Aki Harkivi

International manufacturing transfer of a biomaterial implant product
Master's Thesis

Helsinki Metropolia University of Applied Sciences

Master of Engineering

BI12S Business Informatics

Master's Thesis

Helsinki Metropolia University of Applied Sciences

Author(s) Title Number of Pages Date	Aki Harkivi International manufacturing transfer of a biomaterial implant product 64 pages 4 May 2014
Degree	Master of Engineering
Degree Programme	BI12S Business informatics
Specialisation option	
Instructor(s)	Thomas Rohweder, Thesis supervisor

In 2012 a US based global medical device company, made the decision to transfer the manufacturing of biodegradable implants from its subsidiary in Finland to two facilities in the United States of America. This decision raised some business challenges. How to transfer manufacturing of biomaterial implant products with minimal impact to stakeholders, and how to ensure continuous high quality, safety and production yield of biomaterial implant products when manufacturing is done in the United States. The research goal is to create a best practices process for the transfer, uncover risks and working solutions for the manufacturing steps of a biomaterial implant product. The thesis focuses on transfer of one Biodegradable implant product.

Keywords	Master's thesis; Harkivi; manufacturing transfer; knowledge transfer; biodegradable implants; medical device

Contents

1 Introduction

US based company has decided to consolidate production from its Finland operations to its two sites U.S. by 2014. This is consistent with company's strategy to improve Manufacturing & Operational Efficiencies (US Vice President of Operations 2012).
Products manufactured in company's Finland subsidiary, after this also referred as Finland Operations (OPF), are unique and they have only been manufactured in Finland. OPF is a pioneer in the biomaterials field having over two decades of experience manufacturing biodegradable products and is inventor of proprietary technologies. Employees are skilled, flexible and able to deal with the various situations and issues. Successful research on new biocomposite materials have been carried out for years and co-operation with the material suppliers is tight. Proven expertise in the processing techniques used for composites and use of modern materials. Company has consistently introduced new products, product lines and materials to the market. Quality management system is of a high standard also from the authorities' point of view with practically no auditing deviations. Reliability of customer deliveries and high customer satisfaction based on low number of complaints shows affective and flexible production processes, which also allows small production batches. (Strengths of Finland Operations 2012)
A lot of the points mentioned above are not at the same level in the receiving manufacturing facilities in the US. There is a danger that a lot of the knowledge and efficiencies will be lost unless the transfer of the manufacturing is done properly. In worst case scenario customer deliveries could be impacted and quality issues could even lead to factory shutdowns or costly product recalls (FDA 2014).

In this case the recipient organizations have little or no experience in working with biodegradable materials used in OPF, so transferring that knowledge is important. OPF personnel has a lot of tacit or hidden knowledge developed during the decades of manufacturing biomaterial implants. Finding ways to transfer this knowledge is one of the focus points of the research. Imagine changing a tire in a car. The work instruction guides to remove four nuts and then to remove the tire. When trying to remove the third nut, it is rusted and stuck. Applying too much force can break the retaining bolt and then the car cannot be used until retaining bolt is fixed. Work instruction does not provide answers to all of these of issues. The experienced tire changer would just apply

chemical "rust off" or equivalent, then wait for a few moments and remove the third bolt continuing the process. Polanyi (1966) noted, ''we can know more than we can tell''. The discrimination between tacit and explicit knowledge.

1.1 Case Company Background

US Based company is a major medical products manufacturer specializing in surgical instruments and other medical devices. Company manufactures medical device products in nine different areas Arthroscopy being one of the areas. Company growth strategy has been based on acquisitions especially in 1990s. Little consolidation has been done until recently and company still owns many independent subsidiaries. Company has started implementing extensive consolidation strategy (Company website 2013).

Finland subsidiary (OPF) is independent subsidiary of US Based Company and works in close co-operation with other US subsidiary to provide arthroscopic instrumentation, implants, fixation and tissue repair systems for orthopedic purposes. US subsidiary is responsible for marketing, sales and distribution of these products. US subsidiary has extensive strategic control over the Finland subsidiary as the managing director of OPF reports to US subsidiary Vice president of Operations. OPF exports and sells all the products to US subsidiary using transfer pricing. (Finland subsidiary e-portfolio presentation 2012).

Approximately 60% of the Company's revenues are derived from products designed for the orthopedic surgery markets of arthroscopy and powered surgical instruments. Capital equipment such as powered drills and surgical hand-pieces are marketed to support the sale of disposable products. US based company distributes its products globally through its own U.S. sales network, international direct marketing in nine countries, and specialty distributors in other countries. (Company Website 2013)
Legislation in all the areas for medical device products is strict but stable and major sudden changes are very rare. Recalls do happen sometime and, depending on the issue, can be costly. (FDA 2013, medicaldevicerecall.com/ 2013)

US based company customers are Surgeons, Nursing Directors, GPO's (Group Purchasing Organization), IDN's (Integrated Delivery Network) and Governmental Institutions. Surgeons are the ones that have great influence on decision what products they

use. End users (Patients) are not usually aware what options they have, so many times it's up to the surgeon or doctor to choose the products used. Medical insurance covers most of the incidents, so end users tend to want the best available solution that is recommended by their doctor. Quality products, good relations and proven track record with the customer is paramount for success. Customer input is also very important in developing future products that suite the customer needs. (WHO, US based company investor presentation 2012).

1.1.1 Current state supply chain management

One of the US based company's key performance indicators (KPI) and competitive strategies are the next day delivery of disposable products (implants etc.) and 10 day delivery of capital products (power drills etc.) Customers are served first in first served bases (Vice President of Operations 2013). Demand inputs come mostly from marketing department and historical sales data. Due to next day delivery strategy US based company has to keep enough products in stock to fulfil this promise and that tends to drive inventory costs up. US based company supply chain management (SCM) is traditional and vertically integrated, meaning that they produce many of the components in-house instead of outsourcing. Raw materials and other supplies are sourced close to the main manufacturing facilities which are located in North America. Finland manufacturing facility is the only one located in Europe. Distribution centers are located worldwide in North America, Europe, Asia and Australia. The largest distribution center is located in US (Company website 2013).

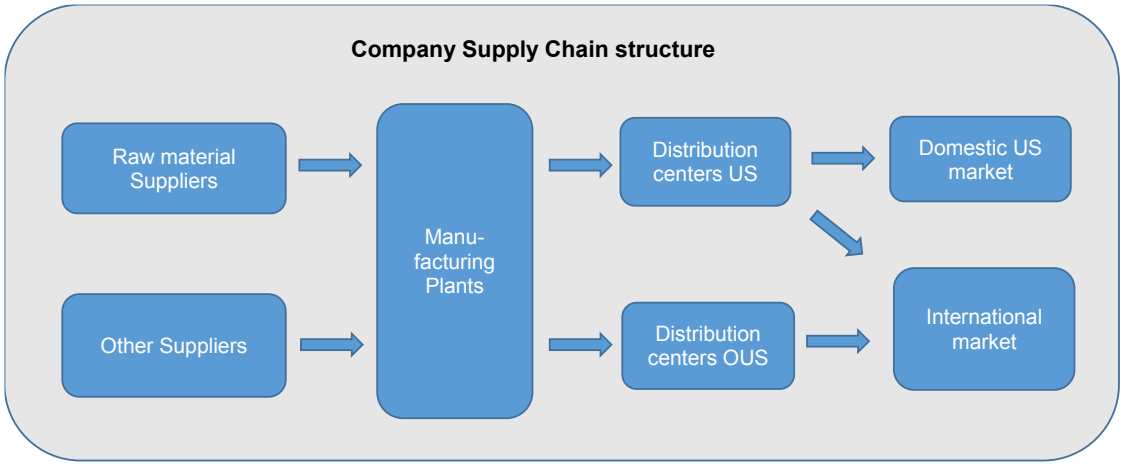

Figure 1. US based company Supply Chain management Structure

Finland subsidiary sources materials and machinery from European market and delivers final products to US based company's distribution centers and semi-finished products to US Manufacturing facilities for further processing.

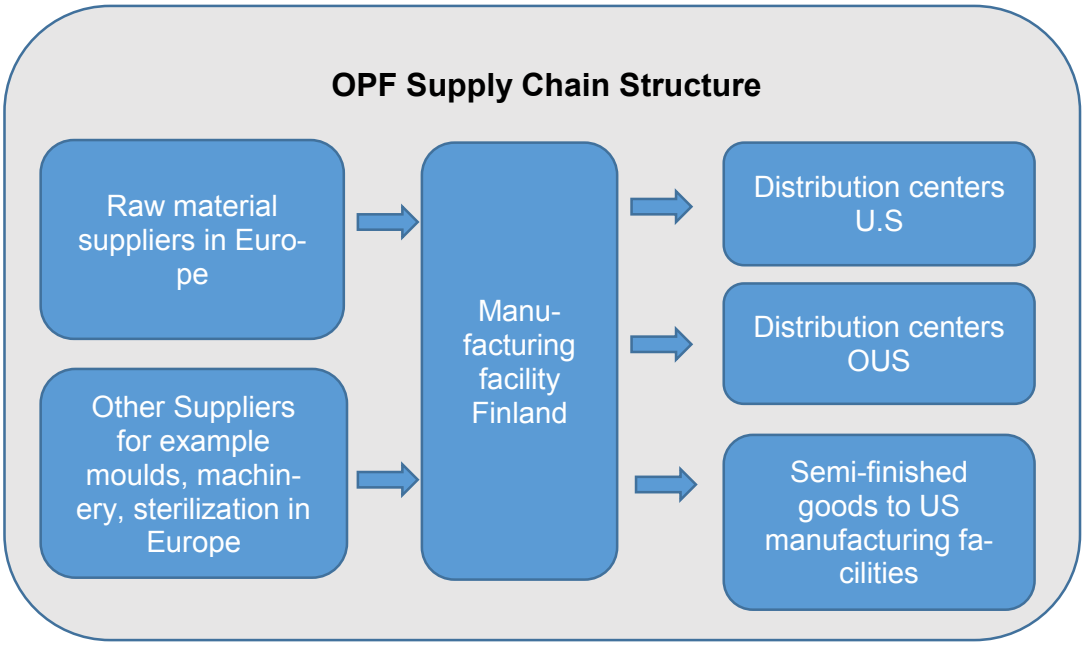

Figure 2. Finland subsidiary Supply Chain management Structure

1.2 Business Challenge, Objective and Intended outcome

US based company's transfer decision has raised some business challenges that were identified by reviewing the transfer announcement presented by Director of Operations and following discussions with Operations management.

How to transfer manufacturing of a biomaterial implant products with minimal impact to stakeholders?
How to make sure continuous high quality, safety and production yield of biomaterial implant products when manufacturing is done in the United States?

Thesis goal, agreed with Operations management, is to create a best practices process for the transfer, make manufacturing process step risk analysis and create solutions toolkit to challenges that will most likely be encountered during the transfer and in continuous manufacturing of a biomaterial implant product in various manufacturing steps.

OPF products are similar between each other, so results should be applicable to other OPF implant products as well. Results would aid with the seamless transfer of manufacturing from Finland to U.S. and solving issues that might rise at a later time in manufacturing processes at receiving site.

1.3 Scope and Limitations

1.3.1 Scope

Research focuses on the transfer and manufacturing steps at the shop floor on one specific product family. Finland subsidiary has 400 different products in their line-up and seven major product families. Main manufacturing methods are extrusion, self-reinforcement, machining, thermoforming and injection moulding. Scope of the thesis is limited to transfer of one biomaterial implant product, after this called ImplantX, which is available in various lengths. This product has been chosen because it is manufactured in machined and injection moulding methods, covering two main manufacturing methods used at OPF. Assumption is that the research will capture common issues and challenges in both manufacturing methods. ImplantX is also part of the successful Sports medicine product line, which accounts for over 30% of US based company revenue. Transfer of Research & Development functions are out of scope for the thesis.

The ImplantX line introduces the latest advancements in biocomposite material technology. Material is a result of extensive research at the Finland subsidiary facility. Material utilizes micro filtration process that yields β –TCP (Beta-tricalsiumphosphate) particles in their smallest form, known as microTCP with average particle size of 5-30 µm. MicroTCP particles are uniformly embedded throughout 96L/4D PLA Bioabsorbable polymer, delivering a stronger biocomposite material. This technology enables reliable fixation during the healing period while promoting bone in-growth to aid in the restoration of patients' natural anatomy both biologically and mechanically. (US subsidiary Arthroscopy catalogue 2012)

ImplantX is for ligament fixation in the knee area. Larger implants are designed for fixation of ligamentum cruciatum anterius and ligamentum cruciforme atlantis. Smaller implants are designed for fixation of other ligaments in the knee area. Product family con-

sists of 35 sizes developed at OPF and the instrumentation for the applying of the implant has been developed by US subsidiary.

Scope of the Risk analysis and Solution toolkit are limited to manufacturing process steps of ImplantX product.

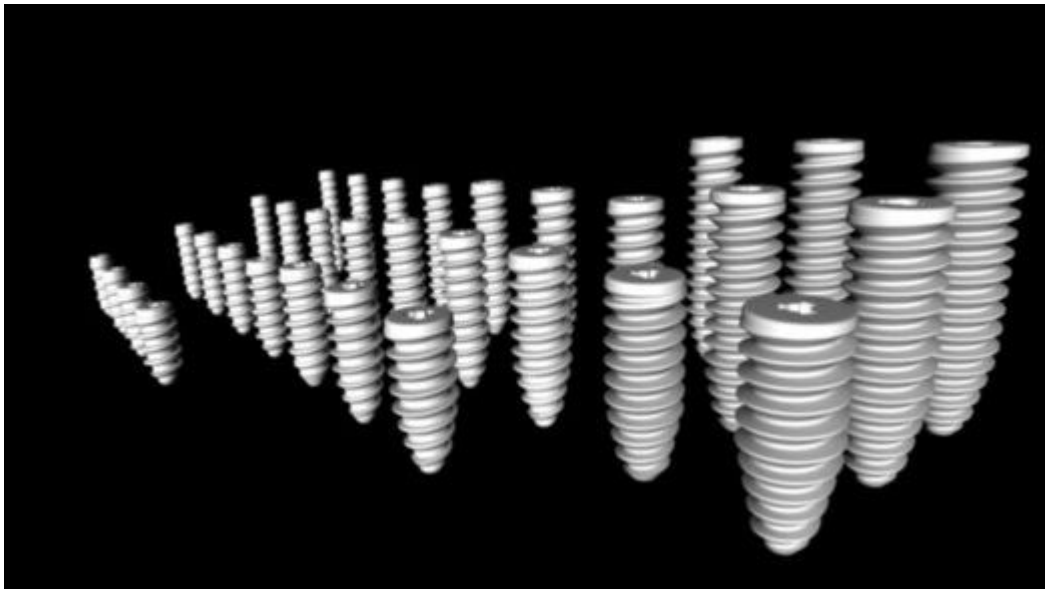

Figure 3. Example of implant product family (OPF e-portfolio 2012)

1.3.2 Limitations

Research has a number of limitations. Research is conducted inside one company and focuses only on one product family. However skills acquired from manufacturing of this product family could, in most manufacturing steps, be applied for other OPF products according to the results from the survey and interviews. Some manufacturing steps had only few responses in the survey, which causes individual answers to gain more precedence. End customer feedback from the case transfer is not available at the moment of writing this thesis, so the case transfer success cannot be definitively evaluated. Conclusive evaluation of the transfer could be done after few years, when all the OPF manufactured safety stock is used and customer feedback from the products manufactured in receiving location is available. Best Practices process built is mainly based on interviews, experience and literature, but has not been tested in practice with empirical results.

2 Methods and Material

2.1 Research Design

The research methodology is empirical and qualitative based on relevant literature, company documentation, a survey conducted in the company and 11 expert interviews including project management and uncovered manufacturing process step experts. Author was part of the transfer, responsible for the information systems and data transfer with a good access for transfer follow-up.

The research design followed the pattern of first getting familiar with relevant literature and company documentation, then internal survey and interviews were conducted. Results from survey and interviews were used in the case review and analysis, which lead to a proposal. Proposal was then subjected to review by OPF and after feedback conclusions were formed.

