

Reducing the environmental impact of syringes in the Intensive Care Unit



Colofon

Master Thesis - Integrated Product Design & Medisign
Industrial Design Engineering - TU Delft

Reducing the environmental impact of syringes in the Intensive Care Unit

Defended on the 25th of February 2022

Written by Margot Honkoop

TU Delft supervision by Dr. ir. Armağan Albayrak

Prof. dr. Ruud Balkenende

Erasmus MC supervision by Dr. Nicole Hunfeld

Executive summary

This graduation project focused on reducing the environmental impact of syringes on the Intensive Care Unit (ICU) of Erasmus University Medical Centre (MC) by designing solutions based on circular economy.

The ICU of Erasmus MC produces an excessive amount of waste and initiated the transition towards a circular ICU. Syringes and their packaging are defined as an impact hotspot product at the ICU, due to the product properties, extensive use (24 per patient per day), and the fact that it is a single-use disposable product. The underlying problem of the high environmental impact of syringes is the current linear life cycle. This needs to be transformed into a more circular system by design, to limit the amount of waste and to reduce the use of natural resources.

The goal of this project was therefore to redesign the syringes, their packaging and their use, according to circular design strategies suitable for medical products, to decrease the environmental impact. The use of syringes should remain convenient and safe for the healthcare staff and patients.

Research was executed to understand the context. This consisted of literature, user and product research. Furthermore, a waste audit and a life cycle analysis were performed. It showed that decreasing the impact of syringes is not only about the product itself. Manufacturing, preparing, using and disposing of all contribute to the environmental impact of the syringe. Various possible interventions were derived from this research. Firstly, adapting the infection prevention protocol and behaviour of the staff could lead to a decrease in unused disposed syringes. Secondly, separating infectious waste from general hospital waste

properly could result in opportunities for recycling.

Thirdly, the syringe itself can be redesigned to reduce the impact by changing the material to a sustainable alternative and redesigning the shape for (partial) reuse.

Lastly, the impact of the filling process could be reduced. It was concluded from research that prefilled sterilised syringes (PFSS) are more environmentally friendly than manually filled syringes because they are produced in large batches and, therefore, have fewer by-products per syringe. However, a life cycle analysis of the filling process of PFSS showed various impact hotspots in this filling process, such as the sterilisation phase, materials used, and left-over medication.

The final design is a process optimisation for batch-produced PFSS, based on circular strategies such as reduce, reuse, rethink and repurpose. Interventions include: eliminating the first sterilisation phase, reduce left-over medication and change from steam to gamma sterilisation. The proposed interventions have been evaluated by discussion.

In the end, the environmental impact of syringes is reduced by optimising the filling process, which resulted in decreasing the amount of waste, material, energy and water usage, while remaining safe and without increasing the workload of the staff of the ICU.

List of abbreviations

COC – cyclic olefin copolymer

EoL – End-of-life

FU - functional unit

GHG – greenhouse gas

GWP – global warming potential

ICU – intensive care unit

LCA – life cycle analysis

LDPE – low-density polyethylene

MC – Medical Centre

PA – polyamide

PC – polycarbonate

PFSS – prefilled sterilised syringes

PICU – paediatric intensive care unit

PoR – program of requirements

PP – polypropylene

PT - pharmacy technician

RTU – ready to use

SZA – Specifiek Ziekenhuis Afval (specific hospital waste)

Table of contents

Executive summary	3	7. Design vision and program of requirements	46
List of abbreviations	4	7.1 List of requirements	46
1. Introduction	6	7.2 Design vision	46
1.1 Project brief	6	8. Ideation of possible interventions	47
1.2 Background on the impact of the ICU	6	9. Design conceptualisation	50
1.3 Problem statement	8	9.1 Choosing a design direction	50
1.4 Research questions	9	9.2 Developing concepts	52
2. Method	10	9.3 Selecting one concept	56
3. Circular economy strategies for disposable syringes	12	10. Detailing the concept: optimising the filling process	58
4. Waste audit at the PICU	16	10.1 Explanation per intervention	60
5. The syringe from a user's perspective	19	10.2 Coherence between interventions	66
5.1 Use scenario	20	10.3 Evaluation	67
5.2 Workflow analysis	24	11. Conclusion	70
5.3 User journey	27	12. Recommendations	72
5.4 Conclusion from a user perspective	29	13. Personal reflection	74
6. The syringe from a product perspective	30	14. Acknowledgements	76
6.1 Product journey	30	Sources	77
6.2 Life cycle analysis of a syringe	32		
6.3 Comparing different life cycle scenarios	36		
6.4 Conclusion from a product's perspective	45		

