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Applying Customer Development Methodology to Industries under Transformation

Case Study of CellaVision

Master of Science Thesis
in the Management and Economics of Innovation Programme

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Abstract

The Customer Development methodology was created by Steven Blank in the mid 1990s. It was developed as a tool for entrepreneurs and startups to discover repeatable and scalable business models. Even though the technique was developed for startups, Blank argues that it can be used for established companies as well. One of the core concepts of Customer Development is that companies must continuously interact with customers to get a first hand perspective of their needs in order to improve the odds for product success. The advantages of understanding the customer needs are obvious, but there are also risks in relying too heavily on their feedback. Christensen (1995) highlights such behavior as a main reason for companies failing to identify the threat of new disruptive technology. Disruptive technology is an issue not addressed by the Customer Development methodology, which bases its assumptions about market demand solely on the customer's current preferences. In industries under transformation, or with long product development cycles, this blind spot of Blank's approach could result in failure to identify competing technology. This thesis investigates how well aware customers are of new technological development in medical technology, in particular in clinical microbiology laboratories. The thesis then continues to investigate how the Customer Development methodology can be complemented with forecasting tools to assess the risk of market disruption.

The thesis is based on a case study at the Swedish medical technology company CellaVision. CellaVision have had close ties with their customers during the successful development of their first product, an automated microscope for analyzing blood slides in hematology departments at hospital laboratories. Over the years, several customers have recommended the company to branch out into clinical microbiology, and this sparked the development of a product in collaboration with a few customers in 2011. However, the CEO at that time decided to cancel the product in order for the company to focus on its core products. Five years later, CellaVision wanted to explore the potential in clinical microbiology again. At this point the landscape had changed because of the introduction of a new technology recognized by Swedish laboratories in 2012, MALDI-TOF. After the technology shift, the prospects for CellaVision's original idea was not as lucrative anymore.

This thesis is built upon 59 interviews with different stakeholders within clinical microbiology, as well as a literature review of previous research. The study shows that customers of medical technology in clinical microbiology laboratories are often unaware of emerging technologies in their field until the products have reached the market. To decrease the risk of developing soon-to-be-disrupted products, the Customer Development methodology should therefore be complemented with tools for forecasting technological development.

Glossary

Bacteriology: The study of bacteria.

CellaVision: The case company of this thesis. CellaVision are today producing automated microscopes for hematology laboratories.

Clinical microbiology: The part of microbiology that is medical. It is concerned with the prevention, diagnosis and treatment of infectious diseases.

Customer development: a methodology for product development popularized by Steven Blank in mid 1990's.

Hematology: The part of clinical chemistry dealing with blood samples. Hematology is CellaVisions current market, and will therefore be used as a reference.

Laboratory managers: The laboratory managers are often responsible for buying new technology, administering the technicians and streamlining the flow in the laboratory.

Laboratory technician: The laboratory personnel that is performing the tests on the samples.

Mass Spectrometry: The technology behind the MALDI-TOF products, presented below.

Matrix-Assisted Laser Desorption Ionization Time-Of-Flight Mass Spectrometry (MALDI-TOF MS): A relatively new technology that is used as a part of the identification diagnosis in clinical microbiology. It uses laser to determine the species of present microorganism by monitoring the time of flight after beamed with laser. Described further in chapter 5.1.3.2.

Microbiology: The study of microscopic organisms.

Mold: A member of the fungi kingdom. Differs from yeasts by their hyphae growth habit.

Technology roadmapping: A technique for technology forecasting.

Mycology: The study of fungi. In clinical microbiology fungi are split up in mold and yeasts.

Parasitology: The study of parasites.

Polymerase Chain Reaction (PCR) Technology: A relatively new technique used as a part of the identification diagnosis in clinical microbiology. Uses DNA replication to detect presence of specific microorganism. Described further in chapter 5.1.3.3.

Turn around time (TAT): the time for that it takes for the doctor to get results from the laboratory.

Virology: The study of viruses.

Yeast: A member of the fungi kingdom. Differs from mold by their single-celled growth habit.

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1. Introduction

According to a survey conducted in 1995, the average commercial success rate of new products spanned between 51% and 62% (Griffin, 1997). Figures provided by the developers of the Customer Development methodology, Blank and Dorf (2012), are even less optimistic, stating that more than 9 out of 10 new products fail. Blank and Dorf (2012) claim that this applies to all product categories, high-tech and low-tech, and to both start-ups and established firms. Blank and Dorf's (2012) main explanation to the high failure rate is the product introduction processes used by companies. Many firms use tools suitable for executing known business, while start-ups are full of uncertainties. Uncertainties are naturally a huge part of any product development, which would explain why large companies also struggle with the same problem. To cope with these uncertainties, Blank and Dorf (2012) suggest increased and improved customer interaction and involvement. However, we argue that the current theories of customer development approach the problem from a static and too one-dimensional perspective, especially when applied to dynamic industries under transformation.

As a practical example of failure in terms of customer development, Blank and Dorf (2012) bring up the billion dollar startup Iridium. The company developed a satellite constellation to offer full satellite phone coverage over the complete surface of the earth. Seven years after its founding in 1991, Iridium had the network setup and the first calls were made in 1998. Unfortunately for Iridium, by that time the market conditions had changed dramatically from when the project was started. Traditional cell-phone networks now covered most valuable parts of the world, and with a much lower cost structure. Iridium's market was soon gone. Blank and Dorf (2012) argue that getting out of the building, repeatedly talking to customers could have saved Iridium billions of dollars. That way Iridium would eventually have learned how small their potential market had gotten while they were developing their product, which would allow them to change strategy.

The approach described above of relying on continuous customer feedback indubitably reduces the effects of unknowns to the development of a new product. Yes – Iridium could have saved billions using the Customer Development methodology, but they would still have spent billions before doing so. Asking the customers what they want right now does not mean that their answer would be the same if asked the same question the following year. Market conditions are rarely static and since the point of reaching the market with a new breakthrough innovation may lay several years ahead, other measures need to be taken to foresee market changes. One reason for changing customer preferences can be new technological innovations that the customers are unable to anticipate. As the famous quote by Henry Ford says – "If I'd asked people what they wanted, they would have said faster horses".

It may of course be true that talking to the customers in some cases could help in identifying a declining market trend as Blank and Dorf (2012) point out. But the question is if it is the soundest way of doing so. In the case of Iridium, the foundational needs of the customers did not change during the time that Iridium developed their product. It can be assumed that customers back then valued similar attributes as we do today, such as geographical coverage and price. Thus, having a near-continuous dialog with the customers during the development process could very well have generated similar response as it did at the outset of the project. What did change was the competition with its rapidly developing network technology. For that reason, companies already in the product development phase need to look beyond the threat of currently existing

substitutes and strive to also identify threats that are yet to reach the market or even not yet invented. The threat of upcoming technologies is currently not addressed by the Customer Development methodology, which is lacking an essential aspect of time. The time aspect is crucial since customer preferences often change as the technological landscape progresses. In industries where product development cycles are long the threat of new technologies is especially important; one such industry is medical technology. This thesis investigates the awareness of new technology among lab managers and technicians within clinical microbiology to see if the Customer Development approach is valid in this context. It is also investigated how the methodology could potentially be complemented. The complemented methodology is then applied to the case of the medical technology firm CellaVision's endeavor of developing a new diagnostic tool for clinical microbiology laboratories.

Research Questions:
Are lab managers and technicians within clinical microbiology aware of new emerging technology in their field?

If not, how can the Customer Development methodology be complemented to account for the threat of new upcoming technologies in clinical markets under transformation?

2. Literature Review

This chapter reviews the relevant findings from the literature study. This chapter first defines the terminology difference between customers and users, and describes the customer development methodology and disruptive technologies. Furthermore the chapter continues to describe common methods to analyze technology trends. The method used is described in Chapter 3.

2.1. User and Customer Definition

From a company strategy perspective it is important to differentiate between the buyer and the user, since that is not always the same individual. Often, the words customer and user are used. Customer is the purchaser, the person who decides which product to buy, while users are the actual users of the product. Users and customers could be the same person when the buyer is also the user, as for most end-consumer products, but within medical laboratories that is seldom the case. In laboratories, the laboratory managers decide which product to purchase while it is the laboratory technicians who end up using the purchased instruments.

2.2. Early Theories of Involving Users and Customers in Product Development

The idea of focusing on customer and user satisfaction within product development theory is older than Blank's Customer Development methodology created in the mid 1990's. Traditionally maximizing market share was the key part of companies general market strategies (Matzler and Hinterhuber, 1998). In the in late 1980's and early 1990's many consultancy firms promoted strategies for customer satisfaction (Matzler and Hinterhuber, 1998). Matzler and Hinterhuber (1998) promote the use of the KANO model, which serves to identify specific product features valued by customers and using this information when developing new products. They argue that understanding the customer needs will generate higher customer satisfaction. This in turn will lead to a loyal customer base, willing to spend more and buy more frequently (Matzler and Hinterhuber, 1998).

Urban and Von Hippel (1988) also highlight the importance of understanding user needs in the development of new industrial products. It can be argued that they get somewhat closer to predicting the future market and reduce uncertainty from unknowns by targeting what they call "lead users" when developing new products. Lead users are defined as users who face needs that will become common in the market, but they face these needs months or years before the rest of the market will do. Lead users are also positioned to benefit greatly from a solution to these needs. Consequently, this type of users will be more interested in finding a solution and therefore also may be more willing to collaborate. However, reminiscing the words of Henry Ford, one can question whether interaction with lead users of the horse would have added much value other than identifying the need for improvement. How this improvement could be achieved would probably still have remained as big of a challenge.

2.3. Customer Development

Customer Development methodology was created by Steve Blank in the mid 1990's. Blank argued that the practices taught at traditional MBAs were only suitable for running large corporations (Blank and Dorf, 2012). These practices worked fine as long as customers, problems, and necessary product features were known. On the other hand, for early-stage ventures in search for repeatable and profitable business models such factors are however rarely obvious. As Blank put it, "startups are not simply smaller versions of large companies" (Blank and Dorf, 2012). To fill the educational gap, Blank therefore created a framework that worked for startups and entrepreneurs, based on his own experience. Although the framework was developed for entrepreneurs and start-ups it does not mean that the framework is not applicable to large corporations as well (Blank and Dorf, 2012). Companies have finite life cycles, and to survive and grow most of them either offer new versions of their core products or turn to disruptive innovation. Both of these processes tend to involve the search for new business models. The development of new products at large companies can thus often be seen as attempts at launching scalable startups within the greater organization (Blank and Dorf, 2012). Blank and Dorf's (2012) intentions with the framework is to solve customer and market risk, in other words to solve the question of whether customers will adopt a product or not.

The winning concept according to Blank and Dorf (2012) is to apply a combination of agile engineering and customer development to iteratively test and search for a new business model and thereby eliminate the unknowns. The iterative approach and close customer interaction allows companies to quickly adjust course in search for a suitable business model. The shorter the frequency of interactions, the less risk of wasting resources on products for which there is no demand. Hence, Blank and Dorf (2012) stress the importance of *getting out of the building,* to get a firsthand understanding of the potential customer needs before making final any decisions about the new product specifics. This needs to be done early and often in the development process. The mission of an entrepreneur is to test a number of hypotheses about the business model. These hypotheses concern who the customers are, what features the product should have, and how to scale the business. Customer development is the process of answering these questions (Blank and Dorf, 2012). Over the past decade Blank's framework has been embraced by tens of thousands of engineers, entrepreneurs, and investors around the world (Blank and Dorf, 2012).

Christensen et. al. (2007) have a similar point of view. They mean that in order to find new opportunities, firms cannot just rely on sales data and desktop research. They need a close relation to the customer to allow for feedback and to be able to observe their actual needs. To understand these needs Christensen et. al. (2007) suggest focusing on understanding the "jobs to be done" that the customer is trying to carry out. Customers do not restrict themselves to a certain product category when trying to a find a solution to their problems. This means that researchers need to thoroughly understand the job that the customer is trying to get done to be able to recognize substitutes from other product categories. Interacting and observing the users will not only generate insights about the functionality of the product, but also a broader understanding of the situation in which the product is used. This can be achieved through surveys, interviews, observations, participation and experimentation. For instance, the customer's pain points of trying to carry out a job may become obvious from the way they act as users and the emotions they express.

