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Product Service Systems in Health Care: Case Study of a Drug-Device Combination

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Abstract

Although often mentioned as an area in which Product-Service-Systems (PSS) possess great potential, the health care sector has not been in the focus of research in the past. This paper briefly reviews the challenges and benefits of implementing PSS and analyses the special characteristics of the health care market. A case study is then reported in which a PSS approach has been developed for a business-to-business, as well as a business-to-customer, scenario, in order to establish and then grow a market for an innovative method to treat brain tumours and neurodegenerative diseases.

Keywords

product-service systems, health care, drug-device combination, market establishment

1 Introduction

This paper presents a case study of an application of PSS to health care. It starts with a summary of the challenges and benefits of the adoption of PSS, and a summary of available design methodologies for PSS. Special characteristics of the health care market are then discussed. Finally, a health care case study is presented, centring on convection-enhanced delivery of therapeutic agents.

1.1. Challenges and Benefits of Implementing Product Service Systems

Despite the great potential of PSS and several very successful implementations in the industrial sector, there is still a certain resistance for a broader adoption of the concept [1, 2]. Putting PSS into practise requires a completely new mindset for both the company providing the PSS and the customer using the offered PSS [3]. A company developing a PSS needs to be ready to adopt the concept [4]. This adoption may include changes in organization and a significant investment of money and time [1]. Companies which have implemented a matrix organization are more like to adopt and successfully implement PSS [2].

Three major functions within a company face major impacts if the decision is made to offer PSS to a customer rather than simply a tangible product.

Firstly, the research and development (R&D) function has to gain the resources and the knowledge to be able to offer value adding services in combination with a product. R&D is also required to obtain the technical knowledge regarding the product and its constant quality improvement [5].

In addition, R&D efforts are not complete after the product launch. PSS providers increase their responsibility over the whole life cycle of a product, from development, through its use, including constant improvement, to the step of discarding and recycling. This influences development priorities. Ideally it moves designers towards a greater focus on developing more durable and recyclable products, as they may also be re-used in a PSS for other customers, or be reconfigured or updated by varying the services associated with the product [6].

Secondly, as the relationship between customers and the company changes dramatically with the implementation of PSS, a company's marketing group is likely to be faced with process redesign [5].

As PSS are inherently streamlining efforts towards the fulfilment of the final use for the customer, a different approach is necessary to collect requirements. In traditional product design, the design input consists of requirements for the product as evaluated by the marketing function. Instead of collecting this information, marketing needs to gather detailed knowledge about the final use for the customer, considering that customers may be more keen on paying for the use or the result, rather than for the operation of a product or the ownership of the product itself [7].

This approach requires a new mindset of the actors within and outside of a company. In order to collect the right data to constantly improve the PSS, the organization and communication infrastructure has to be set up to facilitate exchange between actors during the development phase and also during the performance phase of the product [2, 4].

This is the most crucial part for a positive adoption of the offering. In order to optimize and customize the PSS, users have to be involved early in the development phase to ensure the correct definition of the needs [4].

Thirdly, human capital gains importance when a producing manufacturer is enhancing products by integrating service components. Consequently human resource development is the third major function within a PSS providing company that is heavily affected [4].

For companies, PSS clearly can set the basis of improved design and quality as well as continuous innovation, which can be the strategic approach towards cost-pressure and increased competition in a global market [3].

PSS allows adding value to a product that may be hard for competitors to imitate. Especially in mature markets, adding value often is the only way to secure and further improve the market position of a company. Successfully implementing these changes, however, is not a guarantee of success with PSS. Besides the readiness of the company, customers need to be ready to accept such a concept [4]. Cultural or social barriers to the implementation of a PSS may exist. For example, end users may not feel comfortable with their lack of ownership of the tangible product, which they require to fulfil their needs. In order for customers to provide the required input for designing and enhancing PSS, processes training of those customers would almost certainly be required [4]. However, willingness to

accept such training implies that the customer requires an initial level of acceptance of the concept.
However there can also be clear advantages for the customer. Customers take advantage of better design and quality. Customized products may lead to higher degree of satisfaction with regards to their final needs. The changed ownership structures can also be counted as another benefit for the user. Despite some resistance to this concept, customers in general profit form paying for the use or - even more advantageous - the result. This takes away all responsibilities in terms of operation, availability, maintenance, insurance and recycling from the customer [4].

1.2. Designing Product Service Systems

The focus of a PSS on the final use for the customer, rather than the requirements of a product suitable to be used to fulfil such final use, change the development processes away from those used for traditional product development
Tan et al. [7] analyzed the status of research with regards to development methodologies for PSS and identified a research gap for such methodologies.
In the absence of dedicated design methodologies, most methods for designing PSS are derived from traditional product development. Instead of approaching the design of PSS with a "green-field mindset" [3] often industry tends to design systems using current practise in product design. This inherent limitation may be the reason for the restricted adoption of PSS in industry.[2].
PSS is adding complexity in terms of design. In fact it is adding new dimensions to the development process [6], since it is not sufficient to solve a problem defined by some design input requirements. In addition to this technological aspect, one needs to take in account the social as well as the cultural component. An understanding of the mindset of involved actors (such as users, and providers) is crucial to the design of a sophisticated PSS.
Considering this complexity, PSS designers require methodologies and tools to visualize the network of actors and their needs. The same is true for the graphical representation of immaterial components versus tangible products. Such visualisation allows to better understand relations and to manage the different phases of design.

PSS are complex systems having implications in technology, human resources, marketing, customer relations and communication, so it appears reasonable to derive a design methodology for PSS from involved disciplines, such as social studies, marketing, management, engineering and information science [6]. Nevertheless, those methodologies are not taking in account all aspects of PSS and may form a barrier for further innovation.