1. Introduction

1.1 Project brief

The healthcare sector is one of the most unsustainable sectors, contributing to 4.4% of the global net greenhouse gas emissions and toxic air pollutants (Karlner et al., 2020). In the Netherlands, 5.9% of the national footprint is associated with the healthcare sector. The majority (71%) of these emissions come from the production, use, transport, and disposal of medical products used in the hospital (Browne-Wilkinson, Exter, Bouwens, Souder, & Chatel, 2021). Single-use and disposable products are commonly used in the healthcare sector as a regulation to reduce (cross-)infections and have resulted in better health outcomes (Kane, Bakker, & Balkenende, 2017).

The Intensive Care Unit of the Erasmus MC has noticed their excessive amount of waste and initiated the transition towards a more circular ICU. Therefore, Erasmus MC and Metabolic performed a study in 2019 on the environmental impact at the ICU by doing a material flow analysis and an impact assessment. Metabolic is a consulting company that uses systems thinking to tackle global sustainability challenges. This study resulted in 7 hotspot products that are considered to have the highest impact on the environment (see appendix B). Syringes and their packaging are defined as one of the hotspots at the ICU, meaning that it is a problem area causing significant environmental impacts. On the other hand, it creates the opportunity for sustainable innovation. Therefore, the Erasmus MC is interested in finding solutions to decrease the environmental impact of the use of syringes in the ICU.

1.2 Background on the impact of the ICU

The ICU treats patients with life-threatening illnesses and injuries. The

treatments are often complex and require a lot of equipment, such as syringes, liquids, and protective equipment for the staff (see figure 1). Most of this equipment is disposable and single-use, to ensure the safety and sterility of the products. This combination of complex care and the use of single-use products makes the ICU one of the most resource-intensive departments of the Erasmus Medical Centre (Browne-Wilkinson et al., 2021). Furthermore, the global healthcare sector is expanding quickly due to economic growth and growing world populations (Deloitte, 2020). This increases hospital waste, causing a risk for the world's population of reinfection by this medical waste (Dhote, 2016).

The ICU has a large share in the production of waste, but how much exactly is unknown. The study of Metabolic (Browne-Wilkinson et al., 2021) stated that many products are disposed of unused, due to limited shelf life or due to the infection prevention protocol of Erasmus MC. It states that when a patient leaves after a stay that exceeded 24 hours, the entire inventory of the room needs to be disposed of. This inventory consists of sterile packaged syringes, lines, scissors, bandages, gloves, etc. These are all disposed of without being used and end up being incinerated together with all the used products (Browne-Wilkinson et al., 2021).

Likewise, a study by the Paediatric Critical Care Unit in Harvard Medical School in Boston (Ghersin, Flaherty, Yager, & Cummings, 2020) states that supplies are discarded at the time of discharge of a patient, even when the supplies were safely stored away in a medical cart, because of fear of possible contamination. Nevertheless, so far no waste analysis has been



Figure 1: the material that is used daily for one patient (Marcel van den Bergh / de Volkskrant).



Figure 2: nurse checking syringes in the infusion pump.

done yet at the Erasmus MC. Only procurement data has been analysed to determine the impact of the ICU. Also, no research data is available on the impact of the infection prevention protocol on infections within the hospital.

In conclusion, the current state of the ICU is not sustainable nor circular, since it is based on single-use devices, disposables, and a linear economy. The reason for this is that so far safety, sterility, and infection prevention are currently prioritised above sustainability.