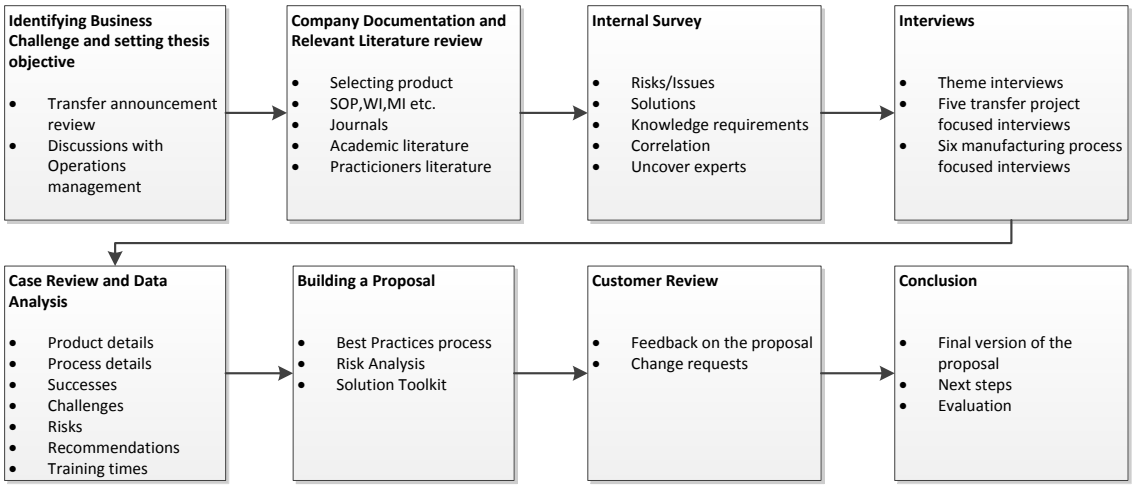

Figure 4. Research design

2.2 Data Collection and Data Analysis Methods

ImplantX manufacturing information was gathered from company's internal documentation including standard operating procedures, work and equipment instructions. Survey questions were focused on the manufacturing steps of ImplantX product. Purpose of the survey was to uncover knowledge experts in the organization and gather information from personnel in order to achieve research goals. Survey was structured by each manufacturing step and answering a step was optional. It consisted of open text fields, choices and lists. Choice questions were limited to four possible answers. Since the survey was targeted for Finnish personnel, the questions were in Finnish language in order to avoid misunderstandings. Survey was built on SharePoint server 2010 platform and users answering the survey used their own Microsoft active directory user account and computers provided by the company. 47% of the personnel responded to the survey.

Survey uncovered the experts of each particular manufacturing step and many agreed to be interviewed for the manufacturing process step of their expertise. The transfer project leadership, project managers and managing director were also interviewed, their interview questions were mostly focused on overall transfer for case review. Total of 11 recorded interviews were conducted lasting from 17 to 45 min. Interviews included open-ended questions concerning the research topics. Additional focusing questions were asked by the author during interviews. Author also engaged in several unrecorded conversations about the transfer with the personnel that helped to highlight focus points.

3 Case analysis of the manufacturing transfer

In spring 2012 US Based Company consistent with their strategy to improve Manufacturing & Operational Efficiencies reviewed Finland operations and set certain targets for improvement. In the end they came to a conclusion that targets could only be met by transferring the Finland operations to United States. US Based company decided to consolidate Finland manufacturing operations to two manufacturing facilities in North America by 2014. Receiving organizations are referred as Rsite1 and Rsite2.

3.1 Transfer in general

Finnish labor laws are very different from the US labor laws according to overall transfer project manager. US based company has done manufacturing transfers multiple times within the North America region, but not international transfers from Europe. There were additional legal issues that management had to take into consideration, Finnish joint negotiation law for example.

According to the project management interviews, once the transfer decision had been made, the project for transfer was not very different from a normal big international project except that the end result was a shutdown of Finland operations. Project schedule was created and responsible project manager for the project was chosen. In this case the project manager came from US subsidiary (Rsite1) and she was overall responsible of the transfer project. Finland Operations (OPF) requested that there would be a local project manager in Finland site, which was agreed, and local project manager was appointed in OPF. Overall Project manager could not choose the transfer team members herself, they were chosen by respective directors from receiving (Rsite1 and Rsite2) and sending organizations (OPF). There was no transfer process template or best practices process available, but the experience of the project managers that have done transfers in US were used in the pre-transfer planning. There was extensive experience of transferring documentation and other practical matters. Original purpose was to copy the processes from previous completed transfers and apply them. However this was international transfer from Finland to US, products and manufacturing methods transferred were very different from the previous completed transfers. This resulted that only basic outline of the transfer process from previous transfers was used and previous experience indicated that estimated transfer time would be about 18 months. Finland personnel was offered a generous bonus system that rewarded the personnel staying for the duration of the transfer. About 90% of the personnel stayed to collect the bonus, which ensured availability of the valuable human resources. Company also offered other kind of support for the personnel in Finland, a job search training for example.

3.2 Pre-Transfer planning

First step was to determine what products are manufactured in OPF, how many catalogue numbers, products and product families there were. Then among those catalogue numbers, how many of them are in product families and how many of them are

components compared to final products, and what effect that has for the transfer. Review of the manufacturing methods was conducted to find out whether product was machined or Injection moulded. Process flow chart was created for each of those families. Machined process products were to be transferred to Rsite1 and assembled into a final device there. Moulded products were to be transferred to Rsite2. Some products didn't necessarily fit into either facilities current capabilities and receiving site needed to be determined separately in those cases.

From equipment standpoint decisions were made to either purchase new equipment to receiving site or to transfer the equipment from Finland. This was based on availability of the equipment, for example Extrudex is fairly common extruder versus the self-reinforcing equipment which is custom made equipment, so determining if it made sense to purchase new equipment in the US or transfer equipment from OPF. Custom made equipment that could not be purchased easily were to be transferred and that required to build up more inventory of those products, because there is going to be some time period, were there is no manufacturing being done. For the machined products, a new machines were to be purchased in Rsite1, which would enabled Finland to continue manufacturing products until Rsite1 was capable manufacturing products, and so there was not going to be that time period where there is no manufacturing. There was planning from inventory standpoint of how much safety stock is needed to cover transfer periods. Finland needed to make more products and determining how long that was going to take had to be scheduled. OPF was suddenly asked to make 10 months' worth of extra inventory in particular products during pending shutdown. This was a challenging resource issue for local OPF management.

There were also determining from the regulatory stand point of what regulatory impact transfer has. There are differences if the final product is already manufactured in receiving site in US or the final product is completed in OPF, and if transfer is considered a major change or not from regulatory stand point. The estimated time the regulatory submissions and approvals would take, also influenced decision on how much safety stock was needed.

Sales Data was reviewed of whether it is related to regulatory impact as well. If there is longer regulatory time period like in Korea for example. How much, what percentage of the product is actually sold in Korea and what is the impact. Sales figures of each product line was reviewed, in which markets and what regulatory impacts there were. Then the amount of additional safety stock was calculated with estimates of other relevant effects. Few product lines were considered for discontinuation like one implant

family, which was sold primarily in China. Product had very low profit margin and it would take a long time to get it resubmitted for regulatory approval. Cost Analysis and payback estimates were made for the products which had very low profit margin and the decisions to discontinue were made on selected products.

3.3 Transfer overview

Order of the transfer was decided according to the project plan to start from latter process steps. First manufacturing process steps to be transferred were Injection moulding, packing, machining and laboratory measurement. Extrusion and Self-Reinforcement processes were positioned to end of the transfer schedule. Safety stocks for final products and components were build based on the project plan. Detailed project plan was available only to transfer product management. Discontinuation decisions were also made during the transfer, which created confusion and delays when building safety stocks and a wrong product was manufactured at times.

There was a team within Rsite1 which was assigned to get manufacturing up and running of the machined implants that were assigned to Rsite1. They had to build a cleanroom, order machining equipment etc. There were people from several different departments assigned to the project. Products transferred to Rsite1 were all component products and final product assembly was already done in Rsite1. Personnel in Rsite1 had worked on those products before and therefore had some background in transferred products.

Rsite2 had their own team assigned and they, like Rsite1, had to build a cleanroom facilities. They were not familiar with implant manufacturing, so they had to get themselves acclimated and learn issues of working with biomaterials and implants. They had to implement new processes in order to ship component level implant products to Rsite1 that were not in place previously. Test laboratory had to be setup in Rsite2 among other things, so there were a lot more activities in Rsite2, if you look at the scale the whole project, then in Rsite1.

Overall Project Manager had no previous contact with anybody in Rsite2 facilities and she was in charge of managing project also between OPF Finland and Rsite2. Learning how Rsite2 and Rsite1 organizations worked together and to get familiar with the team members and their skills was required. There are cultural differences between Rsite1 and Rsite2 even if they are located in the same country. Corporate culture in Rsite1 and Rsite2 is also different, which created barriers for the transfer.

Documentation in OPF was mostly in Finnish, so it needed to be translated into English. This was done by using internal and external service providers. Translations were added to the documents and reviewed by OPF Quality Assurance and Research and development Departments that understood technical issues in processes. They made sure the translations were correct. Documents were then scanned to digital PDF form and sent to corresponding locations in Rsite1 or Rsite2, where they were imported into quality systems. There was a lot of coordinating between three sites for making sure that information was provided when needed, but also trying to make sure, that information was verified by Rsite1 Quality department, so that in the end, the correct final revision of the documents will be the one available. There was a tendency for one-to-one communication, for example someone in Rsite2 was working on something and have been talking to somebody on one-on-one level in OPF asking them questions. They might send information back and forth, and manager needs to make sure that ultimately the final released revision of the document is the one translated and imported into quality system. A majority of the release documents were also scanned and rest of the documents were archived with instructions from the US in the archive boxes and then sent to US for final archive. One of the quality requirements was that document content and meaning cannot change at all, so Finnish part of the document is considered valid in case there is any conflict between English and Finnish text. Also due to this requirement, no indexed PDF –files were used. This limits the future indexing and searching of the PDF documents, but is necessary because OCR (Optical Character Recognition) and PDF transformation tools available in OPF might change some aspects of the content or appearance of the document compared to original. User personal home drive files and email archives could not be sent to US due to legal issues, so this particular data was archived in US based company sales office located in Finland.

Rsite2 also had to have bio-absorbable implants production added to their manufacturing certificates, which they did not have before and Rsite1 had to add Rsite2 as a significant subcontractor onto their certificates. This issue came up when process to do regulatory submission was started and there were additional regulatory requirements that were not known ahead of time.

Resources were being drained. Everybody was asked to do more work, but also maintain the service levels during that time period. Finland operators were training US personnel on how make products during their visits in Finland, while at the same time doing overtime in order to increase safety stock levels. Finland Personnel were kept in-

formed about transfer progress by info sessions held as often as needed, at least once a month. Personnel also received support and information about their options after their role in the transfer was over.

Once the safety stocks were completed for a particular products, the Finland manufacturing equipment of those products was transferred to US facilities and process of ramping up manufacturing of these products in receiving site was started. Transfer progressed in phases by each product family. Process validations needed to be done in receiving site before any actual manufacturing can start. Receiving sites had trouble successfully completing process validations especially with older products. A number of expert visit from OPF to receiving site was done and OPF personnel helped with these validations.

3.4 Knowledge transfer

There were number of people visiting the Finland operations from Rsite2 and Rsite1 during the transfer period. They were learning the use of equipment and manufacturing process steps in manufacturing area. Some had extensive previous experience and some had very little previous experience. Most visits lasted from one week to two weeks. Injection moulding specialist and process engineer from Rsite2 stayed longer, a few months in total. They were learning injection moulding, extrusion, thermoforming and self-reinforcement. They also documented processes by taking video and pictures, and reading the translated work and equipment instructions. Finland personnel also visited Rsite2 and Rsite1 and helped them ramp up their manufacturing. These trips in general lasted from one week to two weeks. None of the Finland manufacturing experts relocated to US. One Research Development Manager and Finland transfer Project manager relocated to Rsite1 and Rsite2. Rsite1 tried to recruit two additional persons, but there efforts were unsuccessful.

3.5 Cultural challenges

Cultural differences between US and Finland affect the transfer and the training. Language was the biggest obstacle at the beginning, especially with technical terms. Operators in Finland were not used to speak English and at first were a bit timid with visitors from United States of America. As time went on they felt more comfortable of interacting and technical language terms became more familiar. Language issues caused training to take more time, because operators had to explain procedures many times and they had to make sure everything is understood correctly. Some operators interviewed expressed a concern that even if US visitors performed the operational tasks they did not really understood why the process is done this way. This could be interpret as a lack of absorptive capability. Language problem did not persist with the office personnel, however there was some miscommunication at times. An example of Rsite1 sending people to pack-up equipment faced a resistance, because persons in OPF thought Rsite1 didn't trust them enough to do the equipment packing. The real reason being that Rsite1 personnel needed to see the equipment before it was dismantled so they have a better change to properly assemble it in the receiving site. OPF office personnel had worked with Rsite1 personnel before, which made communication easier. The abundance or lack of daylight in Finland caused various issues for some visitors. Finnish personnel received positive feedback from US visitors in separating personal feelings from work and general professionalism throughout the transfer. Receiving sites also mentioned how very helpful Finnish personnel were compared to their experiences with transfers inside the US.

Work and corporate cultures differ between OPF and US sites. Finnish tend to be more loyal to the employer and stay longer in service. Manufacturing workers in Finland tend to have more responsibility. OPF operators do machine settings, measuring and reporting. In US the hierarchy has more levels, operators basically just push a button and run the machine. Machine settings are done by technician, measuring by quality personnel and supervisor does reporting. Finnish operators are very straight forward in case of a problem, they bring it out in the open immediately and ask for help. In US they would probably try to solve issue by themselves and only ask for assistance when nothing works or even try to hide the problem exists. It seems more acceptable in Finnish culture to reveal that you do not know and need help then in US. Admitting a mistake or requesting additional training seems difficult for the US personnel. Mistakes are more like unfortunate events rather than lack of skill.

3.6 Implant transfer case

When the transfer project first started ImplantX was being machined in Finland and initial plan was to transfer the machining to Rsite1 and then make the change to moulding in Rsite2. That was primarily due to regulatory reasons. Each of those changes being considered a major change by some regulatory bodies. Decision was made to change the production to moulding in Finland and then move the moulding production from Finland to Rsite2. This eliminated the intern step of transferring machining, in which some of the equipment purchases planning were based on. So there were constantly changes being made to the project plan. Rsite2 was getting their moulding equipment up and running at the same time as OPF was doing validations of a moulded product. Packaging into foil pouches was added into packing process in Rsite2, which had never been done there before. Sterilizing with a special low dose Gamma cycle was added, that US based company in the US has never dealt with before, and the sterilization supplier, which could provide those services, was sourced in the US. Sterilization with low dose Gamma was something totally new to Rsite1 and Rsite2, neither had any previous experience in that process. Rsite2 had to do the moulding validations, but also sealing validations and sterilization validation. All these steps were considered major changes to some regulatory bodies and subject to regulatory submission.

Injection moulding process was rigorously created and validated according to newest requirements in OPF Finland. Primary operator from Rsite2 had 4-5 years previous experience in injection moulding and he spend few months in cleanroom practicing biomaterial injection moulding with Finnish Injection moulding expert. Finnish Injection moulding expert and quality engineer also visited Rsite2 site a few times to verify the processes were running and validations have been completed properly. There has not been any major issues in injection moulding manufacturing after the transfer. Two years supply of raw material billets was manufactured in OPF for this process. Transfer of Compounding and pelleting processes needed for making raw material components for Injection moulding is scheduled to be completed by summer 2014.

3.7 Manufacturing overview of ImplantX

ImplantX can be manufactured in two different ways, Machined or injection moulded. Originally the machined process was used, and after 2011 the injection moulding process was implemented. Both manufacturing methods are validated and have necessary regulatory approvals. Two lathes are used in machining process, the product manufactured in this way is slightly more costly compared to the injection moulded process. One lathe could be enough if it had enough tool slots available. Both manufacturing types presented are also widely used in other OPF implant products. OPF manufactures the finished product, which is then sterilized and delivered to the customer. The control of sales permit is the responsibility of US subsidiary Rsite1's regulatory department.

Manufacturing process includes many steps and these steps generally have sub-steps within production cell. Detailed Documentation is available for each step explaining how each component is manufactured, equipment is setup/used, how process is validated and quality is assured. Documents include work-, equipment- and measurement instructions, and validation documentation. Product specific tools and measuring equipment used during the each process step is listed in the documentation. This documentation was used as a source in the description of the manufacturing steps.

3.8 Machined Process

In this process ImplantX products are created by compounding, self-reinforcement and machining.

