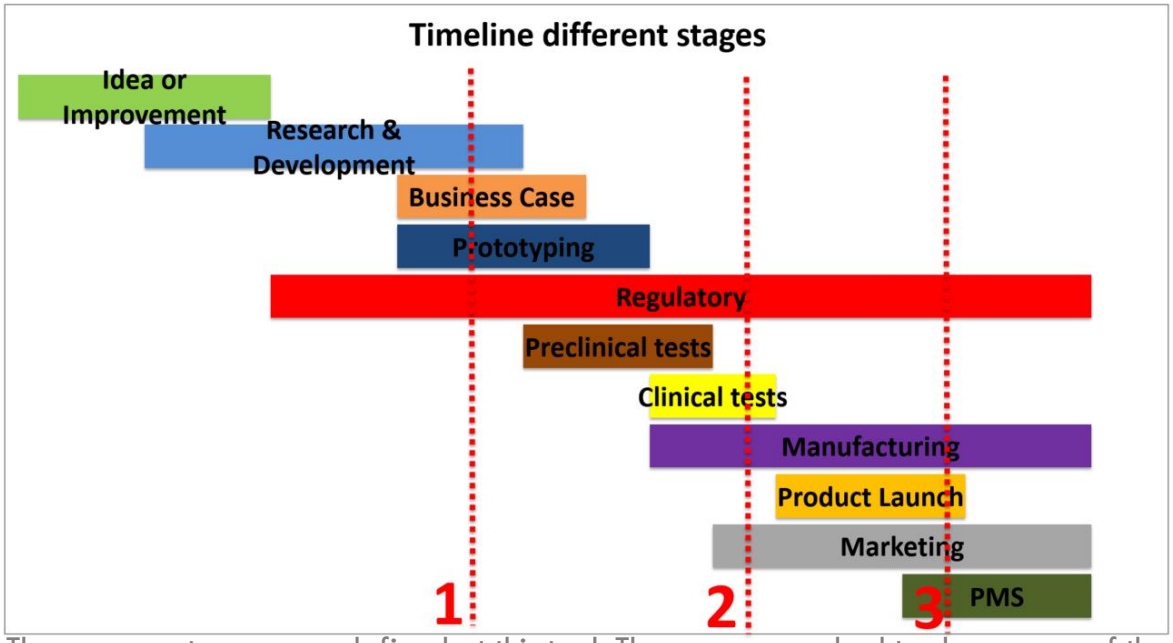
Answers on multifactorial questions are also converted to weights of a specific class, depending on the importance of the question and the selected number of answers.

The questionnaire is implemented in an online tool on the platform of SurveyAnyPlace.

Link: http://su.vc/medtech_compass QR-code:

The evaluation moment; when are they filling in the questionnaire?

The MedTech compass tool is designed for newly established start-up companies that will launch a product or service in the Medical Technology sector. Not every start-up has the same duration of a product development cycle. Depending on the moment the questionnaire is filled in, the team behind the start-up will have encountered a lot more or less information. An average pattern traversed by most product development teams is the following.



Three moments were predefined at this tool. The users are asked to choose one of the moments that describes best their current situation. Depending on this moment, not all the questions will partake in the algorithm to calculate the success rate.

Benchmarking the score of a stage

Not all the stages have the same amount of parameters or questions. Certainly not after omitting certain questions because the different evaluation moments of filling in the tool as described above. For this reason, the calculated score of a stage should be benchmarked. The influence of the number of questions on the score is eliminated by implementing a factor that is calculated with some logarithm based on the thought of how many answers of class B and C can be chosen to get a score of 50% at a stage.

Different trajectories for a MedTech start-up

The start-ups have different long term objectives with their product or service. Some of them only want to prototype a very good idea, others want to build a solid company. Also the number of iterations in the development cycle can be very different. Some companies want to go to the market as soon as possible. They launch the new product or service and develop a second version based on customer feedback. Other companies want to be very confident of their product before they go to the market. These companies invest a lot of money and time in prototyping, biomechanical tests and clinical trials. One immediately feels that there is a big difference between the two extremes based on investments in time and money. Based on these considerations four different trajectories are formulated in this tool. Depending on the specific trajectory, some stages will carry more weight when the overall success rate is calculated.

- Product/Service scenario 1: Develop, design and prototype some product or service. The technology will be intellectual protected with the intention to sell the patent to another company.
- Product/Service scenario 2: Going fast through the development cycle of the product or service with the intention to go very fast to the product launch. At next development cycle iterations the technology will be revised based on the customer feedback.
- Product/Service scenario 3: Paying close attention to the prototyping and testing phases before the product is launched. The company is going slower through the development cycle because they want to be confident about their product before they launch it.
- Product/Service scenario 4: Paying close attention to all the phases in the development cycle and putting a lot of energy in the organization of a solid company next to the product development.

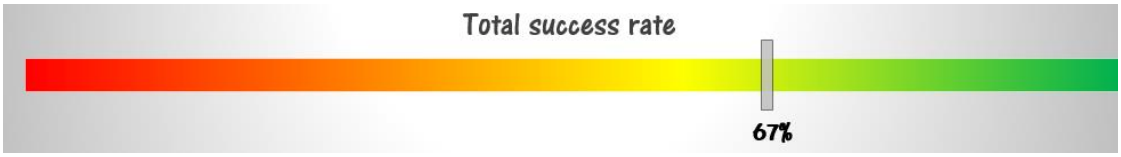
The product/service scenario is determined by some questions about the long term purposes of the company and the time and money they want to invest in the development of the product.