1.3 Problem statement

This project focuses on the hotspot: "syringes and its packaging". The type of syringe that is used most in the ICU is 60 ml syringes (filled with 50 ml medicine). These are used to administer medication to the patient. The syringe is connected to the patient via a tube, called an extension line, and placed in an infusion pump for automated administration of the fluid (see figure 2). The syringe is disposed of after single-use in either the general hospital waste or in specific hospital waste (SZA). SZA is possibly infectious and may not end up in general waste since it can cause diseases in humans and animals.

The syringe is considered as a hotspot product, due to the product properties, extensive use (24 per patient per day), and the fact that each syringe is only used once before disposal (Browne-Wilkinson et al., 2021). Furthermore, the syringe is an assembly of components made of different materials. The disposal is a complex process since the syringes are considered as (infectious) hospital waste. Some syringes are even disposed of unused, due to limited shelf life or due to the infection prevention protocol.

The packaging, to keep the syringe sterile, is hard to separate in the end, as it is a laminate of two plastics. This laminate contributes significantly

to the carbon footprint of the syringe.

However, the underlying problem of the high environmental impact of syringes is that the current life cycle is linear. The impact at the end-of-life of a syringe and its packaging has not been taken into account in the design. This results in syringes being used only once, disposed of afterwards and incinerated in the end.

The linear system needs to be transformed into a circular system by using design, to limit the amount of waste and to reduce the use of natural resources. Design plays an important role here since designing products circularly prevents the production of waste and pollution in the first place. The materials and products used can be designed to circulate back into the loop instead of ending up in a landfill.

1.4 Research questions

The goal of this project is to redesign the syringe, packaging, and its use, according to circular design strategies suitable for medical products, to decrease the environmental impact of the use and disposal of the syringe and its packaging at the ICU. The use of syringes should remain convenient and safe for the healthcare staff and patients. Therefore, the research question is:

How can the environmental impact of syringes be reduced by a redesign, according to circular design strategies, without increasing the workload of the staff in the ICU while remaining safe?

To answer this question, the following sub-questions are formulated:

- What circular strategies are suitable for syringes?
- How much waste is disposed (differentiating between used and unused) on the paediatric intensive care (PICU), and what does it consist of? How many syringes are disposed of (unused)?
- How are syringes used by the staff in the ICU?
- What are the product specifications of a syringe?
- What process does the syringe go through during its life cycle?
- What are alternative life cycle scenarios for a syringe to reduce its impact?

2. Method

The project is divided into four phases: discover (understanding the problem), define (the scope of the project), develop (idea finding and developing concepts) and deliver (design conceptualisation). This is an iterative process, where different methods are used per phase and phases can be performed multiple times. The approach of this project is based on the double diamond design thinking method, as can be seen in figure 3.

Discover the subject

Research is executed to answer the research questions (section 1.3) by using different methods. This is explained in table 1.

Define the direction

Results from the analysis will identify starting points for design solutions. Findings are translated into a design vision and a program of requirements to be used as design parameters and evaluation criteria.

Develop ideas

The ideation phase is about diverging and finding as many options as possible. Thereafter a phase of reverging is performed, to revisit all options generated and cluster them into groups. A roadmap of possible directions is made to cluster the ideas and eventually choose one direction. This is done by discussing the directions with the ICU staff.

After this, concepts are developed.

Methods used:

- Creative sessions with peers (brainstorm with how to's)
- Diverging (restate the problem + how to's)
- Reverging (C-box)

- Converging (clustering, reflection on program of requirements, discussion with the staff)

Deliver a solution

Lastly, ideas are converged to select to most promising options to develop into concepts. This is done with the following methods:

- Select concept on criteria (Harris profile + selecting most relevant criteria of PoR)
- Detailing: literature study, process insights from observations into interventions
- Iterating on the concept by discussing the concept with peers and supervisors
- Validating the concept by a discussion with experts.