> Ultra-high strength, self-reinforced, macroscopical biodegradable polymeric composites can be manufactured by creating the polymeric microstructure, where oriented reinforcing elements and matrix material, which have the same chemical element composition, are bound together. (P. Törmälä 1992)

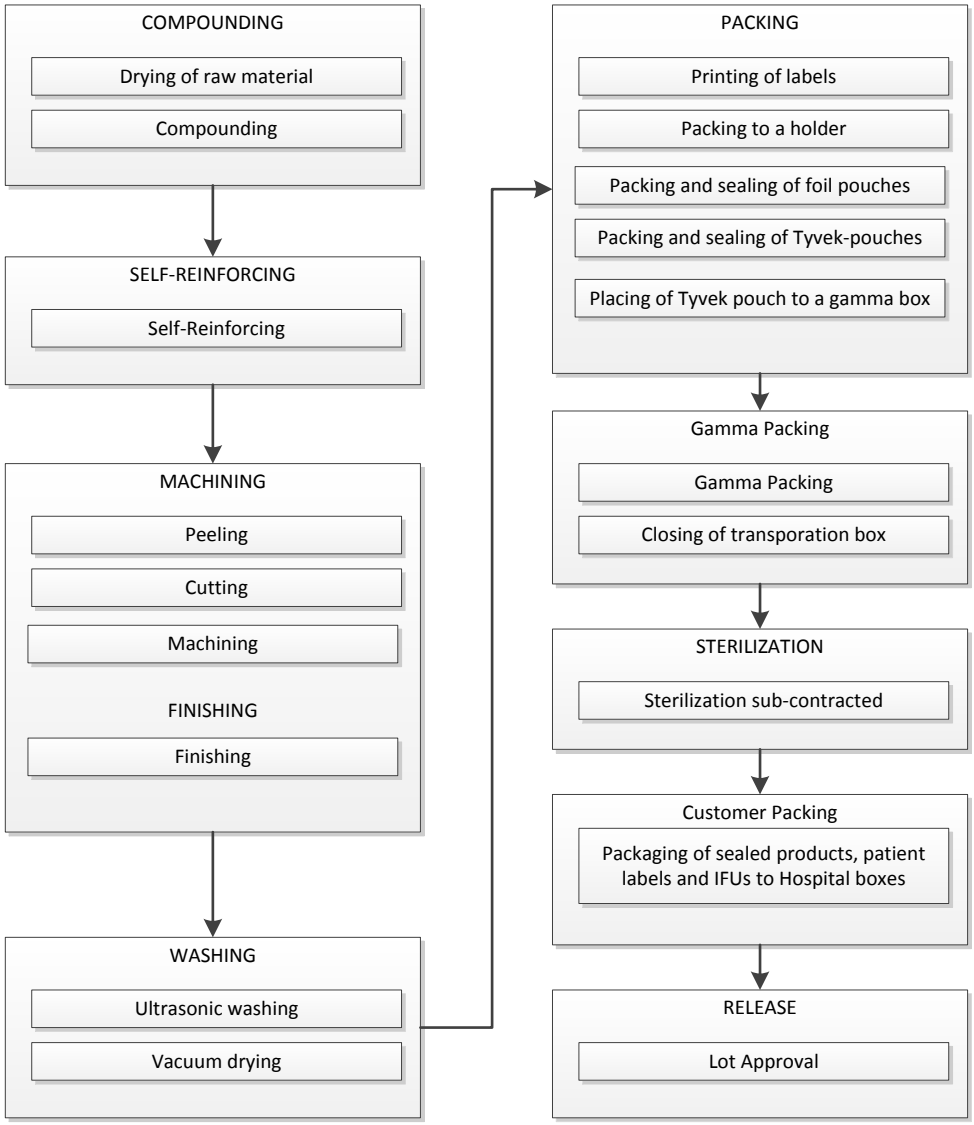

Figure 5. Machined ImplantX manufacturing process

3.8.1 Compounding

In this step composite materials are manufactured from raw materials by continuously mixing bioactive ceramic (β –TCP) to biodegradable polymer (96L/4D PLA) using melt-processing method twin-screw extruder. End result of the process is composite billet, which is a bar used in the following manufacturing steps.

Compounding is done in controlled cleanroom environment. Process step includes drying of raw materials in vacuum oven and compounding them with twin-screw extruder. Single screw extruder cannot not be used to mix liquids and powders to polymers homogeneously, so the twin-screw extruder was developed for this purpose. Process can take an hour to produce a billet.

In-Process quality control consists of following tests: Measurement of billet diameter, Measurement of TCP-content, Measurement of inherent viscosity, determination of monomer content and Visual inspection of the billet.

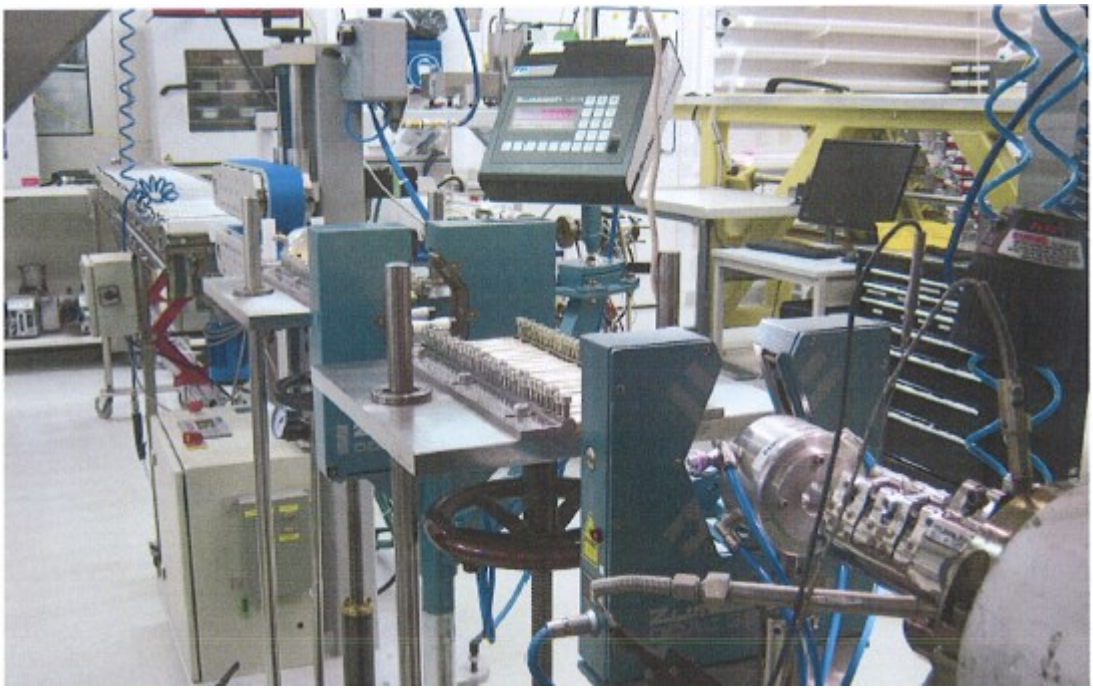

Figure 6. Twin-Screw extruder cell

3.8.2 Self-reinforcing

In this step billet from compounding step is self-reinforced using custom made equipment that with heat and mechanical force slowly elongates the billet causing it to stretch to a predefined ratio and at the same time causing polymer chains to orientate. The result is longer and stronger fibrillated billet that is suitable for machining. Process takes hours to complete and is patented proprietary technology developed in Finland.
Self-reinforcing (also called fibrillation) is performed in controlled cleanroom environment.
In-Process quality control consists of following tests: Determination of shear strength, measuring of the billet diameter and visual inspection of the billet

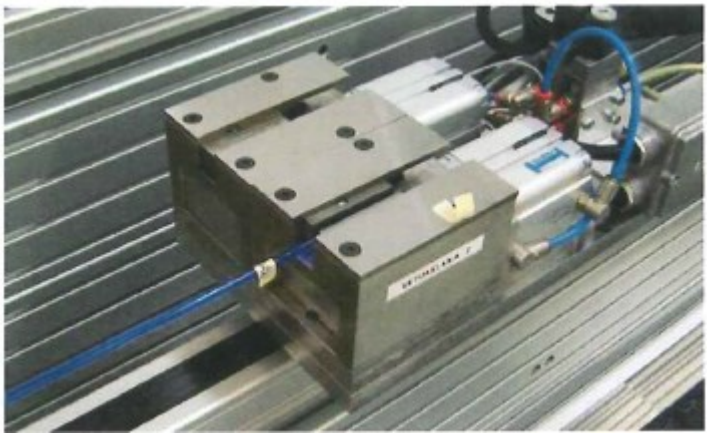

Figure 7. Billet attached to a drawing sled

3.8.3 Machining / Creation of form

This step the final form of the ImplantX is created. Self-reinforced billet is first peeled with peeling equipment, then it is cut into suitable pieces with lathe and instrument hole is made. Pieces are then machined in another lathe, where the final form is created. Then products go to finishing, which as a result of the lean initiatives, is now located at the same production cell then lathe.
Machining is performed in controlled cleanroom environment.
In-Process quality control consists of following tests: Dimensional measurement, instrument testing and visual inspection.

Figure 8. Lathe

3.8.4 Washing

Products are cleaned after machining in ultrasonic washing equipment and dried in vacuum drying cabinet or in similar device.
Washing is performed in controlled cleanroom environment.

3.8.5 Packing

Clean and dry products are then taken to packing where product labels are printed then products are packed into a holder before being packed and sealed with heat sealing equipment into foil pouch. Products are then packed and sealed with heat sealing equipment into Tyvek-pouch before setting products into gamma box.
Packing is performed in controlled cleanroom environment.
In-Process quality control consists of following tests: Tearing test for foil pouches and Tyvek-pouches (visual inspection) and Monthly testing of foil and Tyvek pouches

3.8.6 Gamma Packing

Products need to be sterilized in the outside facility, so they need to be packed well for the shipment. There is also three different kind of sterilization processes used based on the product. So the products are placed in the relevant transportation box with temperature- and Gamma indicators. Finally the transportation box is closed.
This process step does not require cleanroom environment.

3.8.7 Sterilization

Sterilization is sub-contracted and is performed in sub-contractors facility in Germany. Gamma process number 3 is used for ImplantX products.
In-Process quality control consists of following tests: Irradiation dosimeters

3.8.8 Customer packing

After sterilization final product packaging is done. Product labels are printed and attached to a hospital box. Product pouch, patient label and instruction for use is packed into the hospital box. Plastic sleeve is then placed around hospital box.
This process step does not require cleanroom environment.
Product is now ready and waiting for release.

3.8.9 Release

Before production Lot can be approved for release Torsion and Shear strength tests have to be completed. Quality engineer then signs the required release documentation and product is ready for shipping to distribution centers.

3.9 Injection moulding process

Injection moulded ImplantX has 35 different sizes. Process includes compounding, cutting and injection moulding.

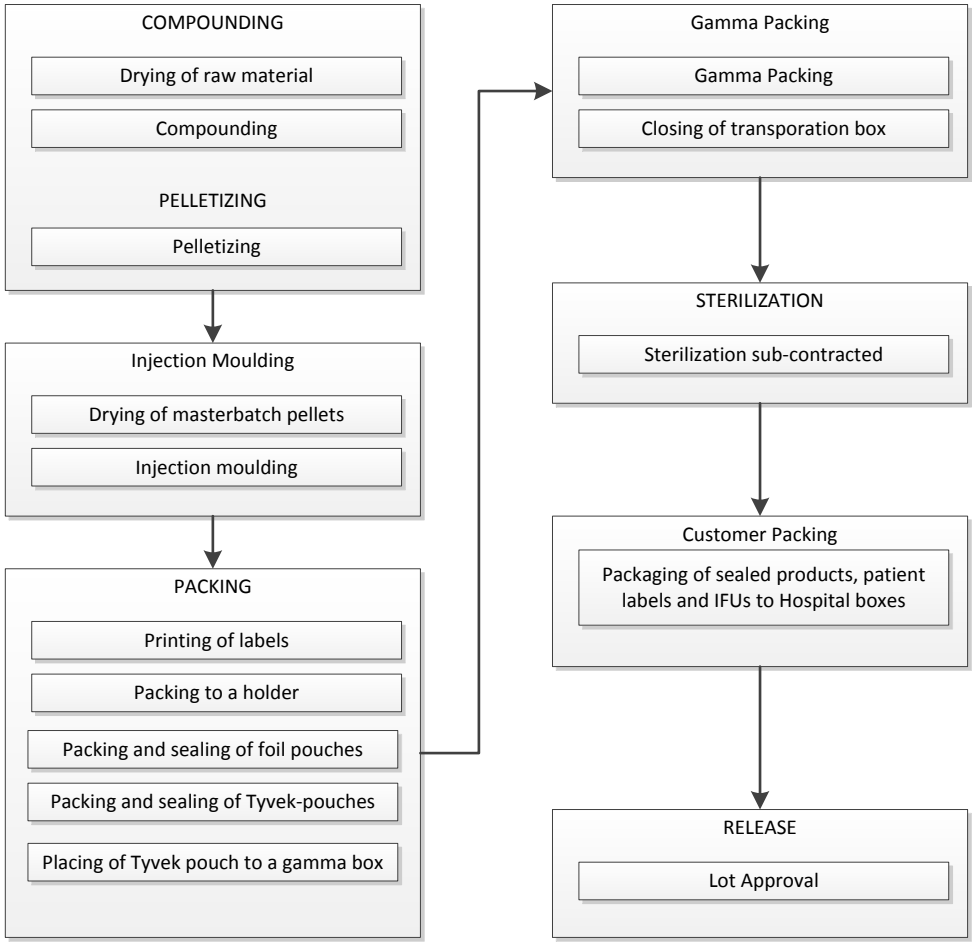

Figure 9. ImplantX Injection Moulded manufacturing process

3.9.1 Compounding and Pelletizing

In this step composite material billets are manufactured from raw materials by continuously mixing bioactive ceramic (β –TCP) to biodegradable polymer (96L/4D PLA) using twin-screw extruder applied in the machined process. Billet is then pelletized (cut) in masterbatch pellets of pre-defined size. Masterbatch is a blend of polymer and additive (ceramic) used as granulate raw material in injection moulding machine.

Process is done in controlled cleanroom environment. Sub-process steps consist of drying of raw materials in vacuum oven, compounding them in twin-screw extruder and pelletizing with pelletizing equipment.

In-Process quality control consists of following tests: Measurement of pellet dimensions, Measurement of TCP-content, Measurement of inherent viscosity, determination of monomer content and Visual inspection of the billet.

3.9.2 Injection Moulding

The final form of the ImplantX is created in this step. The masterbatch pellets are dried in vacuum oven or with hot-air dryer. Pellets are then heated to a liquid state and injected into the mould using Injection moulding machine. Ready pieces are removed from the mould and sent to packing. Each product size needs their own mould, so mould needs to be changed every time a different product size is manufactured.
Injection moulding is performed in controlled cleanroom environment.

In-Process quality control consists of following tests: Dimensional measurement, Measurement of inherent viscosity and determination of monomer content.

Figure 10. Injection moulding machine

3.9.3 Packing, Sterilization and Release

Packing, gamma packing, sterilization, customer packing and release processes are the same as for Machined manufacturing process

3.10 Summary

When reviewing a transfer case it shows that there are many variables in the transfer project and even if the US based company has done manufacturing relocation transfers before, there was no template that could be used in the International transfer. They also encountered some issues that came as a surprise especially in regulatory field. Project plan also had major changes after transfer operations started. Communication of the transfer progress and processing project plan changes is a challenge. In this sense pre-transfer planning seem very important identifying variables and risks associated with the transfer. Ample safety stocks allow time to address these issues, but strain resources in sending organization. Local transfer project manager was essential

in coordinating the transfer project with overall project manager. On-hand training at the manufacturing floor seemed to be effective method of transferring manufacturing knowledge if the trainee had previous experience in similar processes and willingness to learn. Some manufacturing steps are more challenging than others making knowledge transfer of these steps a challenge. It seems that if the product manufacturing process has been strictly validated and documented, it is easier to transfer. Older OPF products have not been re-validated for years, so work and equipment instructions are not as detailed as the newer product instructions. Operator then relies more in the personal experience than instructions. Compounding and Self-Reinforcement process steps seem to be most difficult and time consuming to transfer. Custom made machinery is used in these steps, which makes operating and maintenance a challenge. It also appears that if the manufacturing process is transferred as it is, without changes, there is a higher change of a success and less issues. Cultural and language issues effect the transfer, but no major issues were encountered. Different hierarchy in receiving site can cause issues when trying to keep the process same as in OPF. Some adaptation may be necessary. Rsite2 had no previous experience working with biomaterial implants, so they had more challenges compared to Rsite1, which had some experience. Retaining OPF personnel with the bonus seemed to be a successful way in motivating and preserving valuable human resources during the transfer project.

4 Best Practices on manufacturing relocation based on existing relevant literature

Literature on medical device manufacturing transfers is scarce concentrating on transfers from research and development to manufacturing or outsourcing instead of manufacturing location transfers. Some literature about international technology and knowledge transfer in general is available and there are companies that provide transfer service or outsourcing for medical industry like Creganna-Tactx Medical and Advant medical.

> As many as two-thirds of all relocations by manufacturing operations turn out to be ill advised, says Walter E. Kemp, a Vice President with Michael Paris Associates (MPA). Relocation blunders can be avoided with comprehensive -- and candid -- evaluations. (Relocation:Risky Business 1999)

In 1976 David J. Teece from Stanford University researched 26 technological transfer projects from chemical/petroleum refining and machinery industries in attempt to count the total cost of the transfer. His research revealed that the transfer costs vary considerably and it is not possible to make generalizations of costs involved. One observation he made was that costs decline the more times innovation is applied. Transfer is less costly and easier if the technology is mature. One example could be the transfer of a hamburger restaurant. It can be considered easier because raw-materials, equipment and skilled labor is widely available compared to biodegradable implant manufacturing with special raw-materials, custom equipment and limited availability of skilled labor. Each case seem to be different which makes manufacturing transfers a challenging area to study.

Visits to sending organization at an early stage of the transfer project and hands-on-training is important, "Pull" –type of technology transfers seem most successful model according to Klaus North. "Pull" -type allows recipients to decide which technologies to apply. Competent managers on the recipient side is requisite for successful transfer.