By analysing case studies, Morelli [6] proposed a generic design process in seven steps (see Table 1):

Table 1: Generic PSS design process proposed by Morelli

Design step	*Description*
Definition of value proposition	Definition of the final needs of the end user
Market analysis	Outline of the market players and the network between those players
Product/Service definition	Definition of the architecture and functionalities of the system
Use-case analysis	Analysis of several conditions of use to define functions, requirements and priorities
Tentative architecture	PSS prototype development
Test	PSS prototype testing
Final definition	Refinement of the tentative architecture based on test results

Within each of these steps for PSS design, more specific tools could then be applied to generate a best outcome.

2 The Health Care Market

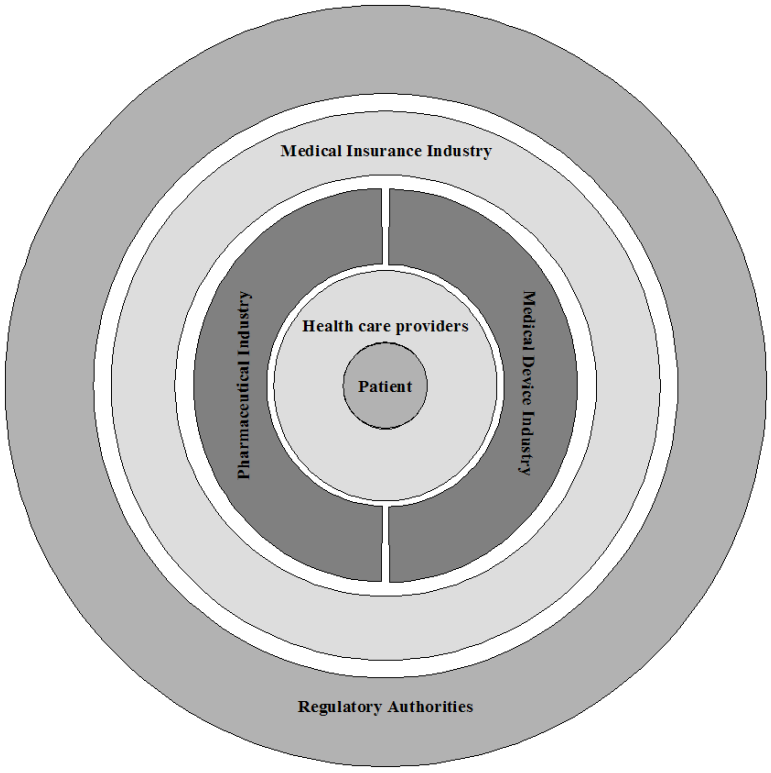
2.1. Special Characteristics of the Health Care Market

More than any other market the health care sector is regulated. This regulation is defined by governmental authorities but also by the industry itself, to mitigate the high risks often associated with development of drugs or medical devices. Considering the actors within this market, different layers of can be identified. These are summarised in Figure 1. Firstly, there are "framework defining" institutions, such as regulatory authorities and governmental, as well as private, health insurance companies.

The layer of "technology providing" companies consists of pharmaceutical companies as well as software and hardware providers. Those companies provide products, services and combinations thereof to different users. Due to the specialization in medical health care, those users most likely will consist of

specialized physicians along the diagnostic and therapeutic workflow (e.g. radiologists for diagnosis, medical oncologists, radiotherapists and surgeons for treatment of cancer). The patients as "end user" form the basic layer of actors in the market, creating the actual need for a specific diagnostic or therapeutic procedure.

Figure 1: Actors in the health care market



Considering the potentially high risks, regulatory bodies require a proof of safety and efficacy to be documented by the approval-requesting company in order to approve the marketing of drugs, medial devices or services. Compliance to all applicable regulatory standards is mandatory for any provider of products or services to enter the market[1].

Governmental regulatory authorities like the Food and Drug Administration (FDA) in the United States influence development costs for drugs, medical devices or services by setting the standards, requirements and restrictions for R&D. Governmental authorities can also shift the focus of R&D within companies by special regulations, An example of this is an accelerated approval process for technology to treat "orphan diseases" (e.g. rare diseases with small

[1] http://www.fda.gov/cdrh/

patient population) , if the unmet medical need is higher than the incentive of the market [8]. Therefore, governmental policies clearly influence the market and its players in the health care sector.

Insurance programs and companies play another major role in defining the framework of the market. Governmental health care insurance programs such as MEDICARE in the U.S. steer the market by their reimbursement policies. Besides the proof of safety and efficacy, those institutions also require additional information of the costs and benefits resulting from the adoption of a new treatment approach, compared to "standard care".

The reimbursement of drugs and procedures has a direct impact on the R&D strategy of technology providers. Studies showed that pharmaceutical companies tend to directly reinvest revenue into new R&D programs (Smith and Summers). The drug pricing set by MEDICARE or other payors affects the expected revenue and therefore has an impact on amount of money invested in R&D and as a consequence on the timelines of development programs.

Pharmaceutical companies as well as medical device companies are driven by market incentives and primarily try to maximize their return on invest. Those companies usually have to manage significant risks during the R&D phases of a drug.

The development process is divided into pre-clinical and clinical phases. The ratio of drug candidates entering the first clinical (human) phase and the succeeding therapeutics actually entering the market is only slightly above 10 to 1 in the treatment field of central nervous system (CNS) and only little higher in other areas [9].

Time to market usually has a direct impact on the revenue of pharmaceutical companies. Potential products are usually first protected in a patent and then further developed to enter the market. Therefore, shorter the development time, the longer is the monopolistic period on the market, which leads to significantly higher profitability of the drug.

Health care providers such as physicians primarily have the goal to treat patents in the best possible way. This group of players in the market can be a huge resource for the industry in R&D as well as marketing. Based on their specialized medical knowledge and their experience in daily clinical routine, physicians are the biggest source of new ideas.

Once those ideas are taken up by the industry, physicians are facilitating the creation of the mandatory data for verification and validation of new products. As a reward for this support, physicians can improve their standing as part of the research community (e.g. by publishing results about new treatment technologies). Being the experts and opinion leaders in their specific field of research, they also have the potential of being a marketing and lobbying resource for pharmaceutical or medical device companies, educating colleagues, but also regulatory authorities and insurance companies, on advantages of new products.