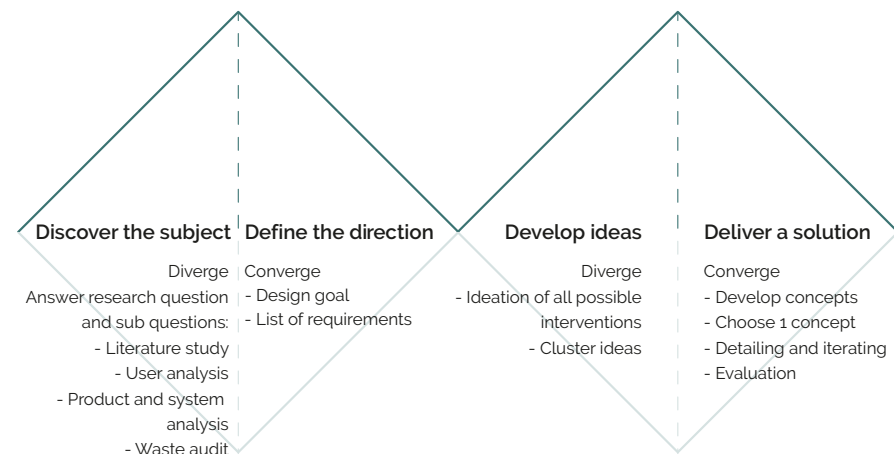


Figure 3: double diamond with accompanying activities of this project.

Table 1: research questions and methods.

Research question	Method	Explanation method
What circular strategies are suitable for syringes?	Literature study	This is done by searching for scientific papers on Google Scholar and ScienceDirect, by using combinations of keywords such as circular economy, sustainability, single-use devices, syringes, healthcare sector, recycling, infectious waste, and sterilisation.
How much waste is disposed (differentiating between used and unused) on the paediatric intensive care (PICU), and what does it consist of? How many syringes are disposed of (unused)?	Waste audit	General hospital waste of the PICU is collected for four consecutive days. The PICU consists of four units; each day one unit is analysed. The waste is collected per unit for 24 hours. All bags of one unit are weighed and opened the next morning, then all items are sorted and counted. Each item is classified as 'used' or 'unused' and then sorted into one of the 14 product categories. All the categories are weighed separately in the end. One of the categories is the "syringes". The full report can be found in appendix D. Besides the general hospital waste, there are also containers for specific hospital waste (SZA). These containers are left out, because of safety reasons and available time. They are only weighed and opened to see what is generally in there.
How are syringes used by the staff in the ICU?	User analysis	Use scenario: observe all the steps of using a syringe in the user environment and interview the users about the use process. User journey (user-centred design): observe different users and their emotions and frustrations during the use process. Afterwards, ask questions about the frustration and general use of the syringe.
What are the product specifications of a syringe?	Product analysis	A workflow analysis is performed to understand the human context of using a syringe. Two traditional contextual design models are used: the flow model and the physical model. The contextual design models help to understand the workflow of the users. The flow model shows the interaction between the different users. The physical model shows where and by who the products are used (Holtzblatt & Beyer, 2017). Analyse the product on materials, different parts, and weight. The weight of the different parts is measured using a KERN & SOHN GmbH 572 Precision balance. The material specifications are retrieved from the technical datasheet of BD Medical, the manufacturer (BD Medical, 2016), and by doing desk research.
What process does the syringe go through during its life cycle?	Life cycle analysis and product journey mapping	Product journey: map the journey of the product from beginning to end with accompanying stakeholders. The life cycle of the product is mapped in a flow chart. All materials needed to fill a syringe are included. Impact hotspots in the process are determined by looking at energy consumption and materials needed per step. A single score indicator, the ReCiPe Endpoint, is used to assess the impact of the (material) hotspots. This indicator combines 18 different impact categories concerning damage to human health, resource scarcity, and ecosystems (Huijbregts et al., 2020). The values of the endpoints can be found in the EcolInvent V3 database. The specific values of the hotspots have been found by calculations. When the values of specific processes are not present in the database, existing information from comparable situations in scientific papers was used to determine a value.
What are alternative life cycle scenarios for a syringe to reduce its impact?	Comparing life cycles	Comparing different life cycle scenarios by doing a literature study scientific research. This is done to investigate to see what possible interventions could be of interest.