A weighted arithmetic mean is taken of the benchmarked scores of each of the stages. The weights for a stage are between 1, 2 or 3 dependent on the importance of the stage for the chosen trajectory.

The results

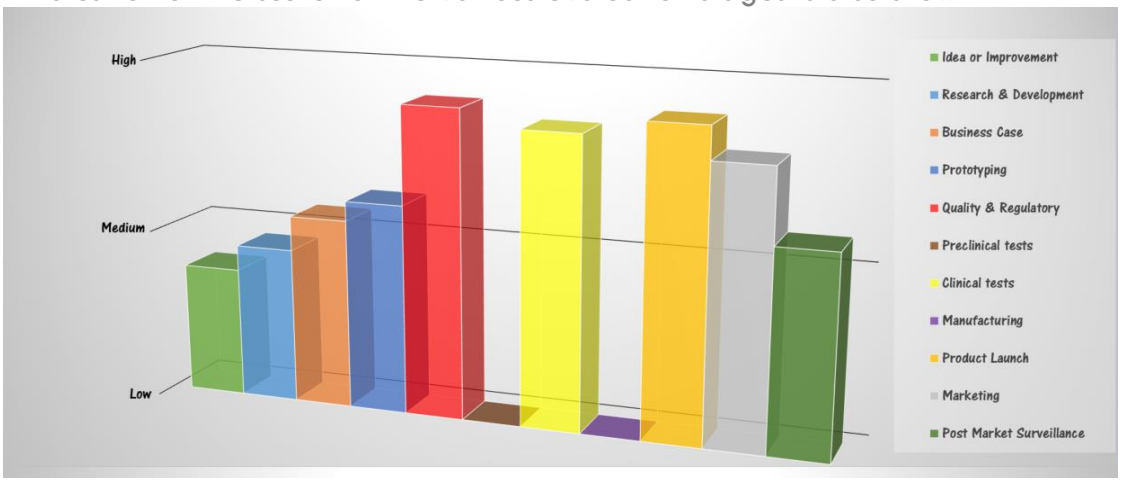
Did you fill in the questionnaire correctly? ✓

To test whether the questionnaire was filled in consistently, some questions were repeated. If these questions always get the same answer, this box is checked.



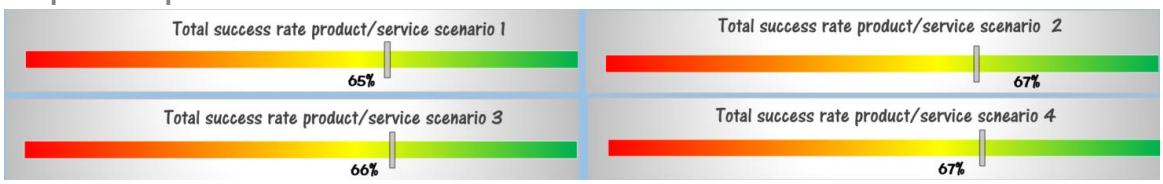
The total success rate is the weighted result of all the different stages, depending on the importance of a stage in the selected trajectory.

An indication of the score for the various evaluation stages is also shown.

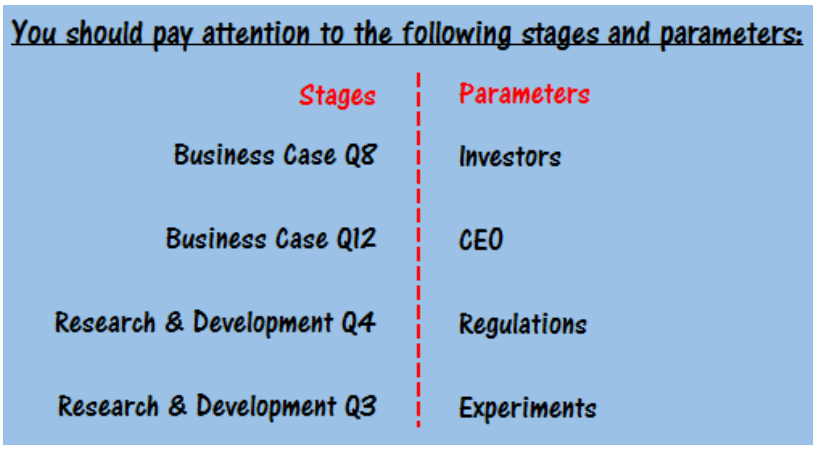


A score of zero at an evaluation stage implies this stage is not included in the calculation of the total success rate. Scores of zero are only possible if the end user indicated that this stage has no significant contribution for the total success rate and those questions are skipped in the online tool.

There will also be a score for the total success rate for the MedTech start-up when it is assumed they would follow another trajectory. The multiple trajectories were described above.



Next, the two evaluation stages with the lowest score are searched. Of these stages, the four parameters that require urgent attention are displayed.



Finally, the scores of the different evaluation stages are compared to the score they would achieve if they indicated a different evaluation moment in the product development cycle.