2.4. Involving Users in Development of Medical Technology

There are many benefits to be gained by involving users in the development of medical technology. In engaging users in the development they are able to help in the excerpting the targeted user opinions, needs, experiences and expectations (Shah and Robinson, 2007). These insights may be crucial to both the long and short term distribution and implementation of the product. Shah and Robinson (2007) list cases where a cooperation between producers and users improves quality, usability, design, functionality, effectiveness and the adoption of medical device technologies.

Even though involving users in the development provides a general value to the product, it does not provide any certainty that the developed product will be successful (Shah and Robinson, 2007). The potential users are not always capable to contribute to some medical technologies, specifically when the technologies are complex (Shah and Robinson, 2007). They might not possess sufficient technological knowledge to understand how the product works and thus can not contribute to the development. Another downside of involving users is the time and resources spent on keeping a tight relationship to the users.

2.5. Disruptive Technology and Core Capabilities

As described in the previous section concerning Customer Development, the upsides of staying close to the customers are quite obvious. However, Bower and Christensen (1995) also bring up the problem of myopia when staying too close to the customers. The concept of disruptive innovation was popularized by Christensen in 1995. Bower and Christensen (1995) pointed out the consistent pattern of leading companies failing to adapt and maintain their positions through technology and market changes. History is full of examples supporting this claim, such the cases of Xerox, IBM, and Sears (Bower and Christensen, 1995). These companies all failed because they stayed too close to their customers. Aggressive investments in technologies necessary to retain the current customers created a myopia that prevented them from transitioning into a new technological paradigm. In early phases, disruptive technologies often do not meet the requirements set by the current customers, which leads to the new technology being ignored by incumbent firms. At the same time its new combination of performance attributes may however appeal to a new emerging market segment. Moreover, the improvement of the new technology may progress much faster than the customer expectations do. This means that it will eventually become good enough also in the aspects that the mainstream customers value. Once it does, it is destined take over the market of the incumbents who are left hopelessly behind in the new development. Bower and Christensen (1995) hence conclude that managers need strive to identify these upcoming technologies. A problem is that targeting a niche market with the new disruptive technology will look financially unattractive to incumbents. If you can't foresee the potential growth, it will be difficult to motivate investments in the technology. A solution according to Bower and Christensen (1995) can be to create an ambidextrous organization, splitting up the established business from the new technology venture. This way sufficient resources can ensured for the new venture, which otherwise could suffer due to prioritization of the mainstream business.

Another factor that explains why incumbents often struggle to adapt to new technological paradigms is described by Leonard-Barton (1992). This factor is core capabilities, which can both promote and inhibit development. A capability is defined as core if it strategically

differentiates a company. Some authors argue that development based on core capabilities, in other words incremental innovation, is more competitively efficient than pursuing opportunities outside of a current strategic knowledge base (Leonard-Barton, 1992). As the environmental landscape changes however, there is of course a risk of incumbent inertia (Lieberman and Montgomery, 1988). Having to replace previous core capabilities with new ones often faces internal resistance.

Despite the concept of disruptive technology being a well-known concept, the Customer Development methodology takes seemingly little consideration of it. With one of the stated goals of Customer Development being to eliminate unknowns, the uncertainties stemming from potentially disruptive technology cannot be ignored.

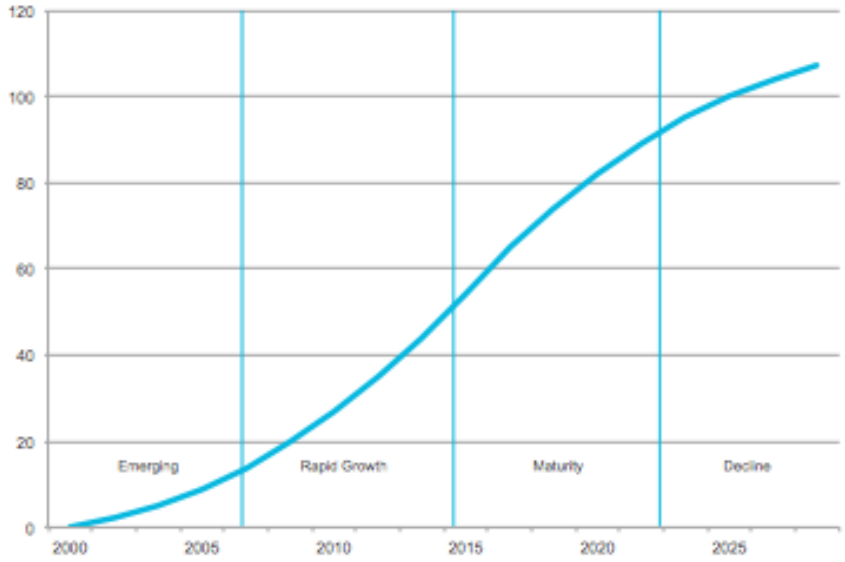
2.6. Forecasting Emerging Technologies

This section presents a number of methods that have been identified as potential tools for filling the gap concerning disruptive technology in the Customer Development methodology. The methods are some of the most well cited papers on technology scanning and technology roadmapping.

2.6.1. Technology forecasting

Technology forecasting focus on transformation in technology, e.g. in the technology's capacity, significance or timing (Roper et al. 2011). Technological forecasting does not seek to project a single definite future. A good forecast should rather project several possible future, of which some may be more probable than others. The growth of technologies is affected largely by differences and changes in their context both politically and socially but also the growth of competing technologies. Thus it is impossible to come up with a single growth pattern that applies to all technologies. There are however general concepts of how technologies develop (Roper et al., 2011).

Technologies typically follow a growth pattern that is S-shaped, see figure X. When the technology *emerges*, the growth of sales are slow as the innovators try to determine the composition of the product (Roper et al., 2011). When the product is established there is a time of rapid growth, followed by an inflection point where the sales growth speed is at its peak, followed by a time of maturity, and finally a period of decline. The speed of this diffusion depends alot on the product, some products *emerge* for decades while others grow much quicker (Roper et al., 2011).



There are many ways to fail at technology forecasting, but Roper et al. (2011) lists three common mistakes: bias, contextual oversights and faulty core assumptions. Bias can be both conscious and unconscious, and the latter is subtle and hard for the decision makers to detect. The best way to protect the forecast from bias is to have diversity in both the team performing the forecast as well as the method used (Roper et al., 2011).

Contextual oversights happen when forecasters do not recognize changes in the context the technology is embedded in. Political or socioeconomic changes can for instance change the direction the market is taking. Another contextual error forecasters do is to overestimate the diffusion rate of a technology. There are four stages that a technology needs to go through in order to diffuse: the knowledge stage, the persuasion stage, the decision stage and the confirmation stage (Rogers, 1983). In the first stage, potential customers need to get to know about the product. Secondly the product needs time to be understood by the customer. Third, the customers need to conclude that return on investment, benefits outweighs the costs for the product. Finally the adopters need to repeat their purchase and/or recommend the product to others. All these stages take time, and thus the time of diffusion should not be underestimated (Alan et al., 2011). The diffusion rate of disruptive technologies is often overestimated since the advantages of the products are not as clear to pragmatic customers as they are to early adopters and forecasters (Moore, 1999).

Faulty core assumptions are troublesome as they, like unconscious bias, often are not recognized by the forecaster. Ascher (1978) noted that the core assumptions are crucial to the accuracy of the forecast. The choice of method selection is either obvious or secondary, if the core assumptions are correct. If the core assumptions are incorrect, the forecast result cannot be corrected by method selection (Roper et al., 2011).

2.6.2. Technology Roadmapping

Technology roadmapping is a technique used to support strategic long-range planning (Phaal et al., 2004). In recent years the the technique has been used for supporting industry foresight initiatives (Phaal, 2002). Many scholars have developed different roadmapping techniques, with different purposes. By summarizing the a vast number of methods and boiling them down into a single customizable format, Phaal et al. (2004) have managed to become well-known authorities on the subject. One possible use for the technique is that it can supposedly improve the odds of survival for companies operating in turbulent environments by providing a tool for discovering potentially disruptive technologies (Phaal et al., 2004). A company's technological roadmap needs to take both internal and external factors into account. The internal factors consist of the company's core capabilities and the external factors include technological trends and competitor activity (Phaal et al., 2004). A framework developed by Phaal (2002) for industry foresight in essence includes the following steps:

1. Exploration of industry and market trends and drivers.
2. Consideration of performance measures and targets.
3. Consultation to solicit views from industry, academia, and other organizations.
4. Assessment of technology evolution and research requirements within the industry.
5. Synthesis and review

2.6.3. Bibliometric analysis

Daim et al. (2006) argues that a method called bibliometrics analysis could be used to complement traditional forecasting methods. Bibliometric analysis is defined as the measurement of texts and information. It has for instance been used to assess a prediction of the future for the fuel cell in the automotive industry, by looking at the number of publications since 1990s (Daim et al., 2006). In that study, the number of publications was assumed as a proxy indicator for technology diffusion. The data was then used to determine the technology life cycle position, the position on the S-curve. Porter (1991) suggested a type of bibliometric analysis by dividing the number of published articles in journals by the number of articles published at conferences. Then a higher percentage of published articles at conferences means that the technology is in the initial stages as the researchers are looking for peer-to-peer response (Daim et al., 2006).

3. Methodology

This chapter will describe the methodology used in this thesis research. The first two subchapters in chronological order are research question, research design and data collection. The third and last subchapter will be a conclusion and reflection of the quality and replicability of this research.

3.1. Research Question

Customer Development is a hot topic in the area of product development. However, due to the static nature of the methodology, it might not be suiting for industries under transformation or industries in which product development times are extensive. In industries with long development times, during the time it takes for a product to reach the market the technological landscape may already have changed. Therefore this thesis aims to complement the customer development methodology with tools that can aid in trying to foresee future market change.

RQ: How can the Customer Development methodology be complemented to account for the threat of new upcoming technologies in clinical markets under transformation?

3.2. Research Design and Data Collection

3.2.1. User Interviews

The first phase of the research was to methodologically research the subjects of this thesis in a literature review. Google Scholar was used as a way of ranking the articles within relevant areas. The first 50 hits on Google Scholar for the main keyword “Customer Development” were reviewed. For the other keywords the first 30 hits were reviewed. The articles that were not accessible through Google Scholar for free were searched for on the Chalmers University of Technology’s online library. If they were not accessible from there either, they were excluded from the review. The remaining keywords used in the literature review can be found in table 9.1. In Appendix 9.1. The article or book with the most citations were considered to be the main literature in respective field, and was given the main part of that chapter.

In parallel with the literature review a first phase of interviews was conducted at clinical microbiology laboratories at three of the largest clinics in Sweden. Those were the Sahlgrenska Hospital in Gothenburg, the Biomedical Center (BMC) in Lund, and the Karolinska Hospital in Stockholm. Larger hospitals have larger sample volumes and therefore have bigger incentives to invest in automated technology, which is what the case company (CellaVision) is interested in. Moreover, Sweden has some of most developed healthcare facilities in the world, which increases the likelihood of finding “lead users”. In 2014, Sweden had the second highest healthcare expenditure as percentage of GDP among western countries, after United States (The World Bank, 2015).

The first phase of interviews focused on what the Customer Development methodology called Customer Discovery. In other words, on understanding the customer and user needs, as well as obtaining a general overview of the process flow within the laboratories. The interviewees were all working at a clinical microbiology laboratories as laboratory technicians or managers. The interviews were conducted in a semi structured manner with a main topic and a few guidelines of what the interview should cover. Semi-structured interviews are useful when researchers want to understand the interviewees opinions and thoughts (Easterby-Smith, 2012). Each interview took between 1 to 3 hours. In total 2 laboratory managers and 10 laboratory technicians were interviewed in the first phase. Asking “why” type of questions is a way to gradually reveal the

interviewees individual value base, this is called laddering, which were used in all interviews (Easterby-Smith et al, 2012). The starting point for each interview was for them to take us through the process flow within each laboratory, complemented with questions along the way, for questionnaire see Appendix 9.2.1.