3. Circular economy strategies for disposable syringes

The circular economy is an economic model of production and consumption that strives to preserve the value of materials and products, by keeping the material or product in the economic system, either by lengthening the product lifetime or by looping it back in the system with sustainability as aim (Hollander, Bakker, & Hultink, 2017). Different strategies exist to create a circular economy: refuse, rethink, reduce, reuse, repair, refurbish, remanufacture, repurpose, recycle and recover (Kirchherr, Reike, & Hekkert, 2017). The environmental losses can be minimised and the value of the product maximised when as little as possible is changed to the original state of the product (Stahel, 2010). The butterfly diagram (figure 4) shows the flow of materials when using circular strategies (Ellen MacArthur Foundation, 2019).

A circular economy in healthcare will help to decrease the impact of hospital waste and could start a vicious circle that enhances public health and decreases the amount of needed medical interventions (Gamba, Napierska, & Zotinca, 2021).

However, implementing circular economy strategies in the healthcare sector is challenging due to the strict regulations of product safety and sterility. The possible decline in functionality or increased risk could be dangerous for the patient. Key aspects affecting circularity in medical products are the financial aspect, hygienic criticality and the existing infrastructure or support structures around a product (Kane et al., 2017).

- Financial considerations of recovery are about whether it is more

viable to dispose and replace the product with a new one, or to recover the product.

- "Hygienic criticality" means the possible contamination of medical products. It determines the design regulations that the product needs to meet to be hygienically recovered. Three categories of product criticality are defined by the Spaulding Scale: non-critical, semi-critical and critical. Critical products are for example products that come into contact with blood and human tissue, in this case, the syringes and their extension lines.

According to Kane et al. (2017), single-use syringes are considered as a "high-criticality product" with a "low value", because they are used only once and are in contact with the vascular system. Products in this category are the most challenging to develop a performance/value retaining strategy for, because of the combination of a high cost of recovering the product and a low cost of disposal and replacement.

Suitable recovery strategies can be determined based on criticality and value (see figure 5). Recommended strategies for syringes are, therefore: design for separation, design for recycling, design for infectious waste management and design arounds.