Patients as the inner core of the market initially create the medical need. In the past, they played a quite passive role in the market, but due to better availability and transparency within the health care market, patients may now actively decide on which physician or institution they choose. Having better access to information about latest developments, patients also want to be part of the treatment decisions and stimulate health care providers to constantly improve quality of care.

Derived from the individual goals of each actor, dependencies between such actors can be identified (see Table 2). Those dependences need to be considered in PSS design.

Table 2: Goals and dependencies of actors in the health care market

	Regulatory Authorities	*Insurance Companies*	*Pharmaceutical Industry*	*Medical Device Industry*	*Health Care Provider*	*Patient*
Regulatory authorities	N/A		Proof of safety Proof of efficacy Documentation QM-System	Proof of safety Proof of efficacy Documentation QM-System	Improved safety and efficacy Minimal impact on daily life	N/A
Insurance companies	Reliable and independent analysis of safety and efficacy	N/A	Documented regulat. approval Proof of cost efficacy	Documented regulat. approval Proof of cost efficacy	High quality of care Standardization Cost efficacy	Compliance to treatment
Pharmaceutical Industry	Guidelines for R&D Accelerated procedures	Reimbursement codes for agents	N/A	Tailored devices and technologies Simplicity Consultation	Input/Feedback Participate in trials	Acceptance of approved drugs Participate in trials
Medical Device Industry	Guidelines for R&D Accelerated procedures	Reimbursement codes for procedures	Consultation Knowledge about mode of action	N/A	Input/Feedback Verification & Validation Publications	Acceptance of treatment procedures
Health care provider (physicians)	Reliable review of safety and efficacy of drugs and devices	Reimbursement for treatment procedures and drug prescriptions	Innovations Appreciation of feedback and consultation	Innovations Appreciation of feedback Easy to use devices	N/A	Compliance to treatment
Patient	Reliable review of safety and efficacy of drugs and devices	Working reimbursement procedures	Improved safety and efficacy Minimal side-effects	Improved safety and efficacy Minimal impact on daily life	Provision of best possible treatment Education (disease and treatment)	N/A

2.2. Product Service Systems in Health Care

The health care sector is frequently mentioned in PSS research to be one of the areas where the combination of tangible products and intangible services appears to offer great opportunity for innovation and improvement [4]. However, actual case studies are lacking in the literature.

Nevertheless, the health care sector is facing the same trends towards servitization as other industry sectors, – in some cases to an even higher degree. Therefore, it appears appropriate to analyse the specific implications for this sector.

Despite the lack of academic research, big medical device companies like General Electric Medical Systems were eager to adopt PSS concepts at an early stage [10]. This strategic transition, however, proved to be a formidable challenge even for such big, well managed companies.

As in other industry sectors, globalisation and its secondary effects have its impact on players in the health care sector. Being in a much more competitive market, the need to differentiate becomes increasingly crucial.

Spending on health care, projected to be 16,2% of the growth domestic product (GDP) in the United States (2007), has grown consistently faster than the overall economy since the 1960s [11]. However, owing to this explosion of costs in health care, the pressure to reduce cost can be considered to be significantly higher than in other areas.

The medical sector, being one of the most innovative segments, is facing an accelerating trend to specialization. Since knowledge rapidly increases and diagnosis as well as treatment gets more and more patient specific, the whole network of actors is gaining complexity.

"Integration" therefore becomes a significant value proposition, which, however, often is a multi-dimensional challenge. The integration of a product into a, for example clinical, workflow is one of those dimensions, often requiring additional services such as consulting, training and education.

Another integration is that of products into other tangible products. Those products may not only include devices but also combinations of drugs and devices, where malfunctions of the whole systems have to be eliminated.

Last but not least, products (e.g. operating rooms) may need to be integrated into, for example hospital, infrastructure for optimal usage.

Considering these dimensions, clinicians, chemists, biologists, software and IT specialists, mechanical engineers, civil engineers, and even architects may be involved in such integration processes. This increasing need of integration outlines a huge potential for service components and PSS in this market.
Another clear benefit of PSS in heath care is the close relationship to the user. The communication between, for example, a developer of medical devices and the end user, namely the physician - probably focused on certain specialties, for example, neurosurgery - faces fundamental difficulties due to the different knowledge background of actors and the different terminologies. A well defined PSS, including a close relationship between developer and customer, facilitates the knowledge transfer and constantly improves the communication between these groups. This ultimately will improve the quality of the provided PSS.
At the same time, medical knowledge is crucial in many cases to actually define requirements and restrictions and to identify the final need for the user. Therefore, a close cooperation between the user and R&D is the key to enhance health care. By constantly collecting data about usage, as it is often implemented in PSS, and by taking customer feedback into account, sustainability can be achieved in this sector as the quality of medical devices enhances the quality of care.
Product service systems may allow establishing new market segments by offering tailored solutions to a customer's need. As the market evolves, such PSS may be modified to address new customer groups or new market scenarios.
However, the readiness to adopt new procedures, technologies and services may significantly be reduced by a risk-adverse behaviour of each of the actors.
Even in highly research driven and innovative areas such as the health care sector, there is a significant barrier for innovations to be taken up by the market, and replace the current "golden standard" of care, owing to the common goal of all actors to minimize their risk. PSS may enable pioneers to enhance their products by complementary service offerings suitable to address this issue.
Supplementary services, for example user training, user monitoring and according retraining, as well as retrospective analysis of usage, allows to minimize the risk considered to be associated with new products and procedures. While training and consulting services often have a direct impact on the risk profile, other services in PSS are designed to generate data for further improvement to mitigate indirectly the risks. For product innovations, additional service components can open up the

market by creating user acceptance. Added services increase the confidence in using new technologies and therefore PSS can reach a certain threshold of security in opening a market, while an innovative product on its own may not reach this level of user acceptance.