A second phase of research was made with focus on the recent and future development of the industry based on knowledge gained from the initial interviews. Once again Google Scholar was utilized and keywords used this time, can be seen in table 9.1. In Appendix 9.1. In this research phase a clinical microbiology conference in Amsterdam called *ECCMID 2016* was visited. During the conference both company and laboratory employees were interviewed. The laboratory personnel were interviewed to get an understanding of Western Europe's process flow in clinical microbiology laboratories. The interviewees were chosen randomly, and the focus of the interview was to find differences in how they diagnose their patients. For questionnaire see Appendix 9.2.2. In these interviews, 13 laboratory employees were interviewed, 3 from the Netherlands, 4 from the United Kingdom, 3 from Belgium, 1 from Germany, 2 from Greece.

Before attending ECCMID the 162 companies that exhibited at the conference wa researched to scout for new upcoming technologies. The companies was research in order to to identify potential future scenarios for the technology roadmapping. At the conference, the more interesting and unique company stands were visited in the exhibition hall to discuss the future of the market. In total 20 interviews with managers and product developers were conducted. These interviews were also conducted in an semi-structured manner where the company product constituted a starting point or the discussion, which eventually ended with thoughts of the future of the market. A basis for the interviews can be seen in appendix 9.2.3.

Another final round of interviews was then conducted at microbiology laboratories in the United States. To obtain a diversified view, labs of different types and sizes were selected for the visits. Due to time constraints the labs were all located in a relatively close proximity of each other, which should be taken into account if trying to generalize any findings. The labs were located on the east coast in the states of New Jersey, New York, and Philadelphia. The laboratories visited were Hospital of Pennsylvania (Philadelphia, PA), Cooper Medical Center (Camden, NJ), University Hospital (Newark, NJ), LabCorp (Raritan, NJ), and NewYork-Presbyterian Hospital (New York, NY). An overview of all the conducted interviews can be seen in table 3.1.

Place for conducted interview	Titles	Number of interviewees	Time per interview
Swedish laboratories	Technicians, Managers	10	1-3 hours
Amsterdam, ECCMID	Technicians, Managers	13	15-30 min
Amsterdam, ECCMID	Managers, product developer	20	30-60 min
North East US Laboratories	Technicians, Managers	16	1-2 hours

Table 3.1. Overview of conducted interviews

3.2.2. Case Study

A case study is an empirical analysis which focuses on a contemporary phenomenon. A case study should be used to answer the research question when the questions are in the form of

“how” or “why” (Yin, 2013). The core of a case study is to highlight one or multiple decisions: how the decisions were implemented, how come they were taken, as well as the outcome of them. Case studies could observe single or multiple cases, and they can be both qualitative and quantitative.

This thesis is based on a qualitative single case study of the medical technology firm CellaVision. This research made in the clinical microbiology market, is an empirical analysis of the automation phenomenon in the clinical microbiology. Chapter 4 of this thesis explains the case company and their situation in depth.

3.2.3. Reflection of Quality and Replicability

The research of this study consists of two main areas, the literature review and the conducted interviews. The research question developed over time after the initial contact with the case company and after the first phase interviews. After the research question was settled the interview guidelines for the second phase interview were prepared.

The literature review’s replicability relies on the Google Scholar algorithm. The algorithm is likely to change over time and therefore a future search with the same keywords may generate different results. However the main articles with the most citations, will likely remain among the top results in the foreseeable future.

Moreover, semi-structured interviews is a great way to get an understanding of the interviewees opinions on the subject (Easterby-Smith, 2012). However, regarding replication of the research a replication of interviews is not possible. Furthermore, the quality will be affected by whom that is performing the interview. The pool of potential interviewees was limited by the language barrier, as they needed to know one of the two languages that the researchers are fluent in, English and Swedish. This lead to the exclusion of some laboratory employees from France and Belgium who were initially approached for interviews. During all interviews both of the researchers carefully took notes to make sure nothing was missed.

Case studies have received criticism because they produce huge piles of data, which grants researchers to draw any conclusions they want (Easterby-Smith et al. 2012). In order to deal with this case studies should have a clear design before any data is collected (Easterby-Smith et al. 2012). In our case the first phase interviews were primarily conducted to form a research question and gain a basic knowledge about the microbiology market. The second phase of research that contains the most information about the future of the market, and is used to answer the research question, was carefully thought through before collecting additional data.

4. Background - Case Company

In markets associated with long development times the cost of developing a product are typically higher than in markets with shorter development times. Thus the costs of cancelling a product in the late stages, or finishing a disadvantageous product, are very high. The medical technology industry is associated with long product development times. and thus during the time it takes for the product to reach the market another product might already have changed the industry landscape. Not only does medical technology have long product development times the technology also need rigorous testing before it can be used in practice at laboratories. This thesis uses the case of the medical technology firm CellaVision to show how the Customer Development methodology can be complemented to account for the threat of upcoming disruptive technology. The overhanging threat of disruptive technology in the industry is magnified even more from the technological transformation that has been taking place in clinical microbiology in the recent years.

CellaVision wants to expand their business from their current position in hematology laboratories to introduce their technology in new clinical markets. They want to do this while relying on their core capabilities in digital image analysis. Current customers have over the years been asking CellaVision to create a solution for clinical microbiology laboratories. According to the Customer Development methodology, the fact that customers are actively pursuing a solution to their needs would be a promising sign for market success. However, when digging deeper into the current industry development it becomes clear that new technologies pose a great threat to CellaVision's potential product.

After recommendations from customers CellaVision started in the late 2000's to research the potential for developing a product to streamline the workflow in blood infection diagnosis. The potential customers back then found that the product idea could be of great help in their work and save them both time and money, just like CellaVision's devices had done in hematology. However, CellaVision's CEO at the time wanted the company to focus on its core business and therefore decided that they could not afford to allocate resources to new products (Stråhlén, 2016). Later on it turned out to be a great decision to cancel the development. In the years following the cancellation, the technological development within the field more or less eliminated all the potential that CellaVision's product idea had initially shown.

In 2012, a new technology called MALDI-TOF MS got its first recognition in Swedish laboratories and it disrupted the blood infection diagnosis (Rydberg, 2016). The application of mass spectrometry (MS) in microbiology for identification of bacteria can be dated back to the 1970s (Anhalt and Fenselau, 1975) but the modern MALDI-TOF MS technology emerged in 1980s (Karas et al., 1985; Karas and Hillenkamp, 1988; Tanaka et al., 1988). In 2002, Koichi Tanaka received the nobel prize in chemistry for his development of the technology. The first scientific papers that showed that MALDI-TOF MS could be used for microbial identification were published in the late 1990s. 10 years later the first benchtop instruments were produced for routine microbial identification (Capocefalo et al., 2015).

In all its essence, MALDI-TOF MS carried the characteristics of a disruptive technology. After the introduction, commercial MALDI-TOF MS databases for microbial identification have developed rapidly and thereby improved the precision of the technology up to a level that satisfies the standards of the mainstream customers. The large format of the instrument initially restricted use to pure research purposes and held back the adoption rate within in the mainstream market of clinical microbiology. After developers in recent years managed to compress the instrument into a more compact format, it did not take long for it to be embraced for routine microbial identification (Capocefalo et al., 2015).

At the time that CellaVision was considering to enter the blood infection market, in 2011, they had never heard of this technology. Before MALDI-TOF there could have been an opening to be able to develop an automated microscope that would be able to add more to the identification than manual microscopy did. It wasn't until 2016 when the company revived its expansion plans by initiating this thesis that we realized that entering the previously attractive blood infection diagnosis opportunity was no longer an option due to the recent technological development. In comparison to the precision and throughput offered by MALDI-TOF MS, CellaVision's potential solution would not stand a chance.

The case above highlights two different problems caused by staying too close to current customers that Bower and Christensen (1995) mention in their work. Firstly, CellaVision listening to their current customers were unable to see the threat of an emerging new technology. They did not only ignore the threat, but even completely failed to identify it since it had not yet entered the mainstream microbiology market in Sweden. Once the technique had been refined into a compact format that suited the mainstream market and fulfilled the stringent quality criteria demanded by it, MALDI-TOF MS quickly swallowed most of the market. Equally unaware of the development of MALDI-TOF MS, the mainstream customers praised CellaVision's new solution. Abiding by the Customer Development methodology, such appraisal would be seen as a big go-ahead sign since the method does not consider upcoming competitive solutions. Secondly, if the new venture had been as promising as the company assessed it in 2011, it was a mistake to let the current business prevent them from entering the new market. It is however the first aspect, the one of identifying the threat of disruptive technology that will be the focus for this thesis.

CellaVision is now, once again, considering to enter the microbiology market. MALDI-TOF MS has removed the need for advanced microscopy identification of bacteria that CellaVision was originally interested in creating. However, most laboratories still use manual microscopy for some initial screening. This is a process that could be automated by CellaVision and an opportunity which will be investigated through this thesis. This time the company wants to make sure that they do not miss the threat of upcoming technologies. Interaction with the customers, in line with the Customer Development methodology, will thus be complemented with other methodologies to evaluate the situation in this thesis.

5. Empirical Setting and Empirical Analysis

In order to understand and predict the technological development within clinical microbiology, one first needs to comprehend what is actually done in such laboratories. The empirical findings therefore starts off with an overview of the purpose and procedures in clinical microbiology laboratories. This is followed by a section about the recent developments and trends within the field. After that, the industry is analyzed from a Customer Development perspective, which is then followed with a section of technology forecasting.

5.1. Empirical Setting

In contrast to CellaVision's current market in form of hematology laboratories, where only blood is analyzed, a clinical microbiology laboratory handles a wide range of different patient samples. The samples can come from any body fluid or tissue. Among the most common samples are urine, blood, tissue, feces, and cerebrospinal fluid (Rydberg, 2016). The laboratory can be divided into four separate divisions, each focusing on diagnosis of fungi, parasites, bacteria, and viruses respectively. With so many different types of samples to analyze, the workflow within microbiology is not as clearly sequentially linear as within CellaVision's current market hematology. This thesis will focus on bacteriology and parasitology in detail, since mycology diagnosis has quite low sample volumes and viruses are too tiny to be examined with light microscopy, which is the technology that CellaVision bases their core capabilities on.

There are deviations within laboratories in what technologies they use due to size and resources. This chapter will present the most common techniques used in laboratories in western Europe and in the United States. The information has been gathered from laboratory interviews as well from the public website of the Swedish Health Authority, Folkhälsomyndigheten.

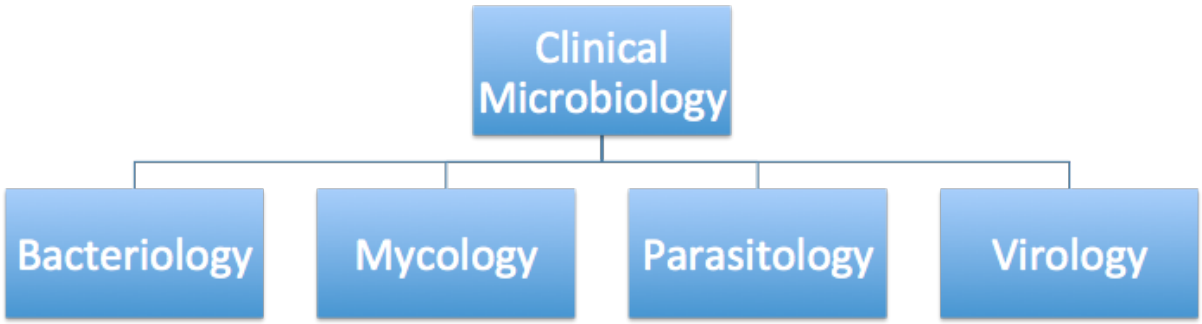


Figure XX: Overview of Clinical Microbiology

5.1.1. Bacteriology

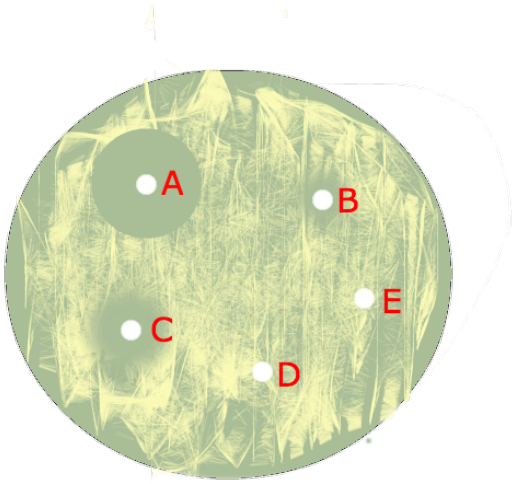
The bacteriology within clinical microbiology can be simplified into two critical aspects; identification and susceptibility. Identification is the act of classifying the bacterial species in question, while susceptibility is focused on antibiotic resistance and on figuring out what combinations of antibiotics can be used to cure the disease.