> Traditionally, the strategic assessment of potential manufacturing transfers concentrates on financial and legal (contractual) issues alone. This analysis is frequently static and based only on a limited range of variables, such as the cost of a single factor. Considerably less emphasis is placed initially on the alignment between potential partners manufacturing capabilities, or the identification of possible difficulties arising from the technological and manufacturing systems in use. In addition, subtle, though no less important, social, political and cultural aspects are usually not recognised in the early stages of a project. As a result, product transfers are frequently more troublesome, time-consuming and costly than originally planned (Tim Minshall and Andrew Steele).

Tim Minshall and Andrew Steele have developed manufactured manufacturing transfer process at Cambridge University.

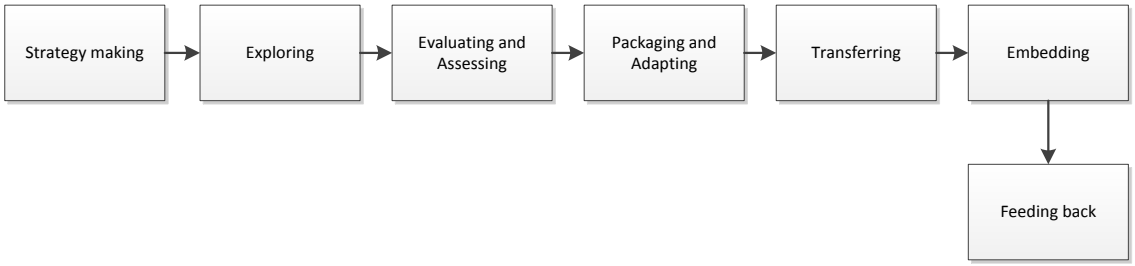

Figure 11. T. Minshall and A. Steele Manufacturing transfer process

Strategy making step includes setting business objectives. Exploring is identifying potential partners and manufacturing sites. Evaluation and assessing step includes evaluating "Fitness for Transfer", which can be interpret as ability of the potential manufacturer. In packaging and adapting step manufacturing transfer package is prepared and processes are adapted as necessary for receiving site. In Transferring step actual transfer activities begin and embedding phase prepares receiving site for continuous manufacturing. Providing Feedback between sites to improve and learn from the transfer project in order to improve future transfers is the last step.
Minshall and Steele also identify manufacturing decision areas that go through process steps described above. Decision areas are facilities, suppliers, material control, Human resources, knowledge, organization and relationships, quality and external environment.

Advant medical company provides manufacturing transfer services and their overall transfer process is described below.

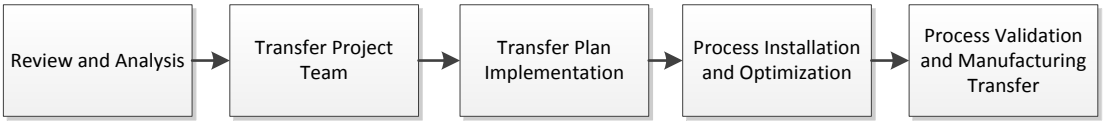

Figure 12. Advant Medical Manufacturing transfer process

Review and Analysis step consists of review of the scope of the transfer, the timeline and costs to develop a precise evaluation of the situation. This is followed by transfer project team selection and forming a communication plan. In transfer plan implementation step a detailed implementation plan is developed including Documentation Control, Quality and Risk Management, Human Resources and Training, Equipment Transfer, Supply Chain Development, Production Line Development, Sterilization Process and Safety Stock Development. In the Process installation and optimization step equipment is installed as it is on the sending site and optimized for efficiency. Final step is the process validations and actual manufacturing ramp-up.

Creganna-Tactx Medical Company's transfer process is slightly different consisting in total of seven steps.

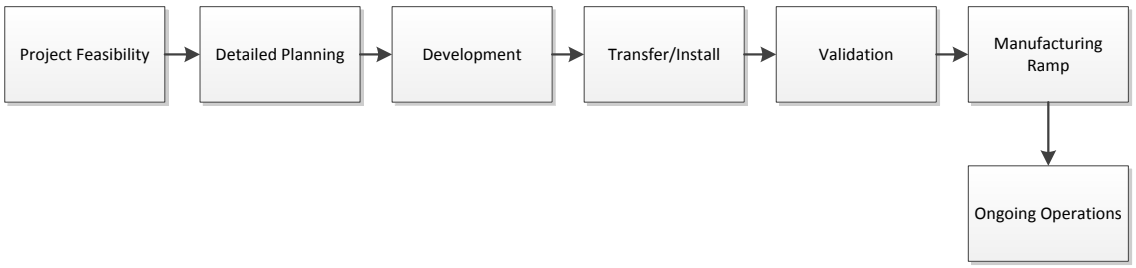

Figure 13. Creganna-Tactx Medical Manufacturing Transfer Process

Starting step is project feasibility analysis where the goal is to understand objectives and requirements, review solutions and develop proposal. Detailed project plan is developed in the next step followed by development, where product development and testing is completed if required. Transfer and installation step equipment and tooling is transferred or purchased. Manufacturing lines are setup and IQ (Installation qualification) is performed to all equipment. Validation phase includes all operative and performance process validations and product validations for finished devices. Manufacturing ramp up meeting the required yield and quality targets is done and ongoing operations

4.1 Manufacturing Knowledge transfer on operative level

Manufacturing knowledge transfer is probably one of the most challenging task in the manufacturing transfer. Ways to transfer specific know-how according to Klaus North

are using expatriate managers, training of new personnel in sending facility, purchase of same key equipment as in sending facility and creating know-how supply source using central planning department. Examples of common knowledge transfer mechanisms are as follows, Joint committees, regular meetings, manuals and documentation, quality control, maintenance, standardization and environmental management. One of the ways to transfer or a transfer case would include: project team, cooperation with equipment vendors and consultants, external training and transfer from simulation/test plant to real size. Joint project teams are also mentioned as one of the mechanisms to facilitate the transfer.

A Standard Operation Procedure (SOP) incorporates explicit knowledge derived from previous experiences in the codified document form. This procedure however is useless until it is actually performed by workers on the manufacturing floor. Workers develop, share and use tacit (hidden) knowledge as they perform their daily tasks. Tacit knowledge is regarded as a key competitive resource for companies and has a significant role on the manufacturing floor. (Davi Nakano, Jorge Muniz Jr and Edgard Dias Batista Jr 2013).

> The act of solving a problem rests on a sense of how the phenomena function; the formal expression of the solution is unlikely to capture fully this procedural knowledge, or even the data and information (or clues, as Polanyi describes it) leading to the solution. Thus, even in the arena of problem identification and solving, the know-how of heuristic search precedes the formal knowledge of the solution. (Bruce Kogut, Udo Zander 1992)

Biggest barrier for knowledge transfer is lack of recipient absorptive capability (Szulanski, 1996). There is not a lot of accessible practical knowledge transfer literature suitable for manufacturing personnel knowledge transfer. In 2012 a practitioner Calixto P.Anaya wrote a book called Knowledge transfer a practical approach, where he describes knowledge transfer program he has been using throughout his career. He especially focuses transferring knowledge from senior employees to junior employees. Based on his experience, knowledge transfer (KT) can be completed in four years. Similar situation is in the case of OPF transfer, at sending organization there are senior employees and receiving site has junior employees at least in the terms of knowledge in manufacturing of biodegradable implants. The transfer program starts by demographics study, which reveals disciplines affected, what are critical knowledge and skills and who are persons that possess these skills. Next step is selecting mentors identified by previous step. Mentors are experts that are dedicated to knowledge transfer in their disciplines. Mentors responsibility is the implementation of the KT program

in their field of expertise. In step three selected mentors conduct competence surveys and map each individuals competence in four levels based on achieved scores. This is current state of competence and then targets will be set. Actual knowledge transfer activities can then begin using targeted selectively training, on-the-job mentoring, job shadowing and using focus groups. Expert interviews can also be conducted in order to transfer tacit knowledge. Transfer activities are monitored and reported until goals are met. Program can then be shutdown. Inspired by Calixto P. Anaya this research uses a survey to uncover the experts, risks, solutions and training estimates. These experts are then interviewed in order to identify and capture some of the most critical tacit knowledge in each manufacturing step. The OPF transfer was scheduled for 18 months, so according to Calixto P. Anya this would not be enough time for confident knowledge transfer. Some of the knowledge will likely be lost during the transfer.

4.2 Cultural transfer aspects

Culture refers to the collective beliefs and values widely shared in specific society among persons at certain point of time (Ralston 1993). Culture can be found at different levels such as the country level and the corporate level. Transfer of knowledge study by Bhagat in 2002 has shown that cultural differences cause major challenges when transferring knowledge across borders. In 1997 Klaus North found evidence in his research of international transfers that the corporate culture determines more than the host country culture with know-how suppliers and recipients priorities. According to Hofstede (1980), every country has its own distinctive national culture. It is important to consider how differences in the national culture dimensions between a subsidiary and parent company effect the transfer.

In 1980 Hofstede identified four dimensions along which national cultures tended to differ: Power distance – expectations and acceptance of inequality of power distribution, Individualism/collectivism – importance of individual goals versus collective goals, Uncertainty avoidance – Acceptance or defense against future possibilities, and Masculinity/ femininity – Gender based dominant values of society.

4.3 Conceptual framework

Based on the review of the case analysis and relevant literature author has formed a conceptual framework of items that contribute to the successful transfer which are shown in the figure below. Overall Transfer items interact with decision variables and barriers or driving factors of the transfer. These factors contribute the success or failure of the transfer. Examples of decision variables are the target location of the transfer, regulatory requirements, knowledge transfer and maturity of technology. Knowledge transfer is probably the most challenging item in the transfer. With each decision variable project management has to develop strategy, methods and assign resources in order to successfully process each item. Barriers and driving factors interact with transfer and variables either helping or hindering progress. Major cultural differences are usually hindering factors in the transfer and extensive previous experience is one of driving factors.

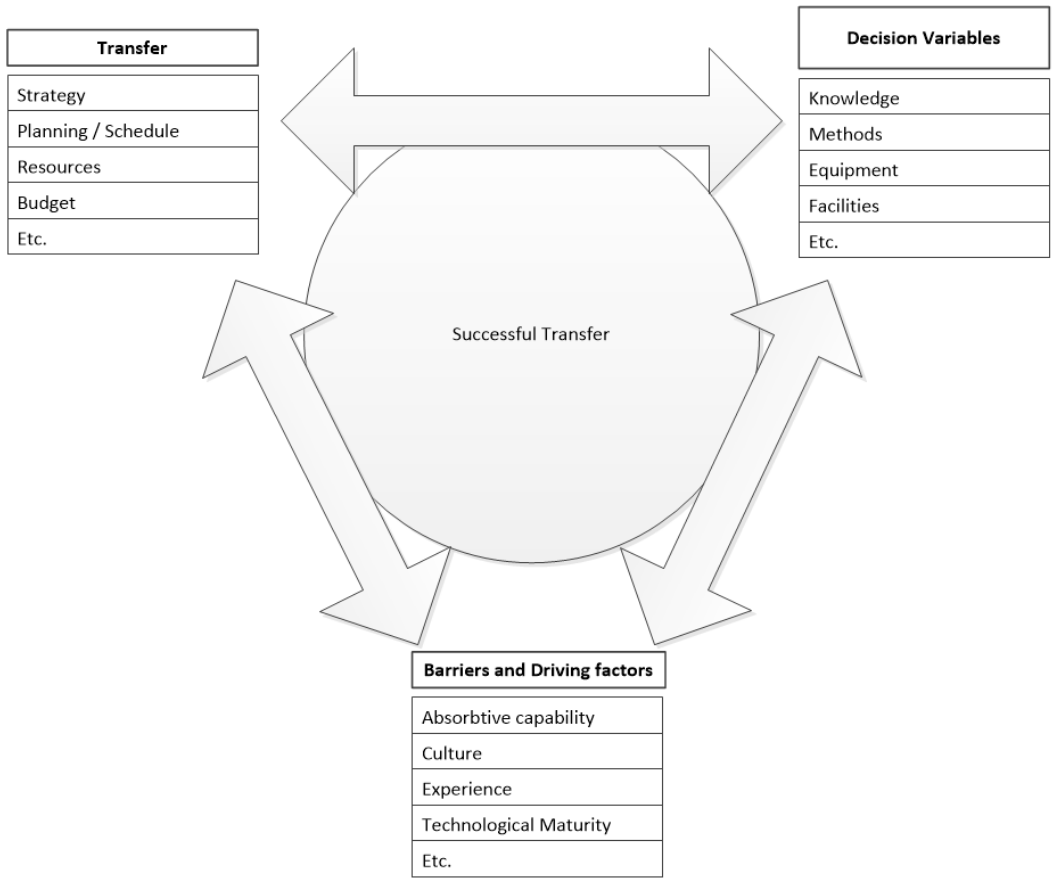

Figure 14. Conceptual Framework

In the figure below, the Manufacturing Knowledge circle represents the total amount of manufacturing knowledge that needs to be transferred. Driving factors are pushing circle inside the transfer circle. Barriers of knowledge transfer, a lack of absorptive capability for example, hinder the knowledge transfer.

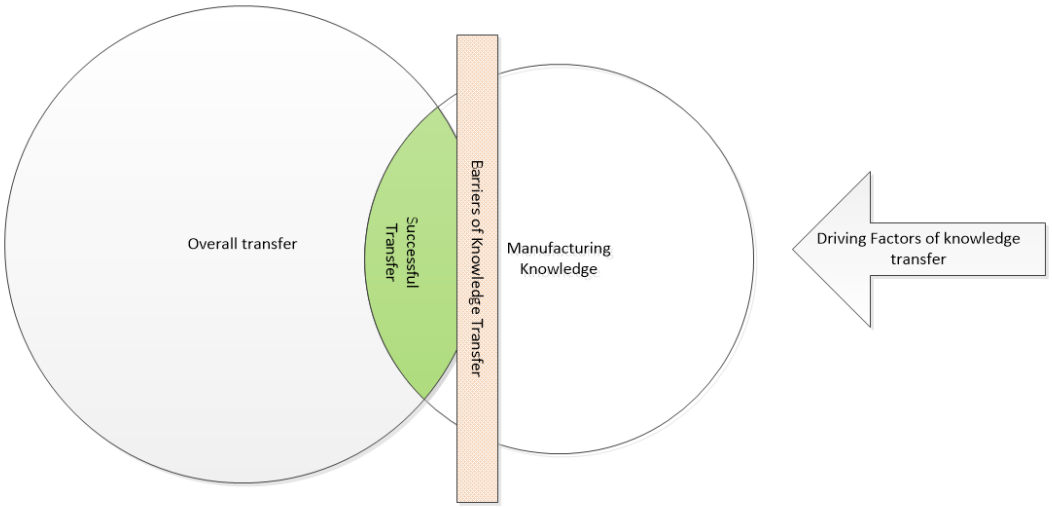

Figure 15. Conceptual framework of the Manufacturing knowledge transfer decision variable

5 Building proposal for the case company

5.1 Best Practices Process

This best practices process has been compiled from case analyses, relevant literature and expert interviews, using especially points where interviewees described how they would have done the transfer if they had the power to decide. The process starts at the point when senior management has already decided that manufacturing relocation should be started.