From PSS provider points of view, this decreases economic risks associated with innovative developments, since the combination of products and services may enhance the market penetration and increase the user base.

3. Case Study: Convection-Enhanced Delivery

3.1. Methodology and Sectoral-Relevance of the Case Study

The seven-step methodology suggested by Morelli (see section 1.3) has been followed in this case study for the definition of value proposition, a market analysis, the product/service definition and a use-case analysis.
Especially for the business-to-business PSS, the testing phase, followed by the final definition, is replaced by individual discussions with contract partners (in this case pharmaceutical companies). Instead of having the market challenging the system, the PSS has to be individually tailored to a specific customer. In this case study only the generic part of the development is reported.

Major parts of the business-to-business model outlined in the presented case study have been applied in a collaboration between pharmaceutical company A and medical device company B (see Table 3) to carry out an multinational clinical trial. This initial model was then modified based on a retrospective analysis of the collaboration. The enhanced model has been validated in several expert discussions, between medical device company B and pharmaceutical companies similar to pharmaceutical company A with regards to business relevant variables. The business-to-customer model has been developed based on expert discussions between pharmaceutical company A and medical device company B, validated in subsequent expert discussions between medical device company B and pharmaceutical companies substantially similar to pharmaceutical company A.

Table 3: Details on companies involved in the case study

Company	*Investor structure*	*No. of employees*
Pharmaceutical company A	Public traded	10-500
Medical device company B	privately held	500-1000

The following case study refers to direct, convection-enhanced delivery of therapeutic agents into brain tissue to treat aggressive brain tumours or neurodegenerative diseases.
This innovative treatment method requires a highly interdisciplinary approach to transfer it from research to market [12]. As the treatment includes drugs as well as

several medical devices, results of this case study should widely be applicable for the more generic, emerging segment of drug-device combinations.
This combination of drugs and medical devices is a recent trend in the health care sector [13]. This is particularly true for the field of local delivery, which necessitates that pharmaceutical companies and medical device manufacturers to work jointly on the research and development issues [14]. In contrast to systemic delivery of therapeutics, where drugs are given by pills or intravenous injection, local drug delivery allows the drug to be placed exactly at the location in the body where it is needed. This leads to a high therapeutic concentration at the target, while the systemic concentration in the body is relatively low, causing less side effects and toxicity.
Regulatory authorities like the Food & Drug Administration (FDA) are also addressing this trend by establishing guidelines [15]. Accordingly, the European Commission has also published guidelines for combined devices [16].

3.2. Technological Background

Despite impressive advances in medicine, the treatment of diseases related to the brain such as certain types of aggressive brain tumours and many neurodegenerative diseases still presents one of the biggest areas of unmet medical need. This is mainly due to the fact that the brain is protected by the "blood brain barrier" (BBB), which prevents it from being damaged or poisoned by substances in the human blood stream. While being vital for healthy people, this barrier becomes a major obstacle for the treatment of many diseases affecting the central nervous system (CNS). Promising drugs for the treatment of primary brain tumours such as Glioblasoma mulitforme (GBM) or neurodegenerative diseases such as Parkinson's, Alzheimer's, Multiple Sclerosis (MS), and epilepsy have failed in human trials over the last decades, although these drugs showed great potential in preclinical studies [17, 18]. Those disappointing results are most likely derived from the fact that the drug molecules never reached their target within the brain [17].
Convection-enhanced delivery (CED) is a promising approach to circumvent the BBB. The drug is delivered directly to the target site within the brain tissue, by placing a catheter into the clinical target and applying a positive pressure gradient to push the drug into the tissue. In practice, this approach, which is superficially

simple, has been found to be highly complex, since the distribution of the drug is heavily depending on patient specific anatomical structures and pathology. Planning therefore is a very crucial part of the procedure and the technique requires a multidisciplinary approach to achieve significant improvement of the patient outcome.

From a technological perspective a tailored system of a safe and effective drug, a patient specific treatment planning system and a dedicated set of devices (such as catheters and pumps) is necessary to ensure the delivery of the correct drug in the correct concentration to the correct target area in a defined period of infusion. The state of the art in this area is represented by catheter systems that promote convection-enhanced diffusion as the infusion mode. Additionally, users, in this case the relevant health-care professionals, need to be trained in the usage of the software and hardware tools provided in order to use them in the most optimum manner.

An overview of the system is as follows. Several magnetic resonance (MR) image series of the patient's brain are acquired for planning purposes. These scans are loaded into a planning software tool in order to plan the exact locations of the drug target and entry points of catheters placed into the target tissue. This planning must be based on the patient specific imaging data as it has to take in account the individual anatomy and pathology of the patient.

The main target of this pre-operational planning is to make sure that a convective flow is established within the solid tissue of the brain and that no drug leaks into the cerebrospinal fluid (CSF) compartment. Secondly, a maximum coverage of the previously defined clinical target volume is the goal of the planning exercise. Once the treatment plan is finalized, the required data needs to be transferred to the operating room (OR).

The neurosurgeon will then place the catheters according to the plan using the planning data for navigational purposes. Once all catheters are in place and are connected to the infusion pumps containing the drug, the patient will be scanned again to verify the actual position of the catheters.

For infusion, the patient will be hospitalized for several days to allow the whole drug volume to enter the patient at the required low, constant flow rate. During and after the infusion there may be several control scans to monitor the treatment.

3.3. Market Analysis and Value Proposition

As outlined above, a system based on infusion via convection-enhanced diffusion (CED) shows promise as a delivery method for drugs to allow them to reach therapeutic concentrations in a significant volume of the brain.

This approach however is technically very challenging. Considerable research is required to develop tools for the delivery of drugs via catheters placed into the solid target tissue.

The current state of the art is represented by the successful development of a software tool to aid the critical step of pre-operative planning of the infusions. This has allowed a deeper understanding of the underlying principles to be accumulated by the development team.