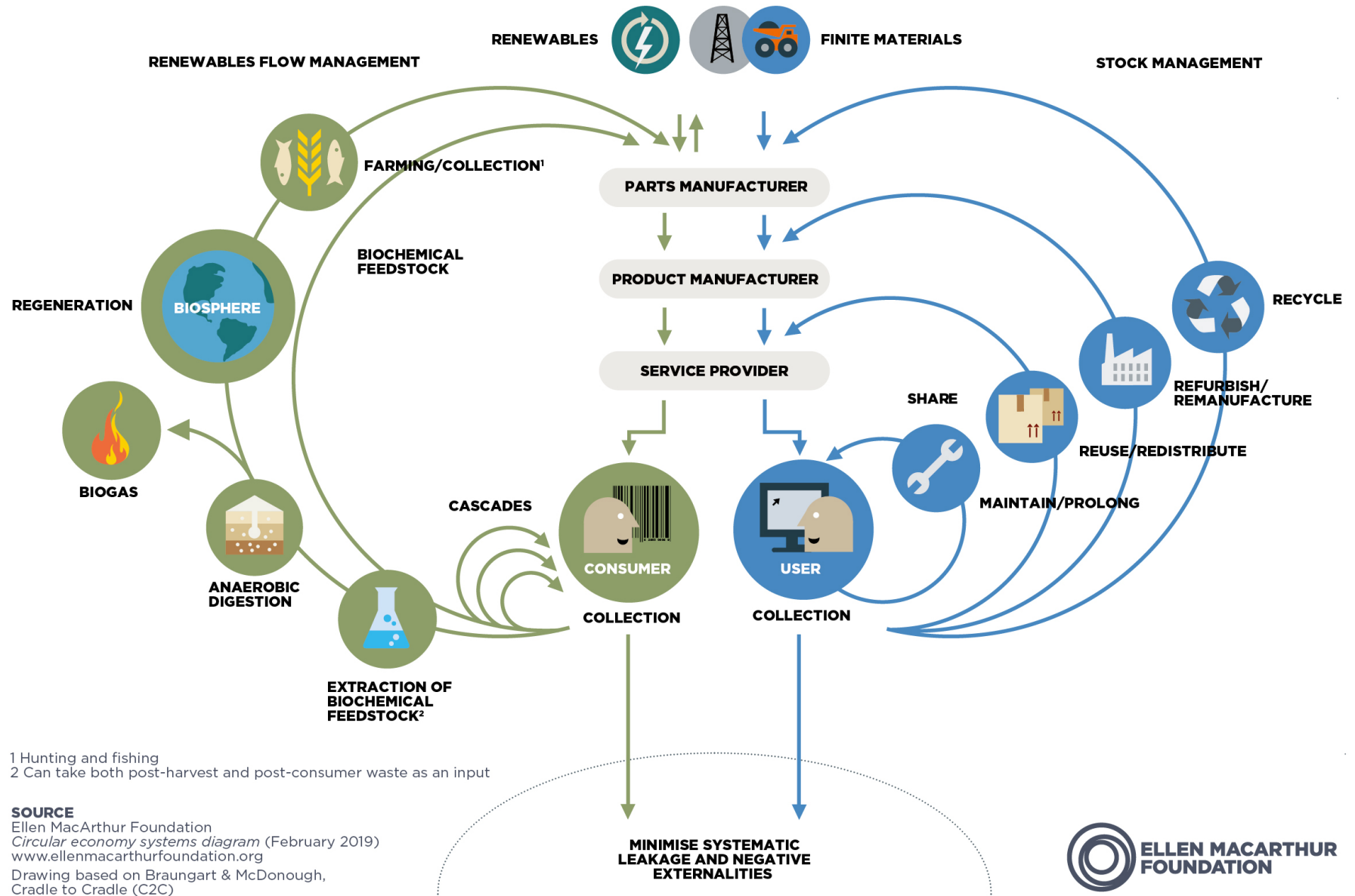


Figure 4: Butterfly diagram that shows strategies to increase circularity (Ellen MacArthur Foundation, 2019).

Design for waste separation

Accurately separating specific hospital waste and general waste could result in a reduction in waste (due to behaviour change of the staff) and costs. Processing specific hospital waste is more expensive than processing general waste, because of possible contamination. Properly separated general waste could even be recovered by mechanical recycling. A study from Gluszynski (2005) showed that training the staff and adapting the protocol to separate the waste more precise results in 50% less waste and decreased the costs of waste disposal by 79%.

Design for recycling

Recycling a product means the recovery of the materials of a product by reconstituting it into a useful new product. Currently, nothing is recycled yet in the ICU. Syringes are mainly made of recyclable materials, as the two largest components (barrel and plunger) are made of PP or PC. The packaging is a laminate of PA6 and HDPE, which is difficult to recycle. The reason that this waste is not recycled yet, is the fact that it is (infectious) hospital waste and could be potentially contaminated. The infectious waste would need to be decontaminated first before it can be mechanically recycled. Many plastic recycling companies do not accept plastic waste from hospitals. For these reasons, the waste is still incinerated and not recycled.

Chemical recycling could also be an option and would immediately eliminate possible contamination. There would be no downcycling with this solution. However, it would require the syringe to be made of suitable plastics, a condensation polymer like poly-esters and polycarbonates, and is a solution for the long term (Joseph, James, Kalarikkal, & Thomas, 2021).

Furthermore, the current low cost of producing plastics from

virgin materials does not make recycling attractive and even is an uneconomical option. Plastics cannot be mechanically recycled indefinitely, as each pass through the recycle stream results in performance loss. Therefore, recycled plastics are often downcycled and made into products of lower quality. To preserve quality, recycled plastics are mixed with virgin plastics (Gamba et al., 2021).