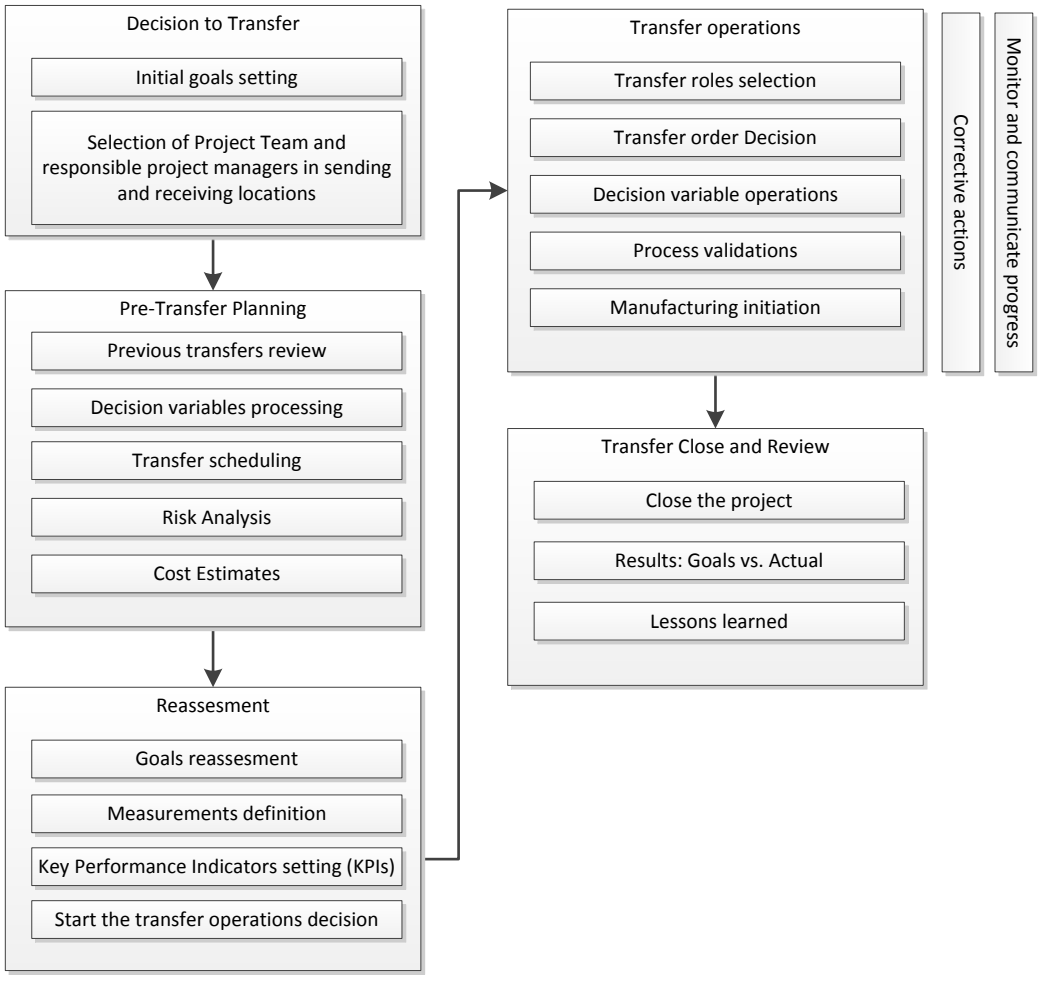

Figure 16. Best Practices process proposal

5.1.1 Decision to transfer

Senior management has become to conclusion that change is needed and they initiate the transfer project and appoint responsible persons into project team. Project team should have members from receiving and sending organizations including project managers. Project goals or targets are set by senior management.

The primary goal is the make a seamless transfer with minimal impact to stakeholders and also achieve financial and operative goals of the transfer.

5.1.2 Pre-Transfer Planning

Project team members should conduct pre-transfer planning and current state analysis, before any actual transfer operations begin by analyzing effect of the decision variables. These variables effect risk level and schedule of the transfer. Kimberly Murdoch suggests creation of the cause and effect diagram based on the risk contributors and process elements like methods and machines in order to uncover potential risks.

Decision variables involved in transfer mentioned by Benita M. Beamon (1998) with input from interviews are described below. List is not exhaustive and project managers could add variables in case they have significant effect on the transfer.

Scope/Product families:	Determining the number of different product families that will be transferred and have any finished goods inventory. Discontinuation of products.
Manufacturing Process	What methods of manufacturing and processes are used?
Maturity of the technology	Evaluate if the technology and methods used are common.
Number of Steps	Determining the number of steps that will comprise supply chain. This involves changing the chains level of vertical integration by removing or adding steps.
Plant	Determining which manufacturing plants will manufacture products, necessary facility improvements and environment.

Distribution Center (DC) - Determining which DCs will serve which customer segments.

Purchasing	Determining and developing critical aspects of the buyer-supplier relationship.
Inventory	Determining the amount and location of raw material, sub assembly, and final assembly storage.
Scheduling	Scheduling the manufacturing and/or distribution.
Regulatory	Regulatory impact, Submission time and cost
Quality Assurance	Documentation, work/equipment and measuring instructions, measuring and release procedures. Translations.
Knowledge transfer	Absorptive capability estimation, Skills transfer, training and technical support
Equipment	Office/Manufacturing equipment and tools
Software and Data	Migration of licenses, files and other data from computer systems
R&D/Patents/Contracts	Any R&D, patents or long term contracts in sending location
Human resources	Retention/hiring of personnel in sending and receiving location.

Determination of what products there are in sending location is the first step. This includes the amount of products, product families and catalogue numbers. How many are components versus final products manufactured and the manufacturing methods/processes used, in this case machined or injection moulded.

Sales data needs to be reviewed. If there is longer regulatory time period like in Korea for example. What percentage of the product is actually sold in that market? Sales percentage product/family in all the different markets is reviewed and regulatory impacts they would have. Some products/families may have to be considered for discontinuation, if for example a product is sold primarily in China and has very low profit margins and would take a long time to get resubmitted to regulatory approval. Analysis of what would be the total cost of transferring, how long would it take to actually make that money back should be done for each product/family using cost-benefit analyses. Products that have very low profit margin and high cost of transfer should be considered for discontinuation.

Good practice is to create a flow chart of product family characteristics and then try to determine the best supply chain structure. What would be the best manufacturing loca-

tion, in this case either Rsite1 or Rsite2, based on each locations expertise and suitability?

Raw materials and other materials like packaging and labelling need to be sourced preferable locally. In the case of very specific materials, sourcing locally may not be an option and this has to be taken into account in lead time. OPF sourced raw materials from Europe from two certified and validated suppliers. The relationship building with those suppliers and their representatives in US is crucial.

The maturity of the technology and uniqueness of the products needs to be evaluated. If the equipment and manufacturing methods used in sending location are common and skilled labor is available in receiving location, the transfer is probably easier.

Any changes to manufacturing steps, methods, processes and quality control should be done in sending location before the transfer. Injection moulded process changes were finished in Finland before transferring the manufacturing to US and initial results of the transfer were positive. Chances made in receiving location would add unknown risks to manufacturing, which has been experienced with other transferred products. It is not recommended to split process into two or more sections. For example billets made in different factory and shipped across country for final processing in another would create a gap in feedback of possible defect billets. Receiving location should first have a solid understanding about the product, before conducting any changes to manufacturing steps, methods, processes or quality control.

There is a need to build up more inventory of products transferred because there probably is going to be a time period, were there is no manufacturing being done in any location. Planning is needed from inventory standpoint, of how much safety stock is needed to cover transfer periods. Sending organization will have to make extra products and that affects the transfer schedule. Sending organization will be requested to make for example 10 months' worth of extra inventory, which requires additional schedule and resource planning in sending location.

Company operates in medical industry, so there is also regulatory impact from the transfer. There are differences if the final products are made in US or in Europe. If the transfer is considered a major change or not from regulatory stand point and how long regulatory submissions will affect the decision on the size of the safety stocks.

All the product documentation, which is in paper or electronic form, has to transferred and in most cases translated from Finnish to English, in this case. This includes work-, QA- and equipment instructions. These documents describe how the products are manufactured and equipment is operated. The time this takes depends on the amount

of products. It took more than a year to complete documentation transfer in OPF transfer with about 400 products. Regulatory related documentation like release documents need to be transferred to an archive according to archiving requirements of FDA and other governmental regulatory bodies.
Products made in OPF Finland are unique and require special manufacturing knowledge beyond what is found in documentation. This knowledge has to be transferred to the receiving site, in order for them to be able to effectively manufacture the products. Knowledge transfer should include engineering knowledge in addition to operational knowledge to get a better understanding of the complete manufacturing process. Knowledge transfer should be a documented process following knowledge transfer process of Calixto P. Anaya for example, where knowledge holders are uncovered by a survey and used as mentors in a documented training program.

Sending site usually has ERP system from where the data can be migrated to receiving organizations ERP system. In this case ERP system was same in Rsite1, so migration there was easy. Rsite2 uses a different ERP system, so all the Bill of Materials, routings, resources have to be input into their system (Manually or with automated tools). Data files need to be copied and sent to receiving site. Legal issues need to be taken into account especially regarding personal files and email archives. Data amounts can be very large (Terabytes), so transfer using encrypted external hard drive or backup tapes media is recommended if the network connection speed between sites is less than 100Mbps.
Result of the planning activities should be project plan, which would then be presented to senior management for approval.

Proposed supply chain structure for receiving sites is described in the figure below. Subcontracting semi-finished components to other units is not recommended at the beginning for the biomaterial implant components due to risk of increased scrap cost in case of faulty batches. This can be done when component manufacturing process is stable and manufacturing experience is cumulated at the manufacturing site. Raw materials and moulds can be sourced from Europe at the beginning, but it is recommended that local approved suppliers are used if available.

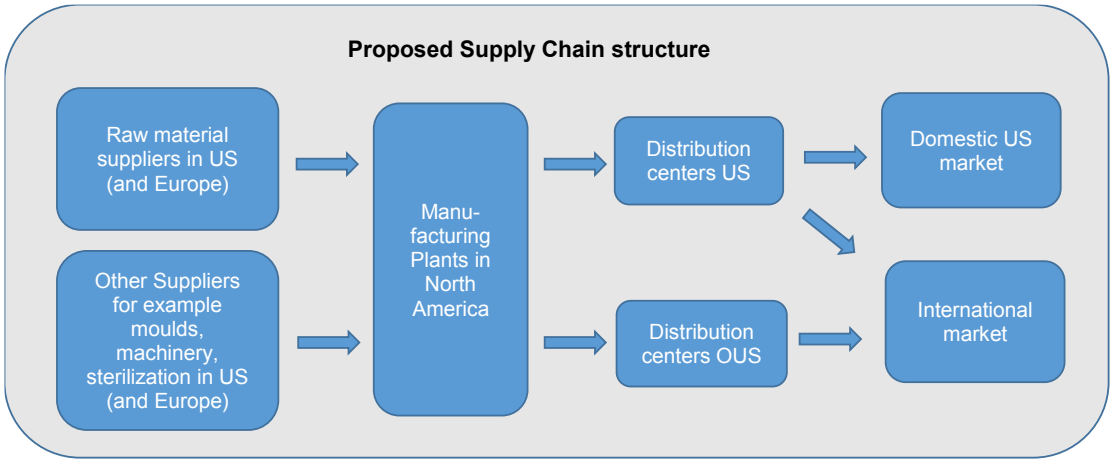

Figure 17. Proposed Supply Chain Structure

5.1.3 Reassessment

After planning step risk analyses and re-evaluation of the transfer is recommended by senior management, answering questions like: Can the goals be achieved with the transfer when this more complete information is taken into account? Are the risks too high and how they can be mitigated? Senior management would reassess and confirm the original decision, modify or cancel. Some products originally included in the transfer goals could be discontinued for example. Senior management would set Goals, measurements and key performance indicators, which will be used to monitor transfer performance. They would accept transfer project plan and actual transfer operations would start.

5.1.4 Measurements and KPIs

Most important KPIs are the customer complaint figures, scrap rate, manufacturing cost and number of backorders. KPI measurement data collected in OPF is comparable to data from other US based company manufacturing units, so it is possible to evaluate receiving site manufacturing unit performance after manufacturing transfer is completed in comparison with the historical data of OPF. Success of the transfer project can be measured by comparing initial transfer schedule/budget to actual costs and schedule. Raise in customer complaint or in scrap rate would indicate issues. Manufacturing yield, cost and backorders show the level of operational efficiency.

US based company uses SQDC (Safety, Quality, Delivery and Cost) strategy to measure its manufacturing performance. A big SQDC board is located at near the rest areas, so everyone can see the performance levels. Quality department is responsible in updating information on the board. US based company also uses earned hours as a way to evaluate manufacturing efficiency. Earned hours is traditional way of looking performance, because results depend heavily on cycle time parameter setup for products. Those parameter have to be kept up to date or the reports will show incorrect data. In this sense adding the reporting of the manufacturing cost and yield would provide more comprehensive results.
Data collected in these KPIs (Key Performance Indicators) includes safety measures indicating accident free days and cleanliness. Quality key performance indicators like product scrap amounts and scrap percentage per month (actual vs. target). Delivery KPIs include demand vs. monthly produced pieces. Cost measures show cumulative scrap in agreed currency and Operational expenditure (actual vs. budgeted). Finance department is responsible of the following items: investments, budgeted expenses versus actual and other management accounting activities. US Based company also measures customer complaints and back-orders. This information is provided to US subsidiary clinical and customer service personnel. Customer complaints have to be processed according to regulatory guidelines.

Listed below are examples of high level performance measures and goals that can be used in the transfer project (Benita m. Beamon 1998).

Cost	Minimize cost, Minimize average inventory levels, Maximize profit, Minimize amount of obsolete inventory
Customer Responsiveness	Achieve target service level (fill rate), Minimize stockout probability Minimize product demand variance or demand amplification, Maximize buyer-supplier benefit.
Activity	Time, Minimize the number of activity days and total cost, Flexibility, Maximize available system capacity.

5.1.5 Transfer operations

Transfer involves people in many departments and for the responsibilities to be clear roles are needed. Roles should be set for every significant manufacturing step and related support functions. Uncovered experts should be assigned to mentor roles and personnel coming for the training in trainee roles given an example. Responsibilities should be clear for everyone.

Transfer order needs to be decided. US based company decided to move from back to front. Meaning that last production steps (machining, packing and injection moulding) were transferred first. Compounding and pelletizing steps were last to be transferred. The majority of interviewees saw this as a proper order of the transfer, minimizing safety stock needs and allowing more time to learn challenging compounding and pelletizing steps.

Risks can be mitigated by having experienced engineers and operators spend time at sending location as much as possible, doing hands on training with experienced mentors and also by trying to maintain a good relationship with engineers that might agree to help even after the transfer is complete. Expert visits from sending location to receiving location and offering a consulting or expatriate contracts to key persons will help at the beginning of the production and mitigation of risks. Persons chosen for the trainee roles should have previous experience in similar field and other positive character trades in order to have good absorptive capability.

Decision variables in planning step have turned into action steps in the transfer project plan. These actions will be performed according to project plan, including the actual transfer operations like building safety stocks, translating documentation, submitting regulatory approvals, training and equipment relocation to name a few.

Transfer progress should monitored and communicated to the personnel in both sending and receiving organizations. Communication plan created in planning step should be followed and project managers should always be informed (copied) even in one-to-one information exchange concerning the transfer topics. Any corrective actions like changes to project plan or responses to emerged issues should be done through controlled documented process.

In the receiving site the process validations will have to be completed before manufacturing can begin including IQ (Installation qualification), OQ (Operational Qualification) and PQ (Performance Qualification). After all the required steps and regulatory issues

have been solved the manufacturing can be initiated in the new location. Experts from the sending site are especially valuable in steps mentioned above.

5.1.6 Transfer close and review

Manufacturing transfer is a project, which comes to an end at some point. Senior management will make decision to close the project and review the results. Some of the results will be revealed later like customer feedback and long term operational performance. In this sense it would be good to revisit the results maybe two years later and compare the results. Lessons learned session is a good venue to discuss and analyze the issues and successes encountered during the project, so they can be taken into account in the next transfer project.

5.2 Required knowledge level for Manufacturing Process steps

Manufacturing knowledge transfer is one of the most challenging items in the transfer variables. Therefore it is recommended that each process step is studied in order to assess knowledge transfer difficulty and estimated training time.

Compounding biomaterial with twin-screw extruder is one of the most challenging processes in OPF. Majority of the personnel have over 20 years of experience in compounding composite biodegradable materials into billets and this is a rare process in medical device industry. Based on the survey results and expert interviews it takes experienced (50%) or Expert (50%) with years of experience to perform and to be trained for this process step. Interviewed expert estimated that five years previous experience in extrusion would be required for successful knowledge transfer, which would take months. According to the survey 67% estimated it takes months to train an experienced person and for 27% it would take years for the person to perform operational tasks independently. Two experts of this process were identified by the survey. Pelletizing process where extruded billet is cut into pre-defined pieces for use as raw-material in injection moulding requires experienced person. Training a person for this process takes months and one expert was uncovered by the survey.

Self-reinforcement process is proprietary process developed in OPF and is unique in the medical industry. Equipment used in the process is custom made. Operators have years of experience in this process. In process speed and temperature adjustments are made by experienced operator in order to produce quality product. Experienced operator needs hands-on training of several months to independently run the process according to the survey and interviewed expert. Two experts were uncovered by the survey. ImplantX process parameters are better validated and more precise then other OPF products, because of three stone system. For this reason the skills acquired in ImplantX self-reinforcement process are not directly applicable to other self-reinforced products.

Machining process step is performed using commonly available lathes, but it still needs experienced person to train weeks (45%) or months (45%) to be able independently perform needed process steps mostly due to material used. Interviewed expert estimated two to three months hand-on training time would be adequate for experienced machinist. This would allow enough practice to get used to the raw-material billets, tool and product changes including some minor troubleshooting. One expert was uncovered in the survey.

Finishing is done after product has been created in the lathe at the same production cell. It is checked, finished and cleaned. Finishing is in some cases done by surgical blade, which is used to remove burrs. Other equipment used is standard industrial ultrasonic washer and drying cabinet. This process step requires eye and hand coordination, and some previous practical experience. Estimated training time on average is few weeks. Two experts were uncovered by the survey.

Injection moulding is another way of manufacturing the product. This step comes after compounding and pelletizing steps. Injection moulding equipment used are standard injection moulding machines common in plastics industry. Moulds and related parts are custom made in Finland. ImplantX has 35 moulds and they are run with two different parameter sets according to the size of the product. This requires less validation runs against doing validation runs individually for each 35 moulds. Majority of the survey respondents (70%) estimate that experienced person is needed for this step and it would take months to train. Person with no experience of the injection moulding takes about one year to be able independently perform this process step. According to the

expert uncovered by the survey, for experienced injection moulding operator hands-on training with mentor takes estimated two months.