Since such knowledge and tools are usually not available within pharmaceutical companies, a joint approach is then required to bring the delivery technology, in combination with a working drug, to the market.

This special technological situation combined with the restrictive regulatory framework leads to two consecutive use cases:

- A business-to-business PSS to provide a "one-stop-shop" for pharmaceutical companies to manage clinical development and to open up the market by getting approval for the drug-device combination
- A business-to-customer PSS to grow market acceptance once the market is opened up by having regulatory approval.

These two cases are discussed in more detail below.

The first scenario is required to open up the market for a drug in combination with the drug infusion systems. In such a scenario, the PSS would mainly be focused on the "business to business" relationship between the medical device company delivering software and hardware tools and the pharmaceutical company providing the drug.

In this scenario, the medical device company has to convince pharmaceutical companies of the potential of the technology. Further, it has to justify, in comparison with current practice, any additional risks associated with aspects of the treatment such as the required surgery.

Identifying information gaps for all actors in the market serves as an indicator of the issues that need to be addressed by suitable PSS in order to enhance the acceptance of the infusion method and create the market. Table 4 shows a list of

actors in the market including their generic goals and the main restrictions they face.

Table 4: Actors and their goals and restrictions

Actor	*Goal*	*Restrictions*
Patients	Optimal treatment	Training/knowledge of doctors
Doctors	Provision of optimal treatment	Knowledge
		Availability of drugs
		Availability of tools
		Training
		Access to innovative developments
Pharmaceutical & Medical device companies	Profitable provision of drugs and medical devices	Clinical input
		Verification
		Validation
		Reimbursement
		Clinical feedback
Insurance companies	Cost efficient, safe and effective treatment	Knowledge about technologies
		Availability of cost data (treatment costs and cost of care)
Regulatory Authorities	Safe and effective treatment	Knowledge about technologies

After the market is opened up by means of the business-to-business PSS, a second "business-to-customer" PSS scenario is required to ensure fast market acceptance and market penetration of the drug-device combination.

The generic value proposition for convection-enhanced delivery, valid for both PSS scenarios is to reliably deliver a therapeutic agent to a specific clinical target within a patient's brain.

In the first, business-to-business PSS, this value proposition offers the pharmaceutical company, as the "user" of the system, firstly, all the required tools (products) to operate the system successfully (e.g. planning software, reviewing software, data management infrastructure) and, secondly, the services (consulting, data management, quality assurance, trainings, review processes, on-site support) to successfully run a clinical trial, minimizing the risk of trial failure.

In the business-to-customer PSS, the value proposition is targeted towards the neurosurgeon, as the "user" of such a system. The user can minimize the risks of treatment by having available the right tools (e.g. planning software, catheters, infusion pumps, etc.) and services (e.g. training, on-site support, etc.).

Creating this market penetration is obviously of value for both providers of the drug device combination.

3.4. Users Analysis

Based on Morelli's proposed methodology, the users of both PSS scenarios have been analysed. In the business-to-business model, a pharmaceutical company in the market of brain tumours would be the customer for the products and services. In the second business-to-customer model, the customer would be any neurosurgeon who wants to treat brain tumour patients with this specific drug-device combination.

Table 5 shows the results of a users analysis for the business-to-business PSS, where pharmaceutical companies are the user.

Table 5: Actors analysis – Pharmaceutical Companies

Pharmaceutical companies	
Goals	Have approved drugs on the market to effectively treat high-grade brain tumours.
Key Problems	The blood-brain-barrier (BBB) prevents large molecules from entering the brain through the blood cycle.
Problem solving strategies	Circumvent the BBB by directly delivering the therapeutic agent to the target tissue within the brain.
Requirements to be met by the problem-solving strategies	Availability of reliable, easy to use technology for direct drug delivery Availability of users capable of using the technology
Current theories	Drug distribution within the brain is dependant on patient specific anatomy and pathology.
Tacit knowledge	To be effective, the anti cancer agent needs to reach therapeutic concentration level within the target volume
Design methods & criteria	Minimal invasive surgical procedures Surgical workflow based on well-known standard procedures Intuitive and fast planning of the surgery Patient specific planning
Users' practice	Pharmaceutical companies are used to perform and manage clinical trials without the technological complexity associated with local delivery of the drug
Perceived substitution function	Technological complexity of local drug delivery
Exemplary artefacts	-

Table 6 summarizes the analysis of neurosurgeons as the target group for a PSS offered, once the market is created and the drug-device combination is available for routine clinical use.

Table 6: Actors analysis – Neurosurgeons

Neurosurgeons	
Goals	Provide best possible treatment approach
	Be well educated and trained for treatment approach
	Minimize impact of treatment on daily life of patient
	Increase survival rates
	Improve quality of life
Key Problems	Probability of recurrence[2] is extremely high
	Prognosis is very poor, independent of the treatment
	Tumour resection[3] (surgery) is highly invasive
	Radiotherapy has major side effects
	Chemotherapy has minimal effect and major side effects
Problem solving strategies	Direct delivery of therapeutic agent to the tumour and surrounding tissue
Requirements to be met by the problem solving strategies	Reliability of treatment method
	Ease of use of required tools
	Appropriate training
	Appropriate on-site support
Current theories	Drug distribution within the brain is dependant on patient specific anatomy and pathology.
Tacit knowledge	Minimal invasive treatment is required
Design methods & criteria	Minimal invasive surgical procedures
	Surgical workflow based on well-known standard procedures
	Intuitive and fast planning of the surgery
	Patient specific planning
Users' practice	Precise placement of biopsy needles in order to take tissue samples from a specified target volume within the brain.
Perceived substitution function	-
Exemplary artefacts	-

3.5. Product/Service Definition

Derived from the users analysis, several service components have been identified as crucial for the success of both PSS scenarios (see Table 7). Those services may be combined with the product (software tool for treatment planning including a simulation of drug distribution within the brain tissue based on patient specific imaging data) to multiply the use of the software features. The software may, for example, not only be used by neurosurgeons to plan treatments. Reviewers auditing neurosurgeons in clinical trials to ensure high compliance to the outlined

[2] return of disease after tumour removal
[3] removal of tumour in a surgical procedure

trial protocol may also use this tool. Outside the clinical field, the software may also be offered in a business-to-business context to help catheter developers in their development by simulating different design methods. Knowledge gathered during the development of the product can be directly translated into services to capitalize on this knowledge.