5.1.1.1. Identification

Identifying bacteria is generally a complex process in modern laboratories. The process consists of many steps and there are thousands of potential diagnoses (Rydberg 2016). Not only are there many different bacterial species, they can also be found in many parts of your body and thus bacteria diagnosis is performed on various types of bodily fluids and tissue. Additionally a high concentration of bacteria is often necessary to facilitate accurate diagnosis, and thus the bacteria traditionally needs to be cultured before analysis. An elaborate explanation of the identification of bacteria can be found in Appendix 9.3.1.

5.1.1.2. Susceptibility

The initial microscopy can only say so much about the antibiotic resistance of the bacteria. Being able to put in more specific antibiotics is important both from the patient point of view of getting better treatment but also on the societal level in order to reduce the risk of bacteria getting more resistant to antibiotics. To improve the precision of the antibiotic treatment, simultaneously as the initial microscopy the bacteria is tested for antibiotic resistance in a Kirby-Bauer test. A number of substrates, impregnated with different types of antibiotics, are attached to an agar plate on which the bacteria has been placed. The plate is then incubated to see how well each antibiotic inhibits the bacterial growth. As can be seen in the picture below, this particular bacteria shows complete resistance to the antibiotics named D and E. In some of the visited laboratories, outside Sweden, a machine called Vitek 2 by BioMerieux was used instead of the Kirby-Bauer test.



Picture: Resistance test

5.1.2. Parasitology

5.1.2.1. General Parasites

Medical parasitology traditionally consists of the study of three major groups of animals: parasitic helminths (worms), parasitic protozoa and arthropods that either directly cause a disease or act as a carrier of pathogens (Baron, 1996). A parasite is a pathogen that both injures and feeds sustenance from its host (Baron, 1996). Infections of humans caused by parasites are in the number of billions, while some parasite infections are fatal not all parasite infections are severe

they can be relatively innocuous. An explanation of the laboratory process for parasites can be found in Appendix 9.3.2.

5.1.2.2. Malaria

Malaria is a particular type of parasite that infest red blood cells. Hence, its diagnosis procedure differs from the one for fecal parasites. The disease poses the largest threat to Sub-Saharan Africa, which in 2015 had 88% of all cases and 90% of the deaths caused by Malaria (World Health Organisation, 2016a). In Sweden there were only 250 positive cases in 2015, but because of the seriousness of the disease, tests run every day in bigger laboratories (Folkhälsomyndigheten, 2016b, Stenström 2016). An explanation of the laboratory process for parasites can be found in Appendix 9.3.3.

5.1.3. Recent Technological Development

This section presents trends in the technological development that have been observed from laboratory visits.

5.1.3.1. Automation

Automation was introduced many years ago within the disciplines of clinical chemistry, hematology, and molecular biology. Clinical microbiology however has for several reasons been lagging behind in the development. The reasons behind this is that the discipline involves high variability of complex sample types, analytical procedures and relatively low volumes of each sample type (Croxatto et al., 2016). In the recent years consolidations of laboratories have triggered the development of automation also within clinical microbiology. Through the consolidation the numbers of each individual sample have increased and thus also the incentives for automation. During the next 10 years the market will likely go through a larger automation change (Burnham et al, 2013).

5.1.3.2. MALDI-TOF Mass Spectrometry

In recent years a technology called matrix-assisted laser desorption ionization time-of-flight mass spectrometry (MALDI-TOF MS) has emerged in the clinical microbiology identification process (Croxatto et al., 2012). The technology has been used for decades in chemistry but in 1975 Anhalt and Fenselau (Anhalt & Fenselau, 1975) proposed it might be possible to use for bacterial identification. It was later shown that it could not only be used for bacteria but also fungi and viruses as well (Giebel et al., 2010). Due to its way of analyzing samples in a completely new way, some of the culturing process is no longer needed, which speeds up the analytical process.

MALDI-TOF MS treats the microbial sample with laser, transforming it into ionised gas form. The ions are then separated according to their mass to charge ratio, and finally the time of flight of the ions is monitored and analyzed. The time of flight is compared to the database of previously identified specimen. The technology thus relies on having an extensive database of diseases, and consequently it gets better as the database continues to grow (Croxatto et al., 2012).

The instrument can analyze urine samples, agar plates, and blood culture bottles (Fournier et. al., 2013). MALDI-TOF has already replaced a large part of the bacterial identification process in laboratories today, but has not yet become routine for identification of fungi and yeasts (Croxatto et al., 2012). MALDI-TOF test can identify about 2000 different bacterial species. To put this into context, about 5-6 of these can be classified using a light microscope (Rydberg, 2016). Although MALDI-TOF is already extensively used in bacterial identification the technology is relatively new in this area and, it still has room for improvements of its database quality, sensitivity and post-

run analysis methods (Croxatto et al, 2012). It is likely to eliminate the traditional identification methods to a large extent (Croxatto et al, 2012).

One of the main advantages of using MALDI-TOF MS is its turnaround time (TAT). In theory, the technology can provide an accurate description of the test within an hour (Croxatto et al., 2012). From our laboratory visits we have seen that in reality many labs expect results after approximately 2 hours (Rydberg, 2016; Elmér, 2016). At BMC In Lund, MALDI-TOF is done directly from the blood bottle, without culturing, and is started simultaneously with the initial microscopy. At the Karolinska University Hospital, MALDI-TOF is not used until bacteria has been cultured for a half day after the sample has been taken out of the incubator. This was due to poor previous results after doing them directly from the bottle (Stenström, 2016). If the sample is a mixed culture, containing several different species of bacteria, which only occurs in about 5% of the samples, MALDI-TOF will not be able to accurately identify the content. In those cases the sample needs to be cultured so that colonies can be tested separately in the machine (Stenström, 2016).

None of the US laboratories visited for this thesis had yet implemented MALDI-TOF, but one was in the processes of purchasing the instrument within a year, and another had plans for implementing it in the future. The US is often lagging behind slightly when it comes to new technology due to strict rules set up by the Food and Drug Administration (FDA).

5.1.3.3. Molecular Techniques

Molecular techniques study physiological processes that occur in microorganisms. Apart from increased automation, the recent decades have brought advances in genome analysis with the conclusion of the Human Genome Project in 2005 with the comprehensive sequencing of the human genome (Murray et al., 2015). Murray et al. (2005) draw a parallel to the human efforts of sending a man to the moon, in the sense that the most important outcome of the project was all the new technologies developed to accomplish the goal. PCR is one of thos techniques on the rise, that builds upon matching DNA molecules in a sample to known parasite or bacterial DNA. If the targeted DNA molecules are present, they will multiply. The process is controlled in an automated device which by regulating heat in different stages starts the chemical reactions.

Real-time polymerase chain reaction (PCR) has revolutionized the process of identifying bacteria and parasites in the laboratories over the past decades (Espy et al., 2006). The technique uses a combination of PCR chemistry and fluorescent probe detection of amplified product in the same reaction vessel (Espy et al., 2006). For real-time PCR this process of amplifying targeted DNA is monitored in real time, in contrast to conventional PCR that only examines the sample after the PCR is completed. Real-time PCR generally delivers accurate results within an hour, and only requires a few minutes of hands-on time. Parasitologist Kawash (2016) at the Sahlgrenska Hospital compares the accuracy of PCR to identification using microscopy by claiming that one would have to look through a sample slide 200 times over in a microscope in order to obtain the same confidence level as for PCR. Still, Kawash (2016) means that the technology is unlikely to replace the microscope on any larger scale in the near future due to the cost of PCR tests. In the US, both in high-end and lower end laboratories included in the study, that had low volumes of stool samples, a PCR device called BioFire FilmArray was used. The cost per sample using this instrument is $140 USD (Burday, 2016; Whittier, 2016). To put this in context, LabCorp, which is an independent laboratory, charges hospitals $11 USD for analysis using microscopy, and this cost includes shipping to the facility (Burday, 2016).

5.1.4 CellaVision's potential product

CellaVision's core competencies are within automation of microscopic pictures and image analysis. Therefore the areas of clinical microbiology that currently use the most microscopy were identified, and as previously stated it is parasite and blood infection diagnostics. According to the first phase interviews five areas within clinical microbiology uses microscopes extensively: blood infection, parasites, fungi, tuberculosis and malaria diagnosis. The process flow to diagnose these five types of samples are shown in appendix, see 9.1.1-9.1.5.

5.1.4.1 Blood infection product

CellaVision could digitalize the gram stained slides and automate the analysis that provide the initial bacterial identification, see Appendix 9.1.1. The process is currently performed manually by loading one slide at the time for examination in a light microscope. The analysis part focuses on morphology (the shape and size) of the bacteria as well as the color obtained from the staining process. The ocular analysis takes from 30 seconds up to a minute according to technicians, while laboratory managers often estimate the process to take about five minutes.

5.1.4.2. Parasite product

Parasite diagnosis is mainly done on feces samples. About 90-95% of the parasite samples at Sahlgrenska are feces (Kawash, 2016). The process flow for feces samples is shown in Appendix 9.1.2. CellaVision could compete against the traditional microscopes, as well as the emerging PCR technique, by replacing the microscopes with an automated alternative. The product would need to locate and and photograph suspicious objects and present them to a laboratory technician, just as CellaVision's current product does within hematology. If this product would be able to rule out some of the negative samples at an early stage it could save significant time and cost for the laboratories.

5.2. Empirical Setting Analysis

This subchapter analyses the findings through interviews and research.

5.2.1. A Disconnect Between User and Buyer

There is a clear disconnect between users of medical technology and the managers responsible for purchasing the technology. Our interviews with laboratory technicians, who are the actual technology users, have in general generated more pessimistic responses towards the potential of automating processes currently involving manual microscopy. The majority of the laboratory technicians also said they were better than the average at performing microscopy. Even though the technicians are not as keen to replace microscopy the ergonomics of microscopy is something that is often brought up by technicians as a problem. Sitting hunched over a microscope for hours can easily result in stiff necks and back problems. Technicians therefore value the idea of being able to review the slides on a computer screen instead, while maintaining the procedure of human analysis.

There is also a noticeable difference between managers and the technicians when it comes to estimating how long it takes to perform particular tasks. Managers believe that the technicians do their analysis more rigorously than they actually do. While laboratory managers on average state that the ocular analysis of a gram stain takes around 5 minutes, the technicians explain

that the analysis takes 30-60 seconds. Since the technicians are the ones actually performing the task, their statements could be assumed to be closer to the truth. That means that they can provide more detailed information about how current instruments are used.

On the other hand most laboratory technicians have very little understanding of the financial aspect of purchasing new instruments. Naturally, managers are more interested and knowledgeable when it comes to this aspect of new technology. In this context the knowledge situation is reversed and when asked about the cost of using certain instruments in their labs technicians can rarely give accurate answers. Two laboratory technicians say that MALDI-TOF testing is very cheap and only cost a few cents per run, completely disregarding the cost of acquiring the machine which is in the ballpark of $200k-$300k. According to many managers the technicians are rarely involved in purchasing decisions to any larger extent. “If they are new and want to see changes, they are quickly squashed by the other technicians”, one manager said. One laboratory technician said “Sometimes they ask us what we should purchase, but I do not think they value our opinion as much”.