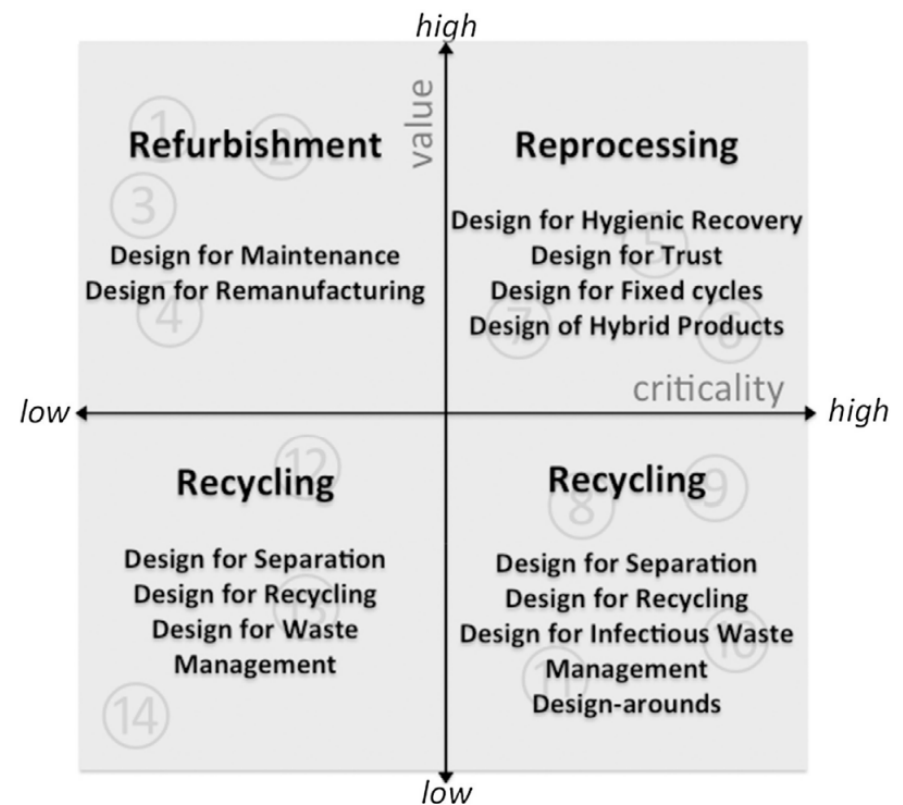


Figure 5: "Design strategies for recovery of circular medical products concerning product criticality and product value" (Kane et al., 2017).

Design for infectious waste management

Waste is managed differently in each hospital, but every hospital has a category for waste that is possibly contaminated. This category of waste forms a barrier to recycling as discussed before. Previous studies state that theoretically, around 10-25% of the total waste of the hospital is infectious (Cheng et al., 2009). Nonetheless, many hospitals dispose of general waste items as infectious as default for safety reasons, even when it's not infectious waste. This results in a higher percentage of infectious waste than necessary (Lee Rushyuan & Mears Simon, 2012). Therefore, designing solutions for infectious waste management could be beneficial to be able to recycle the general waste of a hospital.

Design arounds

Another strategy is to design in a way that the product is not needed anymore (Kane et al., 2017) and replace it with other products with a lower impact. In this case, replace the syringes with another product that holds and administers the medication so that the syringes are not needed at all anymore.

Sterilisation

According to Kane (2017), a disposable syringe "would be unlikely to retain its integrity after a high-pressure steam treatment", and is therefore not suitable to sterilise. However, redesigning the syringe in a way that it can retain its integrity could still be useful. Also, there are more ways to sterilise than only high-pressure steam treatment, such as ethylene oxide, gamma sterilisation and UV sterilisation. If the syringe would not be designed as a low-value product anymore, remanufacturing and reusing could be a viable option. Material properties will need to be suitable to retain the integrity after a cycle of sterilisation and reuse. For example, hot water sterilisation requires the material to stand a temperature of 121°C for about 15 minutes (RIVM, 2018).