Services may also be tailored to both PSS scenarios. The training of neurosurgeons, for example, is required during a trail to minimize failure of the trial due to human error, but this is obviously also is of great importance once the treatment is available on the market.

The presentation of such services as training however may change depending on the target group. While for a small study, the PSS developers can do the training personally, the same training content may have to be provided by a service force if a worldwide trial is carried out. To translate this service into the business-to-customer scenario, with the possibility that any neurosurgeon has to be trained, supporting tools such as e-learning modules have to be applied to keep the quality of training high.

Table 7: Product and service components

Services	*Description*
Planning software tool	The planning tool is the technological basis for the treatment. It can also be recombined with services.
Clinical trial preparation	Results and expert knowledge gathered during R&D (incl. verification and validation) can be offered as a consulting service.
Consulting on CED technologies	
Consulting on trial design	
Consulting on drug selection for CED	
Consulting on patient selection	This service covers the lack of technological expertise regarding CED methods in pharmaceutical companies.
Data management for clinical trials	Software may be used as platform to generate compatible data basis for review processes or retrospective analysis
Quality management for clinical trials	Software may be used as platform to review performance on a patient-by-patient basis. This reduces risk of trail failure, since corrective measures can be taken during the trial.
Training	Software tool and expert knowledge may be used to train all involved persons (neurosurgeons, radiologists, nurses)
Technological background of CED	
Obtaining useful medical imaging	

Use of software (catheter planning) *Placement of catheters (surgical workflow)* *Infusion processes at bed site* *Re-training if required due to results of reviews*	
On-site support	Use in-house experts trained on software to consult with neurosurgeons during the planning phase and the surgical procedure

3.6. Use-Case Analysis and PSS Architecture

Bearing in mind the previously defined product and service components, the two basic use-cases have been analysed to design and visualize PSS suitable to establish a new market and to maintain and grow such a market afterwards.

3.6.1. The Business-to-Customer Scenario

Although chronologically second, the use case for the scenario after the market has been created has been analysed first, as the efforts to establishing the market may be to no purpose if the method of making the drug delivery route reliable, and clinically routine is not designed correctly.

Figure 2 illustrates a (simplified) clinical workflow for a patient eligible for treatment. The figure shows the tools and the environment required as well as the clinical staff involved in the process of diagnosis and treatment. Once a patient enters the workflow, several diagnostic tests will be conducted. For brain tumour patients this will include medical imaging. To acquire these medical images, a scanner, and scanner software to process the information, are required.

The flow of data and the processing has to be integrated into the system to further use this information for diagnosis, patient education, treatment planning and surgical treatment as well as for retrospective analysis and disease monitoring.

Once the patient is referred to treatment, the planning software may take available data from the diagnostic imaging (additional imaging may be acquired upon request) for the treatment planning. A neurosurgeon will then use the software tool to plan the treatment based on the patient-specific imaging data to ensure a high coverage of the clinical target. The finalized treatment plan can then be transferred to the OR, where the pre-planned catheters are surgically placed by the neurosurgeon.

Once the surgical procedure is completed, the infusion of the anti cancer drug will be started at the intensive care station. To monitor the treatment outcome, follow-up scans are performed. The complexity of treatment planning for such drug infusion techniques requires additional services, such as training of neurosurgeons (to plan and actually place catheters correctly during surgery), radiologists (to acquire the right medical images for the treatment planning) and nurses (to correctly maintain the infusion).

As a single component, like a working drug is not sufficient to treat patients and therefore generate the safety and efficacy data required for market approval, an integrated PSS addressing all these requirements is mandatory to get a drug, delivered with a catheter-based infusion technique, onto the market.