The disconnect between user and buyer in laboratories is also apparent in CellaVision’s existing customers. Two of the hospitals visited in the US had CellaVision’s hematology products but did not use them, as the users had problems implementing the new system and felt more comfortable using traditional methods. The managers and technicians both liked the product in theory, but the technicians did not use it in practice. Satisfied customers and best-practice examples are great ways to sell new systems to other customers (Childs, 2016). A CellaVision manager said that educating the users in how to use the product is one of the most important things CellaVision does. If you want to continue to grow as a company, customer satisfaction is a must. In order to have satisfied customers, the users of the products also needs to be satisfied.

5.2.2. Passive Customers in Search for New Technology

Interviews with laboratory managers reveal that their main source of information about new instruments comes from sales representatives. The knowledge of the laboratory managers is based on what products companies have presented and pitched to them. This means that the awareness of products and technologies still under development, or awaiting FDA approval or equivalent, is limited among the customers.

A case of the above mentioned problem can be illustrated from our visit to the Biomedical Center (BMC) in Lund, Sweden, where one of the world’s most advanced clinical microbiology laboratories is located. During our attempt to understand their current unsolved challenges in their laboratory, the laboratory manager described urine analysis as a problematic area for which he was looking for a solution. Despite most of the samples being negative, they cultured every urine sample before they were able to conclude anything. In total 170,000 urine cultures were processed each year, which corresponds to 50% of all their cultures. Of these 170,000, only about 15-20% are positive. Culturing is a very time-consuming process, and with each sample requiring about 2 days of incubation, it is understandably a major cost to the laboratory.

A few weeks after our visit to BMC, when attending a European microbiology conference (ECCMID) in Amsterdam, we came across Beckman Coulter’s Iris IQ200 instrument. This device automatically processes urine samples and microscopically scans them for bacteria, blood cells,

and more. It successfully separates negative samples from positive ones. In other words, it does exactly what BMC in Lund had requested. Even more surprising is the fact that earlier versions of it has been on the market since 2003 and still it had not yet entered the radar of BMC. This illustrates how difficult it is for laboratories to keep up to date with all the technology that is out there, when not even one of the world's most advanced labs is aware of an existing solution to one of their main bottlenecks. As previously mentioned, scouting for new technology is not a high priority at most labs. Instead they tend to rely on the producers to contact them about new opportunities.

5.3. Technology Forecasting Analysis

Since there are so many different new technologies in the field of clinical microbiology, it is very difficult to know which technologies are here to stay. This section starts off by defining the different stakeholders that can be expected to influence the future development. Thereafter, tools that were identified in the literature study of this thesis will be applied to further complement the input provided by customers and users. Technology roadmapping have been combined with bibliometric analysis in order to give an analysis of the future of the field. The scope for the forecast has been defined as the upcoming 10 years, and the analysis has been limited to blood infection and parasite diagnosis.

5.3.1. Stakeholders

The development is likely to be influenced by many different stakeholders, such as society, government, researchers, and influential parties from both external and internal clinical microbiology laboratories. From a societal perspective, there is a desire to suppress the development of resistant bacteria and parasites. Increasing resistance is a big cost to the health care system. Governments want to spend as little money as possible on healthcare and yet increase the quality. The laboratory managers will want the laboratory to become more efficient and save resources by doing so. Still they do not want to decrease the quality of their diagnostics. Like most people, laboratory technicians want to keep their jobs and automation is a serious threat to that wish. Some of them have incentives to support the status quo of microscopy, since they are experts in the area. Other want to work in a more efficient and ergonomic way. Competitors of the microscopy want to increase their market share and profits. The doctors wants decreased turnaround time from the laboratories, as that will increase the quality of care at their hospitals. The hospital managers also want to decrease the costs and thus want the laboratory to deliver their services at a lower price. The patient wants to be treated as rapid and correctly as possible.

5.3.2. Macro Trends

Just as in any industry, the development of the clinical microbiology market is likely to be affected by what is happening on a macro level in society. Thus, in line with the methodology of technology roadmapping, some general macro trends that may have an effect on the future technological development have been identified and analyzed below.

5.3.2.1. Antimicrobial Resistance

Antimicrobial resistance is when a microorganism develops resistance towards a drug that originally was an effective treatment of the disease caused by it. Antimicrobial resistance is a

general term and refers the resistance which can develop in bacteria, fungi, parasites, and viruses (World Health Organization, 2015). Antibiotic resistance refers to the specific resistance only among bacteria. It is a natural phenomenon that occurs when microorganisms mutate during replication of themselves. The use and misuse of antibiotics for humans and animal husbandry accelerates this process, leading to death and disability of individuals that until recently would have been able to live a normal life. Moreover, this puts further economic stress on society since when standard drugs are no longer working, more expensive treatments need to be put in (World Health Organization, 2015).

5.3.2.2. Growing and Ageing Population

The current world population of 7.3 billion is expected to grow to 8.5 billion by 2030 (United Nations, 2015). The ratio of people older than 65 years old and younger people is expected to double by 2060. This means that the current number of working age people who support every retired person will drop from four to two during that period. Thus, cost from strictly age related expenditure is estimated increase by almost 2% of EU's GDP to 2060, which puts pressure on a more cost efficient health system (European Commission, 2015).

5.3.2.3. Shortage of Biomedical Scientists

Any time a patient visits a hospital and leaves a blood, sputum, urine, or any other type of sample, the test will be handled and analyzed by a biomedical scientist. It is estimated that the work of biomedical scientists produces 75% of the content that provides the basis for diagnosis and treatment in Sweden (Englesson and Ribeiro, 2014). In many places around the world there is already a lack of people with this particular training. Statistics Sweden's (SCB) prognosis estimates that there will be a shortage of 21% for biomedical scientists in Sweden by 2025 (Statistics Sweden, 2014). In the U.S., 19.48% of employees in clinical microbiology laboratories are anticipated to retire in the next 5 years (Scott, 2015). At the same time, the need for biomedical scientists is likely to increase due to the aforementioned ageing population. Unless technological advancements can manage to compensate for the decreasing workforce the healthcare system is going to face serious problems as a result (Scott, 2015).

5.3.2.4. Global Warming

The distribution of parasites will be directly affected by the impact of global warming. Moreover, transmission rates of parasites and pathogens are expected to increase with rising temperature (Marcogliese, 2008). This means that climate change is likely to lead to increased parasitic infections around the world (Iacurci, 2015).

5.3.2.5. Increased Travel and Migration

Increased migration also leads to an increasing incidence of parasites in western countries. At the Sahlgrenska Hospital in Sweden, the number of parasite tests have increased by approximately 33% from around 6,000 in 2015 to reach an expected level of 8,000 in 2016, largely due to heavy immigration during the period (Kawash, 2016). Historically the most direct impact of population mobility has been the spread of infectious disease (Saker et al., 2004). Human migration has through history been a source of epidemics (Wilson, 1995).

5.3.2.6. Increasing Wealth

Public health care spending in 27 EU countries plus Norway is estimated to increase from 6.7% of GDP in 2007 to 13% by 2060 (Appleby, 2013). This increased spending covers the increased costs from strictly age-related expenditure at 2% of GDP, but other trends may hold back the impact of healthcare quality.

5.3.2.6. Accelerating change

There are several theories that technological development is not linear but exponential. One of the most famous theories is Moore's Law, which states that the number of transistors on an integrated circuit will be doubled every 18th month (Schaller, 1997). Another theory by Kurzweil (2004) is the law of accelerating returns, says that not only the development of circuits are developing exponentially but technological development in itself is. Kurzweil (2004) says that the 21st century will correspond to 20,000 years of progress rather than 100.

5.3.3. Micro Trends

5.3.3.1. Laboratory Consolidations

Over the past decades, clinical microbiology laboratories have undergone an extensive consolidation process (Rydberg, 2016). According to Van Eldere (2005), the development was grounded in evolving views of health care delivery as an economic activity, as well as changes in medical environment, workforce demographics, and technological development. Through consolidation, cost-efficiency and economies of scale have been achieved for many laboratory procedures (Van Eldere, 2005). This development is likely to continue for some time in order for the healthcare system to cope with increasing sample volumes and financial pressure.

5.3.3.2. Increasing Digitalization

As consolidation of clinical laboratories increases, new challenges arise. At the time when laboratories were located in connection to the hospitals, doctors could easily walk over to the labs to provide or get consultation. This is no longer possible at many hospitals, where their labs have now been concentrated to remote hubs. Digitalization thus becomes an important tool in bridging this gap. With digital gram stain slides or cultures plates for example, laboratort technicians can quickly share their findings with experts in distant locations. Moreover, the digitalization provides a useful aid in the training process of new technicians. Sample slides of rare microorganisms fade in quality as time goes by, so saving these in a digital format can make it easier to train scientists in recognizing these. Currently it takes 2-3 months for new laboratory technicians to become independent in their work, partly because of this reason (Engler, 2016).

5.3.3.3. Laboratory Automation

With laboratory consolidations leading to larger levels of patient samples per laboratory, the need for automation is also increasing. Moreover, labor is a big cost at laboratories so any automated solutions that could take the place of an employee is hugely attractive from a financial perspective. It is estimated that labor, in a typical laboratory, accounts for approximately 65% of operating expenses (MarketsandMarkets, 2015). Another benefit of automation is the potential of quality improvements. Many labs are adopting so called total laboratory automation (TLA) systems, such as BD's Kiestra and Copan's WASP (MarketsandMarkets, 2016). These

types of systems automatically seed culture plates, prepare gram stains, and incolute broths (Franco, 2015). Dr. Engler (2016) estimates that the introduction of WASP in a LabCorp laboratory compensated for the labor of 2-4 fulltime employees. He also believes this development will continue and is actively searching for an automated solution for stool sample analysis.

5.3.3.4. Laboratory Standardization

As a consequence of laboratory automation, standardization becomes necessary in order to optimize the process flow. Not long ago, microbiology laboratories, in contrast to hematology and chemistry, used to handle sample containers of a vast number of varying shapes and sizes (Franco, 2015). There are many benefits from this; cost reductions due to a smaller amount of necessary devices, time-savings for medical staff who do not need to worry about picking the correct containers, time-savings for laboratory staff who will have fewer samples to process, as well as quality improvements for patients (Fontana et al., 2013). The overall transition to a standardized laboratory format in clinical microbiology is not yet completed. There are still many different technologies competing to become standard practice and until that battle is over, full standardization is not possible.

5.3.4. Bibliometric Analysis

In the first step of our technology forecast, the recent technological developments were analyzed in a bibliometric analysis. The purpose was to try and understand the current level of maturity of the technologies to be used for further analysis of new upcoming companies. To perform a bibliometric analysis of competing technologies, the number of articles published on MALDI-TOF and PCR between 1994 and 2015 by searching on each year on Google Scholar were gathered. Since PCR is used in many applications we reduced the number of hits by doing two separate searches, one containing “Clinical Microbiology” and one containing “Parasite”. Below, in Figure x, are the results from this research.

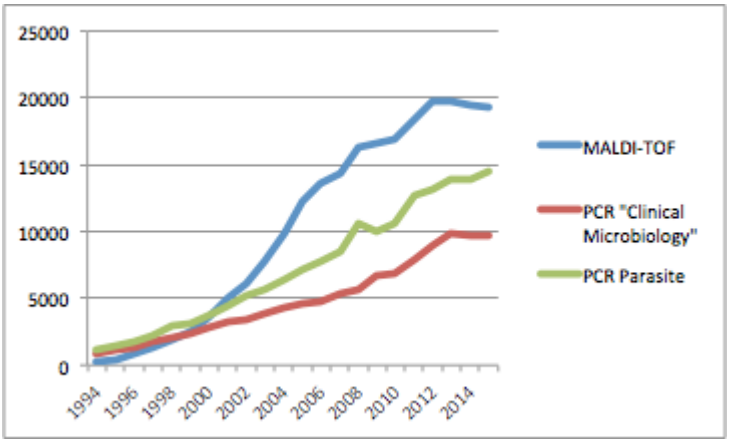


Figure x. Number of published articles per search word 1994-2015.