In packing step the product is placed into product pouches and sealed. This process step is very similar to all OPF products and does not require a lot of experience. Most respondents agree that days or weeks training is enough to perform this process step. Three experts were found with one receiving the majority of mentions.

Products are packed and sent for sterilization in this gamma packing step. No long experience is required, however training takes average of weeks to complete. Survey respondents were quite divided in this step 40% agreeing that training would only take days and 40% that it would take months.

Sterilization step is outsourced to supplier in Germany. The equipment and facilities required are very special. Person receiving back the sterilized products needs to have years of experience and months or years of training in order to verify the validity of the product batch. One expert was found by the survey and she has over 25 years of experience.

In the customer packing step the sterilized product is placed into final customer boxes with instructions for use. This step doesn't require a lot of experience, and training for a new person would take few weeks on average.

In Release step the products are released for delivery after quality assurance has made sure that they fulfil all the requirements. This step requires experienced (56%) or expert (44%) person to perform this step correctly and it would take months to years of training. One expert was uncovered by the survey.

Laboratory is responsible for most of the key in-process measurements in each manufacturing step. It would take experienced person months to learn how to perform these measurements. Equipment used is standard laboratory equipment available in most countries. Measuring processes are the same for the different products, so if the person can perform ImplantX measurements he/she can also perform measurements for other products as well. Two main experts were uncovered by the survey.

5.3 Manufacturing process issues and Risk Analysis

Research results presented below are based on expert interviews and survey results. Manufacturing steps require different levels of experience and training. Persons previous experience significantly reduces training time needed. Experienced injection moulding operator can be trained in two months, but person with no previous experience in injection moulding would take 12 months according to interviewed expert. This time does not include problem solving skills. Manufacturing process in Finland subsidiary has been improved over the years due to operators gaining more experience and with corrective and preventive actions (CAPA process). Possibility of the risks have been mitigated and issues are generally encountered rarely. According to the interviews, likelihood of the risks will increase if the process is changed and/or operator is inexperienced. The issues encountered according to the survey are listed in the following paragraphs and risk factor has been calculated adding scores of probability, severity and how easily issue is detected. Each point has score from 1-4, where 4 is the highest. If many responders brought up the same issue the average from each value was calculated. Maximum score is 12 which indicates a highest risk priority. Risk factor below 6 points indicates low risk priority and 9 points or more indicates high risk priority. According to results there were no high risk priority issues in OPF and maximum score obtained was 8, which indicates medium risk priority. Table 1. shows the possible answers.

Poikkeaman toteutuminen **Probability**	**Riskitaso** **Severity**	**Poikkeaman havaittavuus** **Detectability**
1.Tapahtuu harvoin (1/vuosi) Occurs rarely (1/year)	1. Vähäinen Minor	1. Helposti havaittava Easily detectable
2. Tapahtuu melko harvoin (1/kk) Occurs quite rarely (1/Mo)	2. Kohtalainen Moderate	2.Kohtalaisen helposti havaittava Quite easily detectable
3. Tapahtuu melko usein (1/vko) Occurs Quite frequently (1/vko)	3. Vakava Serious	3. Ei helposti havaittava Not easily detectable
4. Tapahtuu usein (1/pv) Occurs frequently (1/day)	4.Kriittinen Critical	4. Vaikeasti havaittavissa Difficult to detect

Table 1. Risk Analysis choices and scores in Survey

Analysis method is based on the training by the center for professional innovation and education in 2011 and is adapted from GAMP risk assessment method. The purpose is to identify and apply measures on high risk priority issues.

5.3.1 Compounding

The most common error situations in compounding (extrusion) are sensor malfunction, production run failing using validated parameters, feeder malfunction and raw-material issues or contamination. Most of the issues occur rarely with experienced operators, maybe once per month, and are quite evident. Exception are the material issues which are only uncovered in laboratory measurements. Common Pelletizing errors in material are too low or high internal viscosity or contamination, which are visually hard to detect and require laboratory measurements. Pelletizing machine may produce uneven/various length pellets or malfunctions. Incorrect parameters also cause issues. Most of the issues occur very rarely (few times in a year) for experienced operators and are detected with ease except material related issues. Pellet material is not clear because of the additive, so contamination issues are visually hard to detect.

Compounding is the first step in ImplantX manufacturing and one of the most challenging. Inexperienced operator could assemble manufacturing equipment incorrectly. This could lead to machine breakage or fire in the worst case scenario. Scale equipment is very sensitive and prone to errors and could cause so-called displacement increment (reaping), where results are slowly moving toward some direction eventually going under or over approved limits. These issues are detected in laboratory incineration tests. Common issues are related to software. Compounding cell is a system of many machines working together, so operators/maintenance personnel needs to be familiar with the machines working together as complete system (cell). Equipment and raw-material suppliers can help, but they will only be of assistance for their provided machinery or material not the whole cell. Risk in depending too much on this, is that equipment manufacturer could confirm that their machine or device is working and raw-material supplier confirms that material is valid, but the cell still doesn't output valid products. Problem solving, after support from sending site is no longer available, is a major risk especially when training is focused mostly on actual day to day operations with limited or no on-site troubleshooting activities. With only limited number of persons attending the trainings, the receiving site manufacturing knowledge is focused in these persons and should they decide to leave the company before transfer is completed or shortly afterwards is a major risk.

Manufacturing process in Finland subsidiary has been improved over the years and possibility of the risks have been mitigated. Issues are generally encountered rarely. Table 2. shows the list of issues and calculated risk factor from the survey in compounding step and Table 3. In pelletizing step.

Deviation/Issue	Description	Probability	Severity	Detection	Risk factor
Feeder malfunction. Adding additive is not working.	Material is highly powdery and sometimes causes feeder to malfunction. Billet has then no microTCP component. It can be visible detected from the billet. There is no feeder alarm and noise level in the production usually prevents operator to hear the noise that feeder makes when it malfunctions.	2	3	2	7
Sensor malfunction	System alarms of defect sensor	1	2	2	5
Raw-Material issues and contamination	Issue with raw-material is uncovered in the production phase or in laboratory measurements	2	2	1	5
Production run using validated parameters not possible	Product does not fulfill approved specifications or next production step fails. Issue is discovered in laboratory measurements.	1	2	1	4

Table 2. Deviation/error situations in Compounding

Deviation/Issue	Description	Probability	Severity	Detection	Risk factor
Contamination	Dirt or foreign particles in the pellet. Detecting contamination is challenging, because pellets are not see-through due to MicroTCP additive.	1	3	4	8
Pellet IV too high or low	Internal viscosity is out of tolerance.	1	2	2	5
Equipment produces defect pellets, especially the length can vary.	Pellet lengths are constantly measured and monitored, so defect is detected quite easily.	2,5	1	1,5	5
Incorrect parameters	Pellets are not according to specifications	2	1	1	4

Table 3. Deviation/error situations in Pelletizing

5.3.2 Self-Reinforcement

Common error situations include billet diameter being out of tolerance, shearing strength or other mechanical properties are out of tolerance, self-reinforcement is failing using validated parameters and poor billet surface quality. Issues are encountered monthly.

Troubleshooting and lack of tacit knowledge are risks in this proprietary process. Work instructions are not detailed enough to solve issues and to get the feel of the process. Major risk arises when only one or two persons in receiving site are familiar with the process. Measurements are needed quickly after adjusting temperature or draw ratio in order to verify the product properties, so measuring equipment or service needs to be readily accessible or there might be extensive scrap if the measurements indicating issues are delayed, arriving in next shift for example. Changes to in-process measurement would constitute a risk, In OPF, operator does some of these measurements, so there is instant feedback and low level of scrap.

Deviation/Issue	Description	Probability	Severity	Detection	Risk factor
Billet shearing strength too low or other mechanical properties out of tolerance.	Mechanical properties out of acceptable limits detected by laboratory measurements.	1,5	3	1,5	6
Billet surface quality poor	Product surface quality is not acceptable, detected by operator	2	2	1	5
Reinforcement process cannot be run with validated parameters	No valid billet by using validated parameters	1	2	1	4
Billet diameter out of tolerance	Billet diameter either too small or too high. Defect detected by measurements.	1,33	1,33	1,33	4

Table 4. Deviation/error situations in Self-reinforcement

5.3.3 Peeling, Cutting, Machining

Common issues include product being out of tolerance, no instrument hole or hole out of tolerance, incorrect parameters, fractures, contamination, insufficient measurements or equipment malfunctions. Issues are encountered weekly or monthly according to the survey.

Machining can cause burrs in the product and this depends on the tools used and order of machining. More burr the product has, the more time it takes to finish the product in the finishing step. Measurements can also be hard to take. In OPF, the machinist takes measurements and is responsible that the products are within specified tolerances, if machinist has not been properly trained to take these measurements, there is risk for extensive scrap.

Material is difficult to process, because material properties can vary between different billet batches. High quality special tools may be difficult to acquire, because they have been designed and manufactured in Finland. Products with fractures that cannot be detected may slip through QA causing a possible breakage during installation of the product. These occurrences are quite rare.

Deviation/Issue	Description	Probability	Severity	Detection	Risk factor
Out of tolerance	Product measurements out of tolerance, commonly cause is incorrect parameters, incomplete work instructions or incorrect procedure. Deviation is usually detected in the production step.	2,5	2	2	6,5
Missing measurements	After parameter adjustment some measurements have been omitted by machinist. Deviation is detected at the latest in release step causing extensive additional work and potential scrap.	2,33	1,33	2,5	6,16
Fractures	Fractures visible in the product	2	2	2	6
Contamination	Contamination, dirt or foreign particles detected	2	2	2	6
Equipment malfunction	Product cannot be manufactured if equipment is malfunctioning.	2	2	1	5
Insert issue or insert hole off-centre	Failure in making an Insert hole. Could also lead to tool breakage and extensive manufacturing downtime.	1,5	1,5	1,5	4,5
Burr in products	Products may have extensive burrs after machining, which prevent accurate measurements in production step.	2	1	1	4

Table 5. Deviation/error situations in Machining

5.3.4 Finishing

The most common issues encountered are too high paraffin oil content, unfinished or un-cleaned product, product cannot be properly cleaned, visible burrs and drying failure. Products with burrs are encountered weekly, other issues a few times in a year. Measurements can be omitted by human error.

Deviation/Issue	Description	Probability	Severity	Detection	Risk factor
Paraffin content too high	After washing, Paraffin oil in the product. Paraffin oil content is not measured, so detection is difficult. There is issues with equipment or process.	1	2	4	7
Unfinished product goes to next manufacturing step	Human error in finishing and all or part of the product is not finished.	1	1	4	6
Burrs in the product	Product not properly finished. Defect detected in inspection.	3	2	1	6
Product cannot be cleaned	Product not clean and is detected during inspection.	1	2	2	5
Product is not dry	Product is wet or moist after drying. Incorrect drying parameters.	1	2	2	5

Table 6. Deviation/error situations in Finishing

5.3.5 Injection Moulding

Issues encountered are contamination, suction on the base, measurements out of tolerance, malformed instrument hole, insufficient physical properties and scale feeder (Gatetron) malfunction. Most issues occur rarely (once a month) and aside from contamination are fairly easy to detect. Scale feeder issues occur more frequently even daily sometimes.

Instrument hole in the bigger products has had issues that the instrument used in installation does not go all the way inside the product. This can cause product breakage during installation by the surgeon. Feeder (Gatetron) errors have occurred in OPF. One issue is dirt, which can come after maintenance is done for the mould. Mould is cleaned and some grease is applied. Grease is harmless and small amounts could exist with no harm. However OPF quality specifications state that there should be no

grease at all, so some products can have grease at the beginning of the run after mould maintenance. Power outage is a risk for continuous manufacturing if the outage is 10 minutes or longer. After ten minutes raw material in the cylinder becomes defective, because internal viscosity and monomer counts collapse, and manufacturing run has to be stopped. Mould breakage is another possibility. This has not happened in OPF, which shows quality of the moulds, but in case it happens, there are no spare moulds available. Lack of troubleshooting experience and only one trained person for receiving location is a risk. Risk of a considerable tacit knowledge loss.

Deviation/Issue	Description	Probability	Severity	Detection	Risk factor
Instrument hole defect	Instrument hole in the product is malformed. This is detected with instrument gauge. Issue probability increases when the size of the product grows.	2	3	2	7
Contamination	Dirt or foreign object in the product. Due to additive the contamination is not easy to detect.	2	2	2	6
Suction at the base of the product	Visual defect detected by the operator.	2	1	2	5
Out of tolerance	Product out of tolerance. Detected with dimensional measurements.	1,5	2	1,5	5
Physical properties out of tolerance	Product internal viscosity is too low (high) or monomer account is too high (low). Detected by laboratory analysis.	2	2	1	5
Product defect caused by mould damage	Mould is broken. Mould breakage could occur if the foreign object (metal) enters the mould.	1	2	2	5

Table 7. Deviation/error situations in Injection moulding

5.3.6 Packing

Issues encountered include poor seal or no seal, contamination (trash or black spot) and wrong product in the pouch. Issues are encountered weekly.
Sealing issues can occur with the thickest products and sometimes the seal has to be reworked.

Deviation/Issue	Description	Probability	Severity	Detection	Risk factor
Seal defective	Pouch seal is defective	3	3	2	8
Pouch is not sealed	Pouch has not been sealed.	1	4	3	8
Contamination in the pouch	Dirt, black spot or other defect in the pouch. Detected in packing or end packing.	3	2,5	2	7,5
Incorrect product in the pouch	Incorrect product is placed in the pouch.	1	3	2	6

Table 8. Deviation/error situations in Packing

5.3.7 Gamma Packing

Encountered issues include products sent to wrong Gamma program, sterilization failure and gamma radiation dose fluctuations. These issues are very rare and encountered maybe once a year. Products have gamma measurement stickers to verify the correct dose. Other issues are hard to detect. Two Experts were uncovered by the survey.

Deviation/Issue	Description	Probability	Severity	Detection	Risk factor
Products go to incorrect Gamma program	Gamma program used is incorrect. Product properties can change for example internal viscosity	1	3	3	7
Gammasterilisation fails	Failure is detected from Gamma stickers or using external laboratory services tests (Nelson, bacteria culture).	1	3	2	6
Gamma dose varies	Packed products receive varied gamma doses, if they happen to be located at the very edges of the process area. Product properties can be affected.	1	2	3	6

Table 9. Deviation/error situations in Gamma Packing

5.3.8 Sterilization

Issues encountered are too high bioburden levels (microbes on the product), too Low or High Gamma radiation dose and broken package during process. Products have gamma measurement stickers to verify the correct dose and broken packages are quite easy to detect. Other issues are hard to detect. Fortunately these issues are very rare.

Deviation/Issue	Description	Probability	Severity	Detection	Risk factor
Bioburden level too high. Too low Gamma dose	Bioburden level abnormal. Low dose of Gamma3 is not enough to sterilize the product.	1	3,5	3	7,5
Gamma dose too high	Gamma sticker indicates too high dose	1	3	2	6
Package is broken during procedure	Products are not sterile, because package is broken.	1	2	1	4

Table 10. Deviation/error situations in Sterilization

5.3.9 Customer packing

Issues encountered are incorrect labelling, wrong product in the box, heat sensitive indicator is missing and visual defects in the pouch. In OPF this happens very rarely, at most a few times in a year. One expert was uncovered by the survey. If products are subjected to higher temperatures then indicated, during transportation for example, their properties might change. Self-reinforced products loose orientation that can cause products to shrink in length and grow in width.

Deviation/Issue	Description	Probability	Severity	Detection	Risk factor
Label information and product inside the box do not match	Product in the box or label attached on the box is incorrect due to human error. In worst case scenario product will reach end customer.	1	3,66	3,33	8
Temperature indicator is missing	Temperature indicator missing. Indicator has not been attached or has been removed.	1	3	3	7
Pouch or pouch seal defective	Defect is detected in the pouch. Pouches are visually checked before packing to hospital box.	2	2	2	6

Table 11. Deviation/error situations in Customer Packing

5.3.10 Release

Encountered issues include lost documentation, documentation deviation, missing measurement results, non-sterile product has been released and release of products which are out of tolerance. Some of the issues happen monthly like missing measurement results or document deviation, others happen very rarely. One expert was uncovered by the survey.

Deviation/Issue	Description	Probability	Severity	Detection	Risk factor
Release of unsterile products	Product sterilization has not been verified.	1	4	3	8
Release of products out of tolerance	Product properties have not been verified.	1	3	2,5	6,5
Documentation lost or insufficient	Documentation like measurement results are missing. Documents usually misplaced or accidentally thrown away.	2	2	1,75	5,75

Table 12. Deviation/error situations in Release

5.3.11 Laboratory Measurements

Laboratory issues include problems with IV-equipment, product set incorrectly into testing jig, choosing of wrong method, analyzer computer crashes, Gas Chromatography (GC) equipment stops in the middle of the run, equipment not calibrated and incorrect products measured. Issues besides crashing computer are quite rare.