Conclusion

There are many possibilities for applying circular strategies to syringes, such as design for separation, design for recycling, design for infectious waste management and design arounds (Kane et al., 2017) and remanufacturing (sterilisation). Deciding on a strategy depends on the value and hygienic criticality of a product. Syringes currently have a low value, but high criticality. The main barrier to applying circular economy principles in the healthcare sector is the strict regulations of product safety and sterility to ensure the safety of both the staff and patients, and the fact that syringes have a low cost and high hygienic criticality.

Requirements for a redesign:

The product must be designed with suitable circular strategies in mind, to ensure the linear life cycle of a syringe changes into a circular life cycle. For reprocessing, the product must retain its integrity to be reused.

4. Waste audit at the PICU

The Erasmus MC has strict waste regulations to handle the waste safely and prevent infections. The regulations concerning syringes can be found in appendix C. However, waste is often still disposed of the wrong way, and the amount of waste is excessive. The extent of the waste problem is quantified by doing a waste audit at the Paediatric Intensive Care Unit (PICU) of the Erasmus MC. The analysis was not performed at the adult ICU, due to logistic reasons. The full report can be found in appendix D

Results

A total of **107 kg** of waste and **104 bags** were collected and analysed during four days. Figure 6 shows the percentage of each product category found in the waste bags. Table 2 shows how much waste was disposed of used and unused overall, and table 3 shows this for syringes specifically. Data about properly separated versus wrongly deposited waste is not collected, only observed.

In 4 days, a total of **570 syringes** were found. There were 5 to 6 children in each unit, so on average, approximately 27 syringes were used per child per day. The syringes were disposed of in the general waste bins, even when they were still containing fluids like blood or medication. This was remarkable since these are supposed to be disposed of in the waste containers dedicated to infectious waste.

The audit showed that the amount of unused disposed products is **2% to 6%**, mostly due to the expiration of products. Furthermore, the waste mostly consisted of food, protective clothing and packaging. Some waste bags contained almost only of packaging and gloves. These are assumed to be from the pharmacy of the PICU. Other bags only

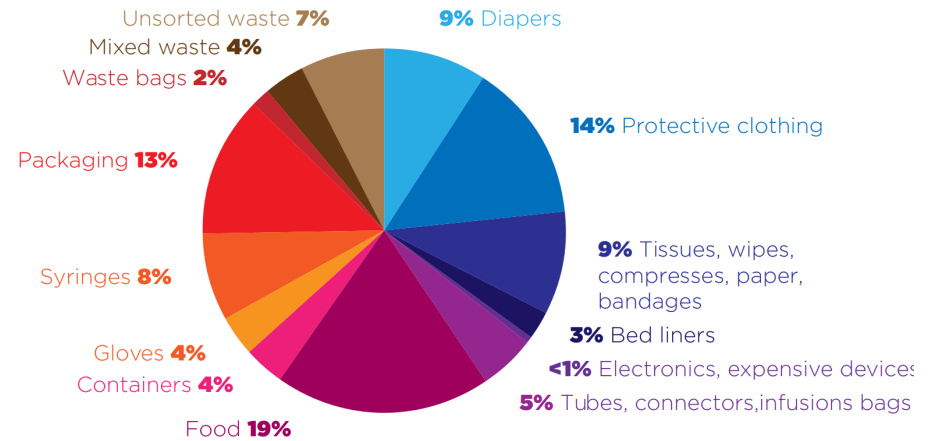


Figure 6: results of the waste audit in weight percentages per type of waste.

Table 2: results of the waste disposed of used and unused.

	Used		Unused		Total	
	Pieces	Weight (g)	Pieces	Weight (g)	Pieces	Weight (g)
All waste	2.353	104.067	154	2.575	2.507	106.642
%	94%	98%	6%	2%	100%	100%

Table 3: specific results of the syringes during the waste audit.

	Used		Unused		Total	Used	Unused
	Pieces	Weight (g)	Pieces	Weight (g)			
Syringes	558	8.055	12	396	570	98%	2%

contained food-related waste, such as coffee cups, empty meal salad packaging and cakes. These bags filled with no contaminated products offer the potential for further separation of waste that is applied now.

The syringe specific results show that in the PICU of Erasmus MC only 2% of the syringes were disposed of unused, most of