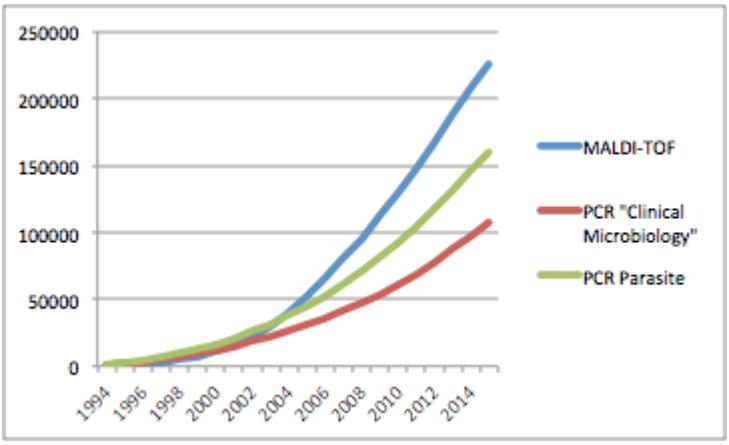
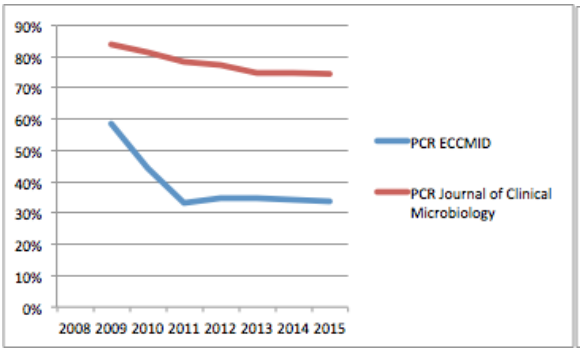


Figure x. Accumulated number of published articles per search word 1994-2015.

The graphs show a slowdown of the number of published papers in the last few years, which could be an indication that the technologies have reached their peak. Even though the development may not be as rapid as in the past decade, the technologies are still under development. When you look at the accumulated number of articles it seems to be in the middle of its S-curve for all three search words. This could potentially imply that there is room for a technology shift in the coming years. The following subchapter, 5.3.5. Future Scenarios, will dig deeper into players and technologies with the possibility of taking the lead in this development.

According to Porter (1991) the ratio of articles published at conferences compared to the number of articles published in journals could be a measurement of how well developed the technologies in question are. Articles published in the leading industry journal, Journal of Clinical Microbiology (JoCM), were compared to articles published at ECCMID conferences over the years. Two keywords were chosen for the comparison, PCR and Mass Spectrometry (MS). The data was collected using the search function at each website respectively. The data at ECCMID could not be traced back longer than to 2008, and the number of articles on PCR on the JoCM website were not available for the year 2008. Therefore the data span over 2008-2015 for MS and 2009-2015 for PCR. The graphs, see figure X, represent the number of articles published on PCR/MS on each respective source divided by the total number of published articles on the same source.

As the charts show, the percentage of articles published on ECCMID compared to the percentage published on JoCM is lower than in the beginning of the sample for both technologies. The percentage of articles on MS published at ECCMID have stagnated since 2011, while in JoCM it continues to be a growing subject. PCR's graph does not follow the same pattern but there was a higher percentage of articles on PCR in the beginning of the data sample than there is now.



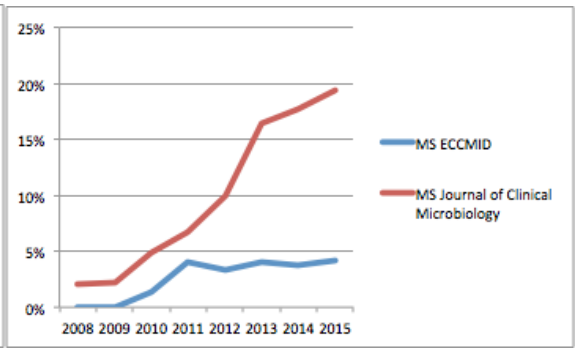


Figure X, Ratio of published articles on PCR/MS on ECCMID and JoCM respectively.

5.3.5. Future Scenarios

Attending the European Congress of Clinical Microbiology and Infectious Diseases (ECCMID), some new interesting technologies were identified. Some of them might have the potential to disrupt the clinical microbiology market, in particularly the blood infection diagnosis market. At this stage it is very difficult to tell which technologies will be here to stay and which will lose the battle of conquering the market. Some of the more promising technologies will be presented in this section. The scenarios are all dependent on each other, and not all are likely to occur simultaneously.

5.3.5.1. MALDI-TOF continues to improve

According to Murray (2012) the most common reason for MALDI-TOF to fail in bacterial identification is that the particular species is not part of the instrument's database. It is very likely that we have not seen the full potential of MALDI-TOF yet. The technology is still under development and the database of microorganisms will also continue to improve. MALDI-TOF has already disrupted a big part of the western market, and if it continues to improve and gets cheaper to produce it is very likely to be sold all over the world. The identification part of the clinical microbiology market will likely be dominated by MALDI-TOF over the next few years.

5.3.5.2. PCR techniques cost reduction

For now, PCR techniques are too expensive to be used extensively in clinical microbiology. It is however likely to replace much of today's microscopy in parasite identification according both laboratory managers as well as Folkhälsomyndigheten, the Swedish Health Authority (Folkhälsomyndigheten 2016c). The technique also has potential to be used in blood infection identification, but the competition for PCR is tougher in this area.

5.3.5.3. Specific Technologies is introduced

Specific technologies is a company, aiming to identify bacteria already in the incubator. All the laboratories visited for this thesis uses a product called Bactec, which separates negative samples from positive by measuring the oxygen and carbon dioxide in the tube. Specific technologies have developed an incubation tube that in combination with their own incubator can identify bacterial species during the growth, using receptors that monitor much more than just carbon dioxide and oxygen levels. In contrast to many other new technologies in the field, this one has the potential of processing a large number of samples at low cost. The incubator will, according to themselves, not be more expensive than a Bactec device and the tubes will be just slightly more than the ones that are used today. If their technology proves to work as they claim, there will not be a need for any of the additional identification steps, including gram staining, initial microscopy and MALDI-TOF. If the technology gets approved for sale, it might totally disrupt the blood infection diagnosis market. They even believe they possibly might be able to evaluate susceptibility of the bacteria directly in the bottle in future. Their product is not yet introduced on the market, but they are doing tests with promising results. Specific Technologies have a former FDA manager in their advisory board, which indicates that they have help with one major difficulty when launching a new medical technology product.

5.3.5.4. Q-Linea is introduced

Q-Linea is using a new type of technique, which they are not willing to go into detail about, but it is not based on PCR nor mass spectrometry. Their product will be able to do both identification and susceptibility testing from blood, without culturing, within hours. Since they claim their product will be able to do both identification and susceptibility testing, there should not be a need for any additional testing, e.g. MALDI-TOF, gram staining or microscopy. However their product will not be on the market until 2019, therefore there is a lot of uncertainty regarding Q-Linea's product. They have not yet revealed any specifics behind the turnaround time (TAT), however they claim to revolutionize the blood infection diagnosis market by reducing the TAT drastically.

5.3.5.5. Accelerate Diagnostics cost decrease

Accelerate diagnostics have developed a product that combines PCR with image analysis to make a product that does both susceptibility and identification. What is unique compared to what is on the market today is that they do both identification and susceptibility directly from blood, without any culturing needed. Their product reduces the TAT from over 48 hours to somewhere between 6 and 8 hours. If their technology is diffused there will not be a need for any initial microscopy nor MALDI-TOF or any additional susceptibility testing. The product is already CE approved and in the process of FDA approval. Two downsides with the product are that it can only test one sample at the time, and the costs of such a test is $100-$200. Moreover, the instrument requires an additional $10k-$100k upfront investment (list price is not yet decided). Representatives from the company itself means that the cost is easy to justify for a laboratory since using the instrument can reduce costs for antibiotics and reduce the length of stay for patients. If they are able to decrease the associated costs, or the market is willing to pay more due to any of the macro trends, they have a great potential to disrupt the market.

5.3.5.6. T2 Biosystems cost decrease and technology improvement

T2 Biosystems uses magnetism to identify the most six most deadly and crucial yeasts that can be found in blood. Their product identifies these yeasts directly from blood within 3 to 5 hours. The product is FDA approved and is already for sale in the US. In the current state the product will not disrupt the flow in clinical microbiology laboratories as it can only identify a handful of the targets necessary. Also for this product, the price is an obstacle, as the product costs $250 per sample run. Company representatives were not willing to disclose the price of the instrument. However if the technology improves to a level where not only fungi, but also bacterial species can be identified, it could become a contender to potentially disrupt the market. The company is currently in the process of getting FDA approval for identifying some bacteria.

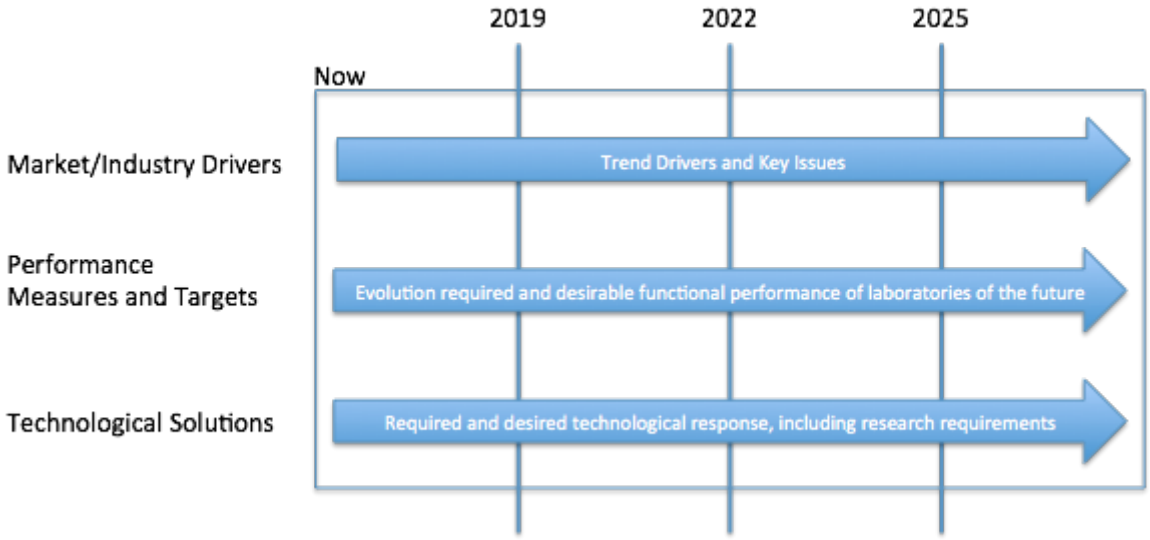
5.3.5.7. New improved vaccines

Research is constantly being made on finding new vaccines for the major global diseases. Malaria and tuberculosis are two of the major diseases that kills the most world wide. In 2015, World Health Organization approved a new testrun of a new Malaria vaccine that had a positive first trial (World Health Organisation 2016a). If vaccines for Malaria become reality, they will be used globally mostly in developing countries but also in the rest of the world. This will reduce the need for laboratory tests for the disease. For tuberculosis there is a vaccine that protects infants and children against the disease, but none that protects adults which accounts for the major part of the cases worldwide. World Health Organization's targets for the disease is to reduce the number of tuberculosis related deaths by 95% and the number of cases by 90% by the year

2035. In 2015, there were 16 tuberculosis vaccines in clinical trials, with a handful of them reaching a phase of proof-of-concept studies. If any of these were to be successful, the number of tuberculosis samples diagnosed in laboratories would decrease significantly (World Health Organisation 2016a).