Misunderstandings of work instructions is one of the biggest risks and causes that process has not been done according to instructions. Most common issue in materials is too high amount of additive in extruded material. Other encountered issues are that product after sterilization step does not pass required mechanical tests and sterilized batch has to be scrapped. In 2005 solvent supplier provided solvent that was in specifications, but yielded incorrect results. This was a wide issue in the area and it took a long time to find the root cause of the issue. Human errors can occur in weighing the samples for example. This is one of the many reasons why Laboratory always uses reference samples to verify the results.

Deviation/Issue	Description	Probability	Severity	Detection	Risk factor
Incorrect process used in laboratory measurements	Raw material, subassembly or final product properties measured using incorrect process. Results are not reliable.	1	3	3	7
Wrong product measured	During measurement material or product codes have been mixed and wrong product has been tested. Results are not reliable.	1	3	3	7
Measurement device is not calibrated	Raw material, subassembly or final product properties measured using not calibrated equipment. Results are not reliable.	1	3	2	6
Product incorrectly setup in the testing gauge	Different products have separate testing gauges and sometimes incorrect one is used.	1	2	2	5
Analyzer computer/software crashes	Computer or software malfunction. Usually in the middle of the measuring run. No danger to end product, but results will be delayed.	2,5	1	1	4,5
Issues in IV-measuring equipment	Equipment used to measure internal viscosity malfunctions. No risk for end product, but results will be delayed.	2	1	1	4
Incorrect method selected with MTS equipment	MTS equipment software has different programmed methods for products. Results are not valid when using the wrong one. Issue is detected by reviewing results.	1	1	2	4
Instrument tool not properly attached	Torsion head instrument is not properly in place. Detected by reviewing results graph.	1	1	1	3

Table 13. Deviation/error situations in Laboratory measurements

5.4 Solution toolkit for manufacturing process steps

Solution toolkit is a set of short instruction on how to address manufacturing step issues described above. More detailed instructions are available in documentation provided to receiving sites. In some cases CAPA (Corrective Actions and Preventive Actions) process has to be initiated in order to find the root cause of the issue and implement corrective actions according to quality assurance process. Instruction of the OPF CAPA process are provided to receiving sites and process is not explained in this paper. Tools given here are a good starting point when an issue in manufacturing is encountered.

5.4.1 Compounding

Solution for assembly issues is more on-the-job practice with mentors, who verify that machine is assembled correctly. On the shelf spare parts are available from Europe within two to three days delivery time. If something major like cylinder or screw breaks, the parts delivery time is months up to six months.

Experienced maintenance person can adjust the equipment when scale equipment displacement increment is noticed.

Close co-operation with the equipment and raw-material suppliers is very important and contacts should be created by face to face visits. K-fare in Germany is a good place to meet the suppliers.

Trained persons should start immediate training for more operators in receiving location to mitigate risk of knowledge centering only on few persons.. Compounding knowledge can also be purchased from U.S. in case the in-house compounding does not work. Operators should also have a basic theoretical training about compounding basics, which was not given at OPF. Consulting or expatriate contracts with OPF experts would mitigate risks

Deviation/Issue	Solution
Feeder malfunction. Adding additive is not working.	Feeder is disassembled and re-assembled. Alarm should installed in case the feeder stops. Operators have noticed that if sieve is left a bit loose, the issue is mitigated.
Sensor malfunction	Replace faulty sensor
Raw Material issues and contamination	Raw material issues are solved with supplier and/or using external services determined by deviation- or CAPA process. Contamination issues follow the same procedure.
Production run using validated parameters not possible	Production run outside recommended parameters is solved internally using deviation- or CAPA process.

Table 14. Solutions for Compounding

Deviation/Issue	Solution
Contamination	Equipment is cleaned and deviation process initiated.
Pellet IV too high or low	Batch goes under deviation process and new measurements are taken from the batch in order to verify the results. If still invalid the Lot is scrapped and Deviation/CAPA process started.
Equipment produces defect pellets, especially the lenght can vary.	Equipment maintenance and adjustment. Especially sharpening of the blades.
Incorrect parameters	Equipment parameters are adjusted through deviation process.

Table 15. Solutions for pelletizing

5.4.2 Self-Reinforcing

Troubleshooting knowledge could be increased by more persons attending extensive training in OPF with proven capabilities to perform the step. Expert visits in receiving facility and consulting or expatriate contracts with OPF experts would also mitigate risks. Most issues are caused by inexperienced operator.

Deviation/Issue	Solution
Billet shearing strength too low or other mechanical properties out of tolerance.	Draw-ratio is to be increased and/or temperature parameters adjusted. In some cases corrective actions via Deviation- or CAPA process.
Billet surface quality poor	Parameters are adjusted and billet scrapped using deviation process.
Reinforcement process cannot be run with validated parameters	Corrective actions via deviation- or CAPA process.
Billet diameter out of tolerance	Stop the self-reinforcement, Select more suitable drag-stone and adjust drawing parameters, often lower temperature and drawing speed.

Table 16. Solutions in Self-reinforcement

5.4.3 Peeling, Cutting and Machining

Change of tools and slight adjustments if displacement increment occurs.
Two machine system used in OPF was found good especially minimizing scrap. Scrap is more expensive then machine time and special tools needed for ImplantX would occupy too many tool slots in one machine system.
Solution for high quality tool purchasing is at least in the beginning to acquire tools from the OPF tool supplier in Finland until equally high quality supplier in US is identified.
Using the same equipment in receiving site and sending site would mitigate risks, because machining programs and tools could be directly transferred. On-site-training would also be more beneficial, because trained persons could apply their new skill the same way as in sending site. No need for process changes and support from sending site would be easier to provide.

Deviation/Issue	Solution
Out of tolerance	Adjust machining parameters or Initiate Deviation- and CAPA process. Improve work instructions.
Missing measurements	More detailed instructions and supervision. Measurements can be completed afterwards with required amount of measured samples.
Fractures	Initiate Deviation process
Contamination	Initiate deviation process and based on severity CAPA process. Root cause analysis with measurements in co-operation with external service providers and corrective actions implementation.
Equipment malfunction	Initiate deviation process. Repair faulty/worn out parts and complete maintenance.
Insert issue or insert hole offcentre	Development and/or maintenance of insert tool. Insert parameter optimization.
Burr in products	Adjust machining parameters

Table 17. Solutions in Machining

5.4.4 Finishing

Solutions for the finishing process are listed in the table below.

Deviation/Issue	Solution
Paraffin content too high	Rewashing of the products. Maintenance of ultrasonic washing equipment, change of process and possible re-validation.
Unfinished product goes to next manufacturing step	Adding another inspector to check the products.
Burrs in the product	Return product to finishing for rework.
Product cannot be cleaned	Add more washing time or intensity.
Product is not dry	Adjust drying parameters and verify the result.

Table 18. Solutions in Finishing

5.4.5 Injection Moulding

OPF does 100% quality assurance verification for the instrument hole with an instrument gauge to detect issues with Instrument hole. Issue with scale feeder is solved by resetting error and restarting the machine. This does not cause scrap products or other issues. In case of power outage lasting longer than 10 minutes the defective material has to be removed and process restarted from the beginning. Mould breakage issues are solved by fixing the mould if possible or ordering a new mould from the supplier. Delivery time from Finland supplier is estimated 4-5 weeks.

Deviation/Issue	Solution
Instrument hole defect	Adjust parameters and/or do surface treatment to the core print.
Contamination	Initiate deviation- or CAPA process. Conduct Root cause analysis and implement corrections.
Suction at the base of the product	Adjust parameters
Out of tolerance	Adjust process parameters like altering switching point, raising or lowering temperature, adjusting speed and/or pressure. Adjust feeding length. If there is any changes to product measurement or form Initiate deviation- or CAPA process, because mould has to be reworked.
Physical properties out of tolerance	Adjust parameters
Product defect caused by mould damage	Sent mould for repairs. If repair not possible the new mould has to be manufactured. Estimated delivery time 2-4 weeks.

Table 19. Solutions in Injection moulding

5.4.6 Packing

Sealing equipment needs to be good and quality assurance tight that no defect products slip through. Extra care when packing bigger products.

Deviation/Issue	Solution
Seal defective	Every pouch is checked and defect pouches are scrapped. Product is re-sealed in new pouch.
Pouch is not sealed	Every Pouch is re-checked in customer packing step. Seals are checked in two manufacturing steps: in Packing and customer packing.
Contamination in the pouch	Defect pouch is scrapped and replaced. If the defect is detected in the customer packing step, the product and pouch is scrapped.
Incorrect product in the pouch	Products, amounts and labels are verified in two steps.

Table 20. Solutions in Packing

5.4.7 Gamma Packing

Solutions for the Gamma Packing process are listed in the table below.

Deviation/Issue	Solution
Products go to incorrect Gamma program	Laboratory measurements after gamma treatment
Gamma sterilization fails	Gamma dose set to required levels
Gamma dose varies	Optimize packing size and shape.

Table 21. Solutions in Gamma Packing

5.4.8 Sterilization

Solutions for the sterilization process are listed in the table below. Co-operation with the service provider and scheduled audits are key to successful operation.

Deviation/Issue	Solution
Bioburden level too high. Too low Gamma dose	Initiate deviation process. Issue verified by using external laboratory tests (Nelson, bacteria culture).
Gamma dose too high	Laboratory measurements verify that product properties have not changed beyond acceptable levels.
Package is broken during procedure	Initiate deviation- and/or CAPA process. Improve protective packaging.

Table 22. Solutions in Sterilization

5.4.9 Customer Packing

Solutions for the customer packing process are listed in the table below.

Deviation/Issue	Solution
Label information and product inside the box do not match	Improve customer packing procedures via CAPA process. Train/choose personnel who are skilled and thorough for this step. Issue can be detected in release step.
Temperature indicator is missing	Improve customer packing procedures via CAPA process. Train/choose personnel who are skilled and thorough for this step. Issue can be detected in release step.

Pouch or pouch seal defective	Visual defects are generally quite obvious. The pouch and product will be scrapped.

Table 23. Solutions in Customer Packing

5.4.10 Release

Solutions for the release process are listed in the table below

Deviation/Issue	Solution
Release of unsterile products	Initiate CAPA process
Release of products out of tolerance	Initiate CAPA process
Documentation lost or insufficient	Find the lost documentation. In some cases new measurements can be made. Initiate deviation- or CAPA process.

Table 24. Solutions in Release

5.4.11 Laboratory Measurements

Human errors cause most issues and recommended solution is providing more training and making improvements to work instructions.

Deviation/Issue	Solution
Incorrect process used in laboratory measurements	Initiate CAPA process and additional training for Laboratory personnel
Incorrect product measured	Initiate CAPA-process and additional training for Laboratory personnel how to handle samples.
Measurement device is not calibrated	Initiate CAPA process
Product incorrectly setup in the testing gauge	Correct instrument gauge is applied and the tests rerun
Analyzer computer/software crashes	Restart the equipment and rerun the measurement. Contact IT department. If problem persists initiate deviation- or CAPA process.
Issues in IV-measuring equipment	Equipment and measurement restart
Incorrect method selected with MTS equipment	Tests are rerun with correct method
Instrument tool not properly attached	Attach the instrument head properly and rerun the tests.

Table 25. Solution in laboratory measurements

5.5 Summary of proposal

Results suggest the importance of transfer planning before actual transfer operations begin. Thorough planning and clear responsibilities will help to identify and avoid issues during transfer which affect the ability to reach transfer goals. Any changes to processes/equipment should be done in sending location before the transfer if possible, in order to mitigate risks. Identifying knowledge holders in the sending organization and using them as mentors in training of experienced recipient personnel is of key importance for successful manufacturing knowledge transfer on the manufacturing floor. Cultural differences have an effect to the transfer and language in particular can be an obstacle at the beginning. A good communications plan would help mitigate cultural related risks. Once committed Finnish are professional and co-operative in the transfer project, and no significant cultural obstacles between Finnish and US personnel were encountered.

In ImplantX product transfer to US, company had to decide between two different manufacturing methods or transfer them both. Choosing Injection moulding method is recommended because it is simpler, rigorously validated and more cost efficient than the machined method. Initial results with injection moulding method has been positive and receiving organization has been able to produce quality products. Combination of thoroughly validated simpler manufacturing process, experienced injection moulding personnel at receiving site and commonly available machinery contribute to the success. Previous to Injection moulding manufacturing step are the more challenging compounding and pelletizing steps. These manufacturing steps provide raw material to injection moulding step and are vital to the process. It is recommended to secure consulting or expatriate contract with one of the process experts with extensive experience in biodegradable raw materials.

Risk Analysis of the manufacturing steps revealed most commonly encountered issues in OPF and survey with the interviews provided recommended solutions. These will most likely assist in the continuous manufacturing of ImplantX biodegradable implant product in the receiving site.

Research results suggest that the skills and processes acquired in transfer and manufacturing of ImplantX can be applied for other OPF biomaterial implant products, with the exception of self-reinforcement step of the machined process.

6 Feedback to proposal

Proposal was sent to the company for review and Managing Director of the company gave feedback in the phone interview. In his opinion the results were very truthful and valid. All the persons interviewed were either manufacturing step experts or deeply involved with the transfer project. Results can and probably will be used in the continuous production of biomaterial implants and in future manufacturing transfer projects. Thesis usefulness as a general guide was questioned, since it has a lot of company related detailed information. No changes or additions to the proposal were requested beyond removing company identifying information.

7 Conclusions

International manufacturing transfer project has many variables, barriers and driving factors that affect the outcome of the transfer. Because of the variables every transfer project is more or less unique. Manufacturing transfer is similar to any other big international project and good project management rules apply. It is recommended to have clear roles. There should be overall transfer project manager and local project manager in each site to improve communication and organization of the transfer project matters. Good planning before starting the transfer operations and identifications of transfer variables is important in order to achieve transfer goals. In this case knowledge transfer was especially important since some of the technologies and equipment transferred were proprietary. Properly documented and validated manufacturing processes and receiving sites previous experience working with biomaterials makes manufacturing transfer more feasible especially if processes are transferred without changes. All the process changes should be done at the sending site prior to the transfer. Cultural and language issues add extra challenges to the transfer, but no major issues were encountered between US and Finnish personnel. Success of the transfer project can be evaluated by comparing receiving site performance versus the sending site.

Author has compiled a best practices process for the manufacturing transfer of the biomaterial implant product, which may be used as reference for similar future transfers. Manufacturing process step risk analysis and solutions toolkit was created based on the survey and expert interviews. Reported results can be used in receiving site especially for transferred biomaterial product manufacturing step troubleshooting. Customer

was satisfied with the results and no changes or additions to the proposal were requested beyond removing company identifying information.

7.1 Next steps

Recommended next steps are to actually utilize the best practices process in the company's next similar transfer project and confirm that it can actually be used as an internal reference. Risk analysis can be used immediately to mitigate risks in relevant implant manufacturing processes of the receiving sites. Solution toolkit can also be used to prepare for possible issues that will most likely be encountered in manufacturing of relevant biomaterial implant products.

7.2 Evaluation

The following paragraphs evaluate the results of the research and its validity.

7.2.1 Outcome versus Objective

The best practices process proposal was created. Manufacturing process step risks/issues and solutions were uncovered and reported. In this sense research objectives were reached as planned. There are some manufacturing processes especially in Gamma packing and Sterilization were no expert interviews were conducted and author has little personal experience, so data in those particular processes is mostly based on the survey and knowledge gathered in prolonged engagement in the case company. Solutions for issues in these above mentioned steps are in some cases so varied that only solutions is to start Corrective Actions and Preventive Actions (CAPA) process in order to remedy the issue. Case company did not have template for manufacturing transfers when the transfer project was started. They can now use the best practices process described in this thesis as a high-level template for basis of the more detailed transfer project plan.

7.2.2 Reliability and Validity

The validity of the qualitative research is a concern.

> There is a general consensus, however, that qualitative inquirers need to demonstrate that their studies are credible (John W. Creswell and Dana L. Miller 2000).

To address the issue of validity author uses lenses of the researcher, study participants and readers. Lenses refer to researcher bringing their study under different viewpoints in order for establishing validity (John W. Creswell and Dana L. Miller 2000).

The author had worked in the case company for over five years before the transfer project was started. After transfer project was initiated the author was responsible for IT related matters in the transfer project. Researcher was not directly responsible for manufacturing transfer steps, but had continuous access and discussions about them with persons responsible. So there was prolonged engagement in the field for almost two years, which was used to validate information received from the interviews and the survey. The end result of the transfer project was the closing of the OPF operations in Finland, which also meant that researchers' position, along with the rest of the workforce in OPF would also terminate after transfer is complete. This has possible implications in terms negativity or pessimism in the views of the interviewees or survey respondents and emphasize some negative aspects of the transfer.