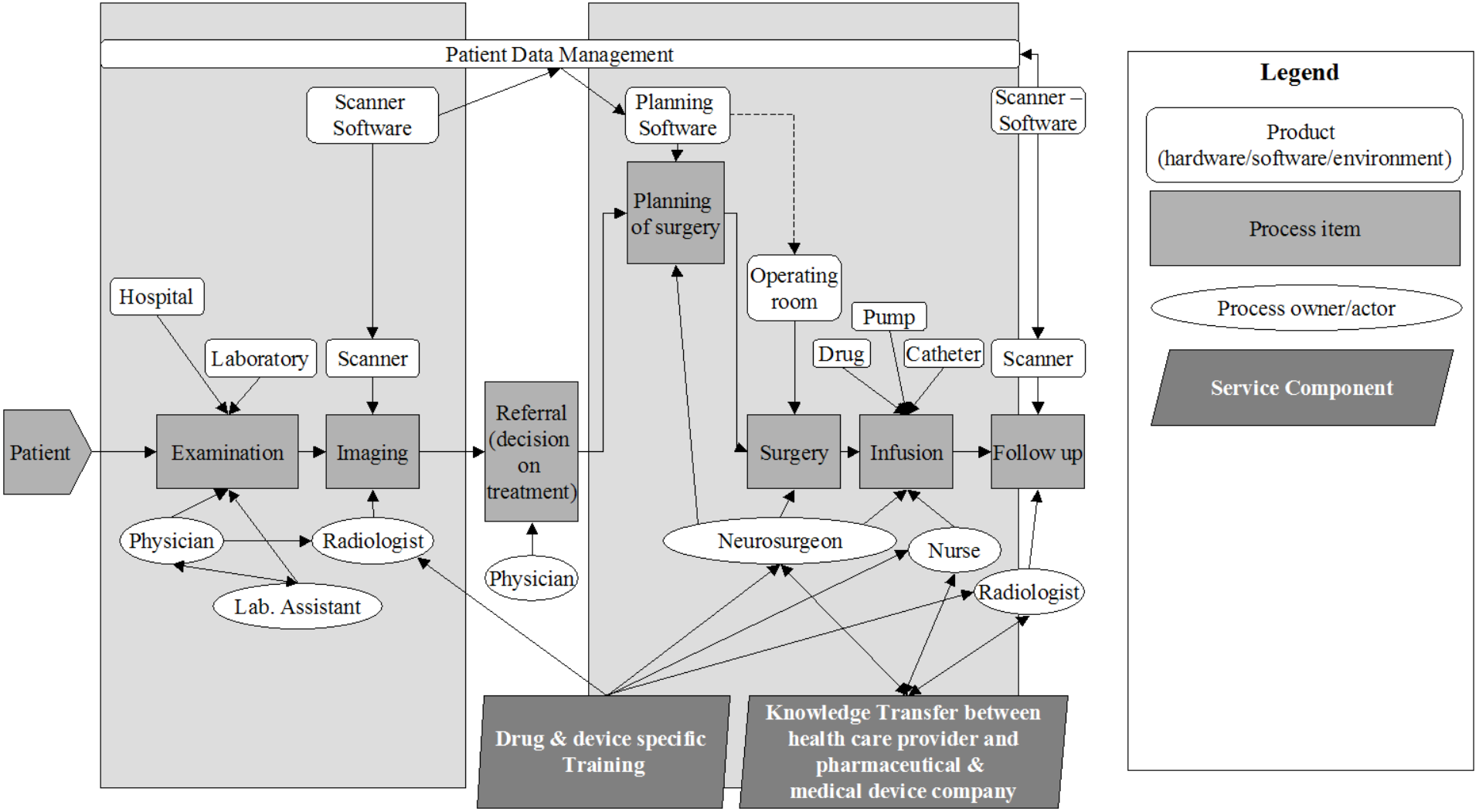


Figure 2: Visualization of use-case for the business-to-customer PSS

Looking at this proposed workflow, the required features of products and services can be recognised.

Table 8 lists the key features identified for the planning software in order to facilitate the catheter planning and placement process.

Table 8: Critical product features

Key software features
Ease of use / no time consuming planning
Automatic image analysis
Outline of clinical targets
Ability to communicate with hospital data management system (PACS[4])
Ability to fuse (overlay) scans from different time points
Compatibility with surgical navigation system
Integration with catheter technology (e.g. consideration of catheter diameter in the planning)
Integration with pump technology (e.g. consideration of pressure fluctuations caused by the pump)

Additionally, the following service-oriented features have been identified for the business-to-customer scenario (see Table 9):

Table 9: Critical service features for a business-to-customer scenario

Key service features
Appropriate knowledge transfer from R&D into clinic
Training on planning software use
Consulting on surgical workflow
Training on catheter handling
Consulting on integration into hospital IT
Consulting on protocols for medical imaging required for planning
Easy access to information for retraining (e.g. web based e-learning tools)
Availability of on-site support, if required
Feedback processes to incorporate users feedback in enhanced developments

3.6.2. The Business-to-Business Scenario

Figure 3 shows a visualization of a use-case scenario[5] as the basis for the business-to-business PSS required in order to obtain approval for clinical use for a drug-infusion method combination.

[4] Picture Archiving and Communication System (PACS)
[5] based on Morelli

A pharmaceutical company developing drugs for brain tumours (or neurodegenerative diseases) would have to make decisions about how newly developed drugs in the R&D pipeline should be delivered to the clinical target. Such a company may also consider further screening of drugs which have been previously developed. Of interest would be those drugs where there is clear indication of effectiveness, but where the drug failed in previous trials for particular sets of reasons. Where those reasons for failure include the drug failing to reach the clinical target, or showing unacceptable side effects when given systemically[6], such drugs may be reconsidered for use in combination with a new infusion system.

This screening process requires an in-depth understanding of underlying principles of the infusion mode, which can be offered to a pharmaceutical company as a consulting service, using knowledge derived from the knowledge base in R&D.

A significant barrier for pharmaceutical companies to actually use infusion as a delivery method for their molecules is that this technology adds to the complexity to the treatment and, therefore, also to the setup of a clinical trial. By offering services to close gaps of expertise and knowledge, those barriers can be eliminated.

By consulting drug companies on the design of the clinical trial in the planning phase and also the management of the trial, risks of trial failure can be mitigated.