5.3.6. Analysis from a Technology Roadmap perspective

This thesis used Phaal et al.'s (2004) framework as a vantage point for the process of creating a technology roadmap for foreseeing the future development of clinical microbiology. Consequently, industry trends and drivers were identified through interviews with laboratory managers, doctors, technicians, and employees at medical technology firms. Furthermore, the research was complemented with desktop research to support and evaluate the findings. The overall trends were then used to identify future key issues with the necessary development from a laboratory perspective. Finally, an evaluation of technical solutions were matched to the imminent laboratory development.



Taking all identified macro trends into account, the overall impact on clinical microbiology point towards an increase workload in the western society. As the population grows, and gets older, the number of patients is expected to rise. Global warming may lead to the introduction of new microbial diseases, that through globalization diseases can spread much more widely and rapidly by travel and immigration. There is also the overhanging threat that traditional antibiotics may become impotent, which demand new, and at least to begin with, more expensive solutions put to practice. Some hope can be put to new vaccines to inhibit particular diseases but on a broader scale, more has to be done in the actual laboratories.

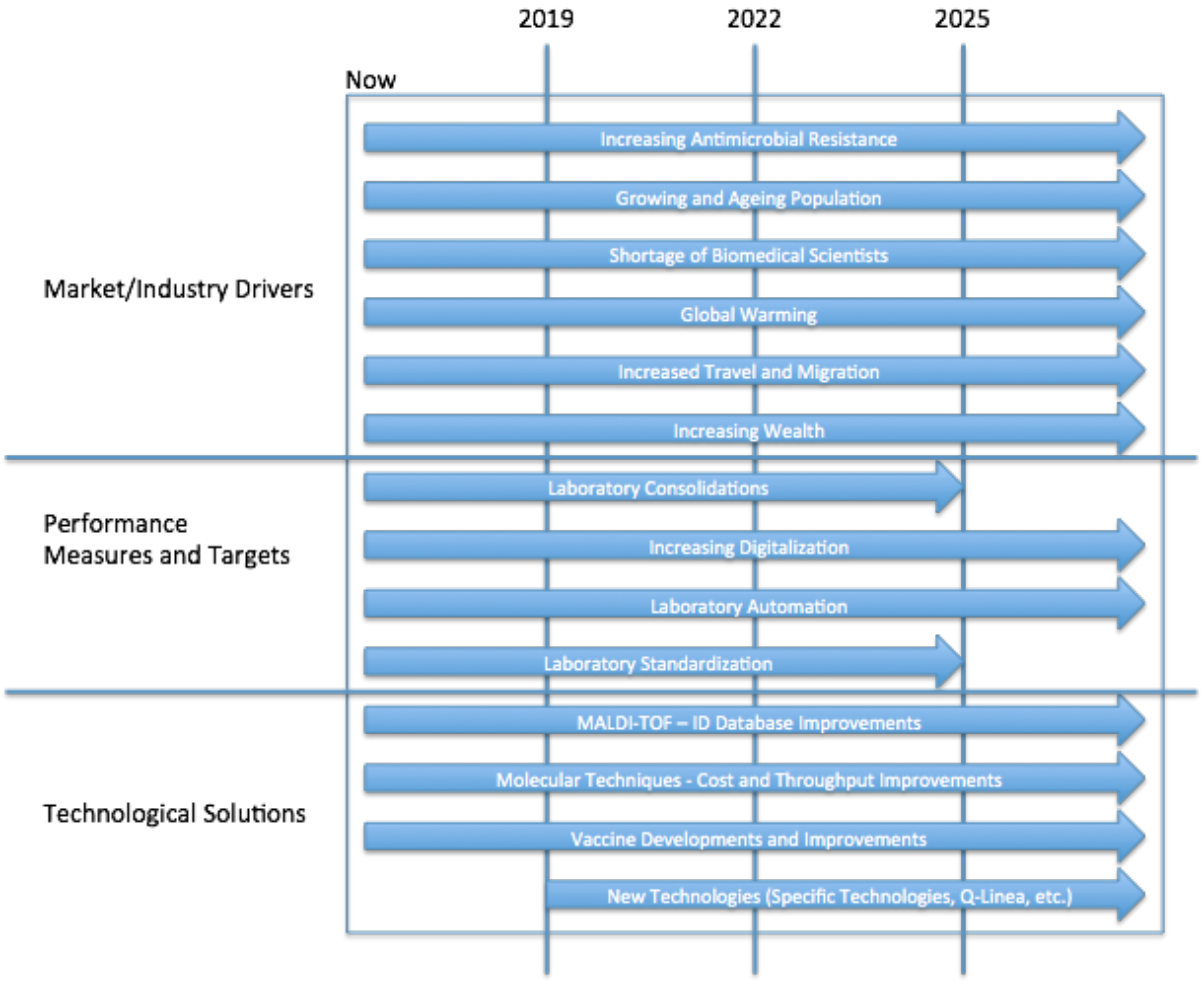


Figure: Technology Roadmap of Clinical Microbiology Laboratories.

The rising pressure on throughput of the clinical microbiology laboratories cannot be expected to be solved by increasing the workforce. There is already a shortage of biomedical scientists and that situation is prognosed to remain for decades. Hence, faith is put in technological development, much in the form of automation, standardization, and digitalization of increasingly consolidated laboratories. MALDI-TOF and molecular techniques have improved the efficiency and throughput of laboratories in the recent decade. They will most likely continue to do so for some time, but the bibliometric analysis also indicates that they may have reached their peak of development.

There are many new competing technologies on the verge of introduction. Many of them currently have limitations of different sorts, such as high cost per sample or low throughput capacity. Kurzveil (2004), claims that technological development is exponential, if that holds true for this area it is likely that some of these new technologies will improve greatly in the coming years and overcome such barriers. When they or any other technology do so they have a great possibility of disrupting the diagnosis process in clinical microbiology laboratories. Even if the cost reductions are not exponential but linear, it is still a question of when not if new technology will replace microscopy.

Most stakeholders benefits from introducing superior technology that will decrease the TAT, improve quality of results and reduce cost. Society, companies, governments, doctors and

laboratory managers all benefits from these improvements. Competitors as well as laboratory technicians might oppose the technology, but they are not crucial in the adoption of the technology since the findings from interviewing managers and technicians show that the technicians are not involved in purchase decisions to any larger extent.

6. Discussion

There are many benefits to be gained from involving the customer in the development of new products. Getting a better understanding of customer needs is a great way to increase the possibility of launching a successful product (Blank and Dorf, 2012; Shah and Robinson, 2007). We argue, however, that the knowledge gained from customer and user interactions also needs to be complemented with an understanding of the environment and competition where you would operate. The market conditions may change during the time a product is developed and that needs to be taken into consideration, especially in industries under transformation or with long product development cycles.

One such industry is medical technology, and particularly unstable at the moment is the clinical microbiology laboratory, which is currently undergoing a period of technological change. Further complicating the use of Customer Development in this context is the disconnect between managers and technicians found in this thesis when visiting laboratories in Sweden and the United States. Most managers do not have a good understanding of the bottlenecks in the technician's work flow. Most technicians have little understanding of the financials behind buying a new product, such as return of investment and depreciation of a product. Including both groups in a development process is a necessity in order to get a product that will be both used and reasonably priced.

Adding to the difficulty for smaller medical technology companies in applying Customer Development is that they often sell their products through large distributors. With the distributor market being dominated by a few large players it is hard to get direct feedback from the end-customers. The distributors are often very protective of their customer base out of fear of the medical technology companies cutting them out as middlemen and switching to direct sales.

In order to involve technicians an extra incentive might be needed. One manager said that technicians have no incentives to do anything outside their ordinary tasks, they get no benefits from putting their best foot forward. There is also a potential conflict of interests in this case, where the technicians may feel threatened that the new technology can render their services obsolete. Manual microscopy is what they have been trained to do. Many technicians take pride in their skills and see their work as a form of art. Since their jobs might be in danger, their willingness to aid in the development of new products could therefore be questioned. Including users is necessary in order to avoid that customers buy instruments that the users end up not using. In the short term, such sales do not hurt the company, but in the long run it is not a sustainable business model for a medical technology firm.

Many technicians and managers at laboratories were positive in theory to a potential product automating microscopy in their department, both for parasite and blood infection diagnosis. There is a need due to the constantly growing pressure on laboratories and lack of trained biomedical scientists, and at the same time the technology could improve the ergonomic situation by reducing back problems. However, the technological forecast performed on the evaluated market suggests that technological change is imminent. If one of the multiple

potentially disruptive technologies identified in this thesis manages to overcome their respective barriers of cost and throughput, the future need for microscopy may completely disappear.

Since laboratory managers mostly get their information from salesmen pitching their products, they have limited knowledge about the future of their field. Some managers said that they, or one of their colleagues, visit technology conferences but there is no consistency, and very little time invested in researching. Consequently, when customers rely heavily on the producers to inform them about new opportunities, they sometimes miss out on products that are actually already on the market, such as in the case of BMC's urine analysis. It is impossible for companies to visit every laboratory in the world, and if they do not, their potential customers may not know they exist. This highlights the problem of applying Customer Development to this field and strengthens our belief that other methods need to be put to practice in order to foresee the threat of new disruptive technologies.

The bibliometric analysis findings also show that the the technologies could be discovered earlier than when asking the customers. At ECCMID there were articles published in 2010 and 2011 on mass spectrometry, therefore we argue that attending conferences is a good complement to the customer interaction in advocated for by the Customer Development methodology. If the customer does not know what is happening on the market, other measures need to be taken to find out. The bibliometric data also suggests that MALDI-TOF and PCR might reach its peak in the upcoming years, and leave space for a new technology. It should be noted that the bibliometric data includes other technologies comparing themselves to the respective technologies, which may skew the data but it is still an indicator of technology popularity.

Bibliometric analysis provided great additional information to the technology roadmapping. However applying it to very new technologies, such as the technology behind Accelerate Diagnostics and the other companies presented in this project to provide no new insights, the data amount were too low. Roadmapping was found to be a great tool to understand the factors behind the change in the industry. Although it is not possible to predict the future with certainty it provided this thesis with a way to understand the drivers behind the change better.

7. Conclusion

This thesis has highlighted a number of difficulties for smaller medical technology companies in applying Customer Development for new product development. In general we think that the methodology provides great value, as long as you are aware of the weaknesses of the methodology. The initially identified main weakness was the lack of attention paid to the developing technological environment. In some industries, such as commodities for example, this may not be a huge problem. In medical technology, where product development cycles are often long and where technological progress in some areas is rapid, it is however of utmost importance since the customers often have little knowledge of the ongoing technological development. Combining the Customer Development methodology with technology forecasting methodologies can raise awareness of potentially disruptive technologies of the rise. Since forecasting is not an exact science it is impossible to assess the accuracy of the method at this time, but what is clear is that in applying it the developer will gain a more extensive view of the future competitive situation. This can help in the assessment of project risk, which is what the Customer Development methodology is all about.

Along the course of this thesis, other weaknesses than lack of forecasting have also been found. One of those is the conflict of interest that can occur when developing products that to some extent are looking to replace the need of the users. In such situations it can be difficult for the developer to assess the intentions of the users during interviews. This cannot be compensated for by strictly focusing on interaction with customers/purchasers, since a clear knowledge difference was found between laboratory technicians and laboratory managers. Therefore multiple key targets in different positions need to be interviewed in order to maximize the customer feedback. Since the laboratory managers are the decision makers, their financial needs can in some sense be considered more important to understand for the developer than the user needs in the clinical microbiology laboratory.

CellaVision

Christensen suggests creating an ambidextrous organization to develop new technology in isolation. Many new technologies are not related to CellaVision's core competencies. The technologies are very advanced in the field so acquiring knowledge is expensive. Hedging the bets by investigating several new technologies is thus impossible for a small company like CellaVision. The conclusion from the technology roadmapping assessment is that is a highly competitive market, with little advantages to gain from CellaVisions current capabilities to break into the market. The market landscape is also likely to undergo a large change over the upcoming years and the uncertainties are very high. Therefore the likelihood of being disrupted is evaluated to be very high.