Persons interviewed were either part of project management or experts with years or in some cases decades of experience. Compounding expert for example had extensive theoretical and practical knowledge of the process and Doctor of technology degree. He travelled and consulted at the receiving site multiple times and was very involved with compounding transfer project. Most of the process experts had similar case. Process experts were uncovered via survey by asking participants to identify the go-to person in case they had an issue in manufacturing process step which they did not know answer to. Interviewer answers were compared and for example in the question of the transfer order, most interviewees agreed that starting from end steps of the process was the correct decision. Survey results were compiled and risk calculations were done in order to uncover highest potential risks and solutions. Project management which was actively involved in the transfer project had direct knowledge of what was going well and where there were issues. Based on their experience, experience of the process experts and relevant literature results were achieved.

References

Acronyms www.all-acronyms.com 2013
Advant Medical (2014) http://www.advantmedical.com/
Beamon, Benita M. Supply chain design and analysis: Models and methods 1998 Int. J. Production Economics 55 (1998)
Bhagat, Rabi S. and Kedia, Ben L. and Harveston, Paula D. and Triandis, Harry C. Cultural Variations in the Cross-Border Transfer of Organizational Knowledge: An Integrative Framework 2002 The Academy of Management Review, Vol. 27, No. 2 (Apr., 2002), pp. 204-221
Creganna (2014) http://www.cregannatactx.com/
Creganna Manufacturing Outsource Process: Your Template For Success 2014
Creswell, John W. and Miller, Dana L. Determining validity in Qualitative Inquiry Theory Into Practice, vol. 39, number 3, summer 2000.
Differences in Managerial Values: A Study of U.S., Hong Kong and PRC Managers Ralston, David A. and Gustafson, David J. and Cheung, Fanny M. and Terpstra, Robert H. 1993 Source: Journal of International Business Studies, Vol. 24, No. 2 (2nd Qtr., 1993), pp. 249-275
Finland subsidiary Discussions with R&D Manager 9/2012
Finland subsidiary DMR009: ImplantX version AC. 2012
Finland subsidiary e-portfolio presentation (2012)
Finland subsidiary ImplantX Survey 2013 Aki Harkivi / OPF personnel
Finland subsidiary info sessions 2009 - 2012.
Finland subsidiary Interview with Finland Transfer Project Manager 06/2013
Finland subsidiary Interview with Laboratory specialist 09/2013
Finland subsidiary Interview with Managing Director 09/2013
Finland subsidiary Interview with Production Team Leader 09/2013
Finland subsidiary Interview with Production technician 06/2013
Finland subsidiary Interview with Production technician 06/2013
Finland subsidiary Interview with Production worker 06/2013
Finland subsidiary Interview with Research Development Manager 06/2013
Finland subsidiary Interview with Senior Project manager 06/2013
Finland subsidiary Quality catalogue 2012
Finland subsidiary SOP400 AB Extrusion and Compounding 2010
Finland subsidiary SOP401 AC Self-Reinforcing 2013
Finland subsidiary TO4001 AA Ruiskuvalu 2011
Finland subsidiary TO4119 AJ Tuotteiden pakkaus puhdastilassa 2012
Finland subsidiary TO4128 AD Pakkaus: Asiakaspakkaus 12/2011
GPO Healthcare GPO (Group Purchasing organisation) Gpo-healthcare.com 2013
Hofstede, G. (1980), Culture's Consequences: International Differences in Work-related Values, Sage, Newbury Park, CA.
Kogut, Bruce and Zander, Udo Knowledge of the Firm, Combinative Capabilities, and the Replication of Technology 1992 Organization Science, Vol. 3, No. 3, Focused Issue: Management of Technology (Aug.,1992), pp. 383-397
List of recalls in US http://www.fda.gov/MedicalDevices/Safety/ListofRecalls/default.htm
Martin, Kevin C. Dr. and Perez, Arthur GAMP 5 Quality risk management approach PharmaceRsite2l Engineering, The official Magazine of ISPE May/June 2008, Vol. 28 No. 3
Miller, Raymond G. Ph.D. The Center of professional innovation and education (CfPIE) validation of computer systems on 14-15th of march 2011

Minshall, Tim and Steele, Andrew International Manufacturing mobility

http://www.ifm.eng.cam.ac.uk/research/cim/manmobility/ accessed 2014.

Murdoch, Kimberly Robyn Development of a Robust Work transfer Implementation process Massachusetts institute of technology 2004.
Nakano, Davi and Muniz Jorge Jr and Dias Batista, Edgard Jr Engaging environments: tacit knowledge sharing on the shop floor 2013 (JOURNAL OF KNOWLEDGE MANAGEMENT VOL. 17 NO. 2 2013, pp. 290-306)
North, Klaus Localising Global Production 1997
P. Törmälä Biodegradable self-reinforced composite materials; Manufacturing structure and mechanical properties 1992 Clin. Mater. Volume: 10, Issue: 1-2 Pages: 29-34
Polanyi, Michael (1966), The Tacit Dimension, New York: Anchor Day Books.
PR Newswire Association LLC. Relocation: Risky Business (1999)
Taschner, Dana http://medicaldevicerecall.com/ 2012
Teece, David J. The Transfer and Licensing of Know-How and Intellectual Property : Understanding the Multinational Enterprise in the Modern World 2008
U.S Food and Drug Administration (www.fda.gov) 2013
Universal technical resource center inc. http://www.utrs.com/technology_transfer.html 2014
US Based company Arthoscopy catalog (2013)
US Based Company Discussions with US Vice President of Operations 9/2012
US Based company Investor & Analyst Day Meeting 08/12 presentation
US Based Company RSite2 Interview with Process Engineer 08/2013
US Based company website (2013)
US subsidiary RSite1 Interview with Overall Transfer Project Manager 08/2013
Wikipedia OCR http://en.wikipedia.org/wiki/Optical_character_recognition

Appendices

Short summary of the interviews is described below.

Summary of the interview with Finland Transfer Project Manager 19-June-2013.
Interview first focused on the person's role in the transfer process as a local transfer project manager and then about case product transfer. Case transfer has been relatively successful when injection moulded method is concerned. Key points were that the process was quite new and recently developed at the sending site. Manufacturing process was rigorously validated, which helped the transfer process. Next topic of discussion was the transfer and operational organization at the sending and receiving sites. The resource differences and necessity of a backup resources was discussed and the need of a local transfer project manager in sending and receiving sites. After this there was discussion about training and knowledge transfer. Few people were sent from US for a training in multiple processes, which might be too demanding and concentration of only single process may have provide better results. Cultural differences were also discussed and differences between working culture and hierarchy was discussed. Finnish operators have much broader responsibilities then US operators, which mainly push a button and run the machine. If the problem comes, the technical specialist will come and fix it. Problems are discussed openly in Finland, which is not the case in US, where there are generally more levels of hierarchy. No major issues with the language. Next the interviewee was asked how she would have done the transfer if she could decide. The regulatory issues should be addressed at early phase and maybe earlier on-site support in receiving site would be good. Engineering level support reception could be improved on US side. Next discussion was related to measuring the success of the transfer. No breaks on deliveries to customers and products that are according to specifications should be primary goals. Scrap levels also tell a lot about performance. Then there was discussion about risks and how to mitigate them, raw material is challenging especially making small products. Manufacturing should be transferred "as is" and any changes should be made in sending location. Processes should be kept as is and find a way to work with them in receiving site.

Summary of the interview with Finland Laboratory specialist 26-Sep-2013.

Interview first focused on the person's role in the transfer process as responsible for laboratory measurements transfer training and support, then about case product laboratory measurement transfer process. Visits from receiving site were conducted and then they purchased duplicate equipment for the receiving site. After receiving equipment several visits to and from receiving site were conducted. Next topic of discussion was the laboratory measurement process. She explained all the measurements in detail, filler content measurement and verification methods for example. Next the interviewer was asked about error situations or other issues that have been encountered and possible solutions. Human error, according to her, is one of the most common reasons why measurements fail. How language and cultural differences affect the laboratory transfer was discussed and no major issues reported in that sector. Risks after transfer were discussed and one solution suggested was the building of contacts with the people, that you might assist them even after transfer is completed. Risk is that only few persons in receiving site are familiar with the complete measurement process. All the product laboratory measurements are done using same process, so it can be applied to other implant products as well.

Summary of the interview of the Managing Director 17-Sep-2013

First topic was his role in the transfer process as a local Managing Director and then the transfer pre-planning matters were discussed. There was some room for improvement in the pre-planning process. Estimated timetable was based on previous transfers was set to 18 months and receiving sites were set as two sites in US. Transfer activities were next. All Finland legal requirements in that were fulfilled and via bonus program personnel was committed to the transfer project. Safety stocks were built in order to make sure customers will always have products available during transfer period. Transfer process order was discussed and importance of setting clear roles for transfer project members came up. Training plan could have been improved and transfer project plan could have been better communicated. Sending expatriates to receiving sites would have mitigated risks according him. Local Transfer Project managers in the sites helped with a lot of practical issues, especially mitigating language and cultural issues. Usually when people spend time working in the same project, issues become common and that lowers barriers caused by cultural differences.

Finland subsidiary Interview with Production Team Leader 19.Sep-2013 an expert of finishing and packing process.

First her role in the transfer project was discussed and then there were discussion about product finishing and packing process. Training process was discussed and it would be good if trainees from US have enough time to practice finishing and packing process. Common issues in finishing was discussed and in packing process especially with thicker products the product sealing into pouches can be a challenge. Pouches are rechecked when they return from sterilization to mitigate risks. Packing is similar with the other products, so skills acquired can be applied to other products.

Finland subsidiary Interview with Production technician 26-June-2013 an expert of machining process

His role in the transfer process as machinist specialist was the first topic and the product machining process in detail was discussed next. ImplantX is manufactured using two different lathes with one operator. Special tools are used in machining. If the settings are not correct, burr can form on the products, which makes measuring product difficult for example. Finishing step is also more time-consuming if there is lot of burrs. Machinist is the one controlling the whole process. Asking how the technician would himself do the transfer, he answered that he would transfer process as it is in Finland using the same machinery and 2-3 month on-site training time for machinists would be enough for basic manufacturing. Machining programs could be directly transferred and support from Finland and on-site training would be easier if the same machinery was used in receiving site. Troubleshooting and problem solving training would require more time than 2-3 months. Biggest risks after the transfer is complete according to the technician were related to difficulty of the raw material used (Billets). Billets should be manufactured at the same facility in order to provide fast interaction with billet creators and machinists, otherwise there is an extensive risk of scrap. Process does not allow errors and tools used need to be of highest quality. Quality controls make sure that there is a very small change that any defect products reach customers.

Finland subsidiary Interview with Production worker 27-June-2013 an expert of self-reinforcement process

Her role in the transfer process was discussed first, she acted as trainer for US personnel. Self-reinforcement process was described next in detail and then common er-

ror situations and solutions were processed, like incorrect temperature settings. Settings has to be sometimes adjusted in the middle of the process and at times result is based on operators gut feeling (experience). Technician was asked how the knowledge has been transferred to US and she answered that by on-site trainings next to machine. Trainee has been taking notes and done actual hands-on practice. Cultural and language issues were effecting the training at the beginning, because common technical terms were lost and communication with foreign language was uncomfortable at first. When releasing that person understands and technical terms came more familiar, then training became easier. Future risks include having no problem solving support from sending site and getting a feeling of the process, which can only be acquired through experience. Risks could be mitigated by having experts from sending site to help ramp-up manufacturing and make sure process runs correctly. ImplantX billet self-reinforcement process is slightly different from other products, so acquired skills cannot be directly applied to other self-reinforced products.

Finland subsidiary Interview with Production technician 18-June-2013 an expert of injection moulding process

Technician's role in the transfer process was transfer of injection moulding (IM) process, extrusion process and coordinating equipment transfer. Next injection moulding process was discussed. Product implantX had 35 different sizes, which meant 35 different moulds. IM knowledge transfer has been done by training two persons on the factory floor and then making visits to receiving site. Trainees also took notes, pictures and videos of the process. One of the trainees had previous experience in IM and this made transfer much easier, because he was familiar with the basics and only working with the difficult biodegradable raw material needed to be learned. This would take about two months compared to a person with no experience in IM would take a year to learn the process. Next the issues and solutions were discussed and one of the issues encountered is the power outage. If it lasts more than 10 minutes the raw material in the injection machine cylinder becomes defect and process has to be started from the beginning. In case of mould breakage, mould has to be repaired or new mould ordered from approved supplier. Discussing about risk mitigation, he said that expatriate expert from Finland to receiving site for 6 months would mitigate possible risks encountered. Training more expert in receiving site should be started at once. He also said that scrap rate is a good measurement of the transfer success. Skills acquired in manufacturing ImplantX are transferable to other similar products as well.

Interview with Finland subsidiary Interview with Research Development Manager 19-Jun-2013 expert of extrusion process

His role was transferring functions related to compounding process. He has over 20 years of experience in compounding and biodegradable raw materials. ImplantX compounding process was discussed in great detail. Extrusion billets are made with twin-screw extruder by mixing polylactide and bioceramic components. End result of the process is a billet. It would be good for the trainees to learn theoretical and practical side of the process on-site before transfer. Knowledge of material, process and equipment is required. There was extensive discussion about possible issues and it is possible to assemble the machine incorrectly and, in worst case scenario, cause machine breakage. This can cause even six month gap in production, because some parts are custom made and have long delivery times. Process transfer success can be measured by laboratory measurements of product properties (IV, internal viscosity) and other specifications. Troubleshooting and problem solving after support from Finland operations are shut down is one of the risks, which can be mitigated by sending expert expatriates. Material and machine manufacturers cannot really help with technical compounding related issues. Compounding is the first process, so if it does not work properly the following process steps suffer, therefore this process step should be first to be transferred and planned properly, according to him. He confirmed that acquired compounding skills are transferrable to other similar products.

Finland subsidiary Interview with Senior Project manager of ImplantX 11-Jun-2013

Discussions began about the implantX product, what purpose it is used for and manufacturing methods. Next was a discussion about the communication between sending and receiving site now and before the transfer. Exchange with the one of the receiving sites had been active and good, with emails and video conferences. Knowledge transfer of engineering knowledge in addition to process knowledge is important, so that the more complete picture of the product and its properties is understood. Success of the transfer can be measured with manufacturing, scrap% and amount of customer complaints. Risks were discussed and because there are no replacement moulds, the mould breakage could cause 4-5 week delay in manufacturing. Material related risks can be mitigated by sending material experts as expatriates. There is still a risk that a lot of tacit knowledge is lost. There are probably a lot of steps in manufacturing that are

not documented in detail and are known to current operators, which have done decades of this work. The discussions continued on the ways to transfer this tacit knowledge to receiving site.

US Based Company RSite2 Interview with Process Engineer 21-Aug-2013

His role was as a supporting engineer and trainee in learning all manufacturing steps of ImplantX. Responsibility was to bring knowledge of the processes to receiving site and to start manufacturing there. Next there was discussion about manufacturing process training and methods. Hand-on training in combination with some training in theory with the people who know best is the best way according to him. The most difficult to learn is the processing of the raw material. Looking at pressures, temperature and clarity of billets is going to take experience. Cultural factors were discussed and he had previous experience from European culture, so for him difference was not that big, but some other people did not like European style of living. Daylight was different compared to US during summer months. Language was a hurdle at the beginning, but Finnish operators became much stronger when time past and felt more comfortable talking to US personnel. Office staff speaks pretty good English, so it was not a big hurdle. Next topic of discussion was how he would have done the transfer if he could decide and maybe more time for learning the raw materials is needed and transfer processes should be transferred "as is". Everybody should know there role and support other departments. He felt that no expats were needed and couple of week's trips for troubleshooting would be enough.

US subsidiary RSite1 Interview with Overall Transfer Project Manager 21-Aug-2013

Her role as a coordinator between all three facilities was discussed first. Then the topic of pre-transfer planning was discussed and how that progressed, identifying products, markets and manufacturing methods. Finding a suitable manufacturing facility of the two available, planning the amount of safety stocks that needed to cover transfer period and regulatory impact. There was also a lot of other matters that needed to be taken into account. Then discussion progressed into actual transfer activities, which included building cleanroom facilities in receiving sites, purchasing or transferring equipment, translating documentations, training personnel and other actions needed. Some process changes were done in sending site before transfer and that was a good idea according to her. Cultural and language differences were discussed and she thinks that

Finnish people have been very professional through the whole transfer and very helpful. There has been some miscommunication due to language issues according to her, but no major issues were encountered. Next discussion was about the things she would have done differently and one was that maybe she would have sent more people to train and a bit earlier. Risks were discussed next and understanding how this type of raw material responds to the manufacturing processes was the biggest concern. Risks can be mitigated by having engineers and operators spend time in sending location and possible try maintain contacts, that they might even be able to call them afterwards. After this discussion the measuring the success of the transfer was discussed and getting manufacturing up and running in the receiving sites without backorders or any kind of interruptions for delivery to customers would signal success. Then in the long run change in the complaint rate of products made in US compared to ones in Finland could be measured.

Finland subsidiary Discussions with R&D Manager 9/2012

These discussion were related to the company structure and products in general. There were multiple unrecorded discussion during September.

US Based Company Discussions with US Vice President of Operations 9/2012

There were multiple unrecorded discussions about company strategy, customer delivery goals and manufacturing best practices. Manufacturing process steps should be transferred "as is" for example.