[6] given orally or intravenously

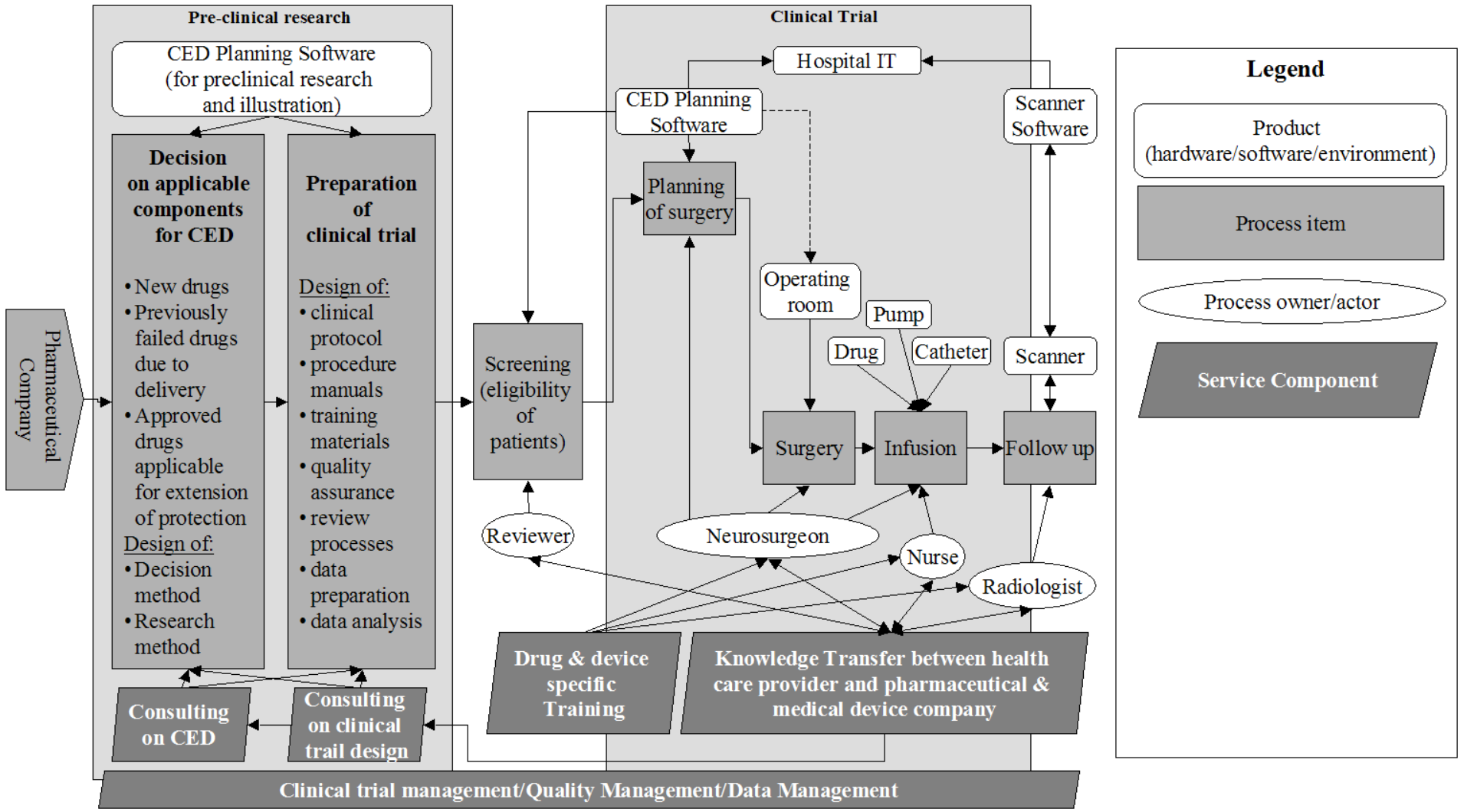


Figure 3: Visualization of use-case for the business-to-business PSS

Table 10: Critical service features for a business-to-business scenario

Key service features
Consulting on clinical protocols and procedures
Availability of training materials
Data management for clinical trials (especially processing of imaging data)
Quality management of clinical trials (review and audit processes by means of the planning software as a review tool)
Training on planning software use (for neurosurgeons)
Training on infusion procedures (for nurses)
Training on imaging protocols (for radiologists)
Consulting on surgical workflow (for neurosurgeons)
Training on catheter handling and placement (for neurosurgeons)
Easy access to information for retraining (e.g. web based e-learning tools)
Availability of on-site support, if required
Analysis of patient data during the trial to minimize risk of trial failure
Analysis of data in the light of predefined research questions
Feedback processes to incorporate users feedback in enhanced developments

The analysis of the presented case study suggests that further research on PSS applied in the field of health care is required to identify areas where benefits of PSS match unmet needs in the health care sector. Subsectors within the health care sector will have to be analyzed with regards to potential added benefit by means of PSS. In addition, guidelines for designing and implementing PSS in a health care market environment have to be developed and validated in order to facilitate adoption in the industry.

4 Conclusions

Product Service Systems in health care have not been in the focus of PSS research in the past, although the concept holds great potential to address major challenges in this sector.

The cost explosion and additional cost pressure resulting from globalization is a serious threat to the industry also in the health care sector. PSS is a useful tool to reduce costs and resources while maximizing the outcome. Companies can capitalize on the knowledge they generate during the research and development process of a product, by selling this knowledge in separate services. In addition,

products may also be reused in combination with several different services. This is especially true for software products, which can easily be recombined with services to provide additional benefit for a customer group or to exploit new markets.

Due to the high degree of specialization in medical health care and increased complexity of technology, integration of technologies, products and services becomes a whole field of new service components expected by the customer. Products (tools) and information have to be available at the right point and in required quality during more complex clinical workflows facing a significant increase of actors and interfaces caused by specialization and digitalization of patient data.

PSS offers the chance to establish an extremely close relationship to the user. This is of special benefit for developers in the health care sector, since the knowledge gap between developers (e.g. engineers or software developers) and physicians is generally quite wide. From a company's perspective PSS creates an access to customers as part of the R&D and quality management processes owing to this close relationship.

In a business-to-business scenario, closer relationships can be established between business partners. Those business relations are more likely to be of a cooperative nature, since PSS ultimately focus on the final benefit for the end user, which streamlines efforts of all partners towards the same goal. This stands in contrast to, for example, supply chain thinking, were each participant in the chain tries to maximize its revenue on the following company in the chain and in fact may not beware of the final customer. Processes can be optimized on a higher level by having this common final goal.

The interdisciplinary approaches required for the success of combinations of drug and drug-delivery techniques set a high requirement on communication between users and developers.

Since PSS causes the designer of those systems to focus on the final customer need, it is a very helpful tool for strategic considerations. The combination of products and services may have the critical mass to establish the market, while a product on its own may face too many barriers. Those barriers for a market entry can be specifically eliminated with additional services. In addition, knowledge created during the development process can be sold as consulting and training

services leading to increased revenue but also creating additional benefit for the user.

Once on the market PSS can increase market acceptance compared to a product without supplementary services. Especially in the launch of a PSS, this can lead to a broader base of potential customers, for example if services are offered that educate customers in using a product that usually would just be used by a small group of experts. Additionally, the market penetration can be increased, if services and products are designed for an easier user adoption.

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