CellaVision needs to consider the difference between customers and users in their development. Focusing on the managers is necessary as they are making the purchasing decision but they also need to develop the product together with users so that it is used when it is implemented. Managers are overestimating the time that the technicians spend on performing their tasks, which in the short term is good for CellaVision to sell the machine. But the technicians do not

use the machine after the purchase, it is not sustainable in the long run. Hence CellaVision need to avoid the scenario where their products are sold but not used. These issues could also be addressed by educating the technicians in how to use the product, but then the benefits for the users must exist and be apparent.

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9. Appendix

9.1 Search word overview

Search word(s)	Number of articles reviewed	Phase
Customer Development	50	1
Disruptive Technology	30	1
Lead User	30	1
Technology Scanning	30	1
Business Opportunity	30	1
Business Potential	30	1
Industries with long development times	30	1
Industries with long development cycles	30	1
Medical technology development	30	1
Technology Scanning	30	1
Technology Roadmapping	30	1
Technology Forecasting	30	1
Scenario Planning	30	1
Bibliometric Analysis	30	1
Clinical Microbiology Automation	30	2
Maldi-tof	30	2
PCR Microbiology	30	2

Table 9.1. Search words used in the literature review

9.2 Questionnaires

9.2.1. Swedish laboratory employee questionnaire

- What are the main bottlenecks in your part of the laboratory?

- What are the main bottlenecks in the clinical microbiology laboratory in general?
- How would you like to improve the laboratory?
- What factors are the most important when you are deciding to purchase a new instrument?
- Where do you use microscopy today?
- How much time do you spend using the microscope on an average day?
- What do you think of a product like CellaVision's in clinical microbiology?

9.2.2. European laboratory employee questionnaire

- What do you do at the laboratory? (Technician, manager, etc.)
- Is the flow similar to the flow we have identified in Sweden? We showed them the flow of samples in Swedish laboratories, see Appendix 9.3.1.-9.3.5.
- What are the differences? How come you have that technology? What are the benefits?
- What factors are the most important when you are deciding to purchase a new instrument?
- What are your main bottlenecks?
- What do you think of a product like CellaVision's in your laboratory? Why do think so?

9.2.3. Company employee questionnaire

- What type of technology do your products use? (PCR, Mass spectrometry, New/other, etc.)
- What benefits does your product provide?
- In your area of clinical microbiology, which trends do you see? Why do think that is? Do you see any competition from upcoming technologies/companies?
- Do you think there is a place for CellaVision's product or capabilities on the clinical microbiology market? Why do you think that is?

9.3 Process flow of samples in clinical microbiology

9.3.1. Blood infection diagnosis process flow

9.3.1.1. Blood bacteria identification

Most common bacteria samples are urine and blood. Blood infections is the most crucial to act upon. Blood could contain any type of microorganism but bacteria is the most common (Rydberg, 2016). The doctor will order the tests that he/she believes is needed to diagnose the patient. For blood infection samples blood is mixed with nutrient broth and put in an incubator to be cultured. If no growth can be observed after 6 days, the samples are flagged as negative, i.e. there is no infection. Modern incubators have sensors that continuously monitor the blood culture bottles and flag samples that show bacteria or fungal growth (Elmér, 2016). Since bacteria consume oxygen and produce carbon dioxide, the incubators can detect bacteria presence by monitoring the oxygen and carbon dioxide level within the sample (Becton-Dickinson, 2001). Positive samples are stained with a method called gram staining, in all laboratories visited for this thesis the process was carried out by an automated machine but traditionally was done by hand. The staining takes about 15 minutes and normally bacteria can be located in the microscope within a minute if a sample has been flagged (Elmér, 2016; Rydberg, 2016; Burday, 2016; Whittier, 2016; Glaser, 2016; Stenström, 2016). By observing what the bacteria look like in the microscope after the gram stain, it is possible to conclude some initial information about the bacterial species.

Urine samples are plated on an agar plate, instead of the incubator used for blood, either by hand or by an automated system. If there is visible growth on the plate the identification process begins, which is the same as for blood bacteria. Many of the cultures are negative. In Sweden, about 70% of the cultured urine agar plates were negative (Rydberg, 2016). In other parts of Europe, as well as the US, a machine called iQ200 by Beckman Coulter was used to sort out some of the negatives before culturing. Since the samples are cultured, which makes the bacteria multiply in numbers, it is not possible to draw any conclusions from quantity of bacteria found in the samples (Rydberg, 2016). Instead, analysts look at the bacteria morphology, how the bacteria cluster, and the color of them. The initial microscope classification of the bacteria is useful for the doctor so that they can put in some initial antibiotic treatment before getting more detailed information about the disease (Rydberg, 2016).

To get an exact identification of the bacteria the procedures and workflow differ somewhat between labs. In Lund, which has one of the world's most advanced laboratories, they started using the relatively new method of MALDI-TOF Mass Spectrometry in 2012, and it is nowadays used extensively around the world (Rydberg, 2016). More about this technology can be read about in section *5.1.3.2 MALDI-TOF*. Before MALDI-TOF MS was approved for use in bacterial identification, the laboratories mainly performed analysis of biochemical reactions, phenotypic characteristics, colony morphology and gram staining (Croxatto et al., 2012). Figure XX below illustrates the process. When all of these techniques are combined they provide an accurate identification but it takes between 24-48 hours to get results, and since it requires well trained laboratory technicians for correct interpretation it is an expensive process (Croxatto et al., 2012). There are also other automated products that are used on the market, particularly in the US, where MALDI-TOF has not become mainstream quite yet. In advanced laboratories in the US they mainly use either a machine called BioFire FilmArray or Cepheid GeneExpert, which are based on PCR technology. PCR is further explained in *5.1.3.3. Molecular Techniques*.

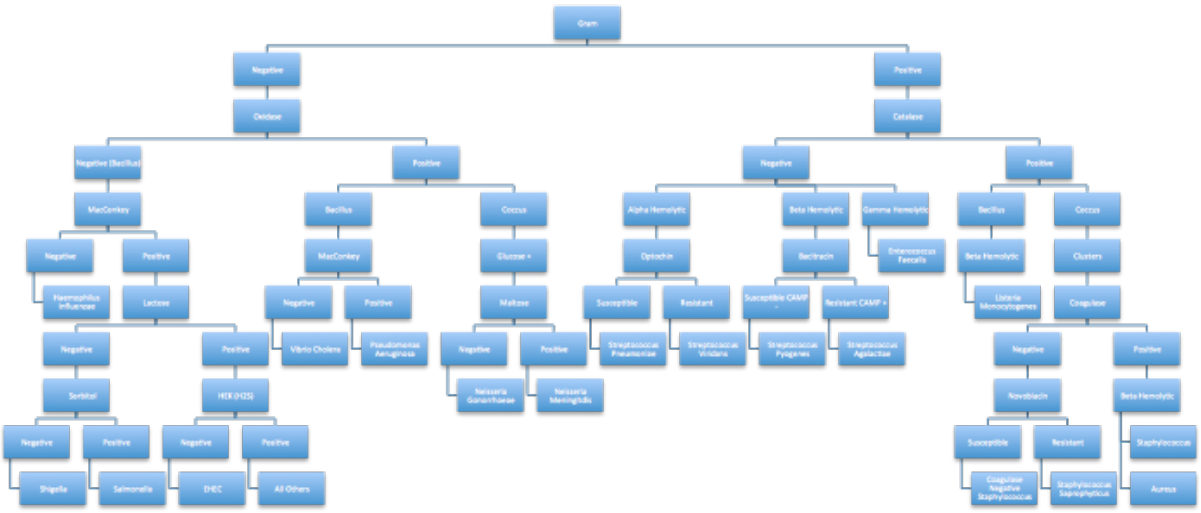
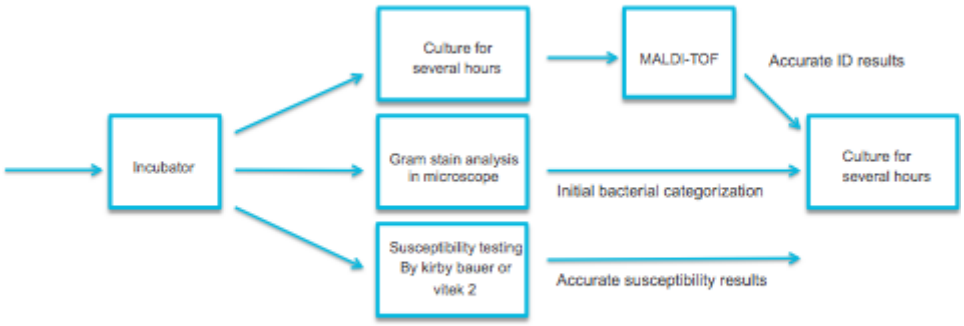
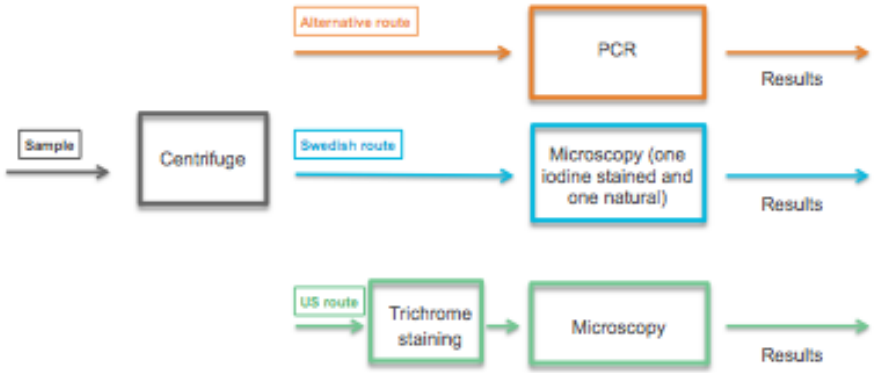


Figure XX: Bacterial Identification Chart (Wayne State University - School of Medicine, 2016).



9.3.2 Feces process flow

In the laboratories included in this thesis project, feces samples account for 90-95% of all parasite samples. When diagnosing parasites from feces samples, there are mainly two techniques, microscopy and PCR. When microscopy is used, the sample is centrifuged and concentrated to non-liquids in the bottom of the flask. In Sweden, two drops of the bottom sediment is then placed at two different locations on a glass slide for examination. One drops is mixed with iodine, and then a cover glass is placed on top of each drop for examination in a microscope (Stenström, 2016). In the US, to slides are prepared instead, both stained with trichrome (Engler, 2016). The microscopy examination takes between 5 and 15 minutes. Using PCR instead of microscopy still requires preparation in terms of centrifugation. The bottom sediment is then placed in an automated PCR machine, which generates results within one hour.



9.3.3 Malaria process flow

The standard way of diagnosing Malaria is to perform microscopy in two steps, called thick and thin film. One of the US laboratories included in the thesis instead used an automated test called BinaxNOW for its malaria testing. However, the use of it still requires a technician to perform the thick film analysis in order to rule out negative samples.

In the first step, the thick film, a few drops of blood are put on a slide and left to dry. Malaria attacks the red blood cells from the inside, and thus the blood cells need to be bursted in order for the parasite to become visible. The slide is therefore stained with a technique called Giemsa, which causes the red blood cells explode. The slide is then washed carefully and left to dry again. After that the slide is examined in a microscope to try and locate any parasites. This process is time consuming. In order to rule out a sample as negative, 200 microscopic fields need to be viewed. Only If the thick film is positive, the thin film microscopy process is performed.

The thin film preparation is similar to the thick film. Instead of a few drops, one drop is smeared on a slide, and that drop is fixated with methanol. After that the slide is stained, washed and dried. The slide is then microscoped to identify the type of Malaria and in which stage of development the parasite is in. There are five different types of malaria species, and they are generally classified according to six different stages of development (Stenström, 2016; World Health Organisation, 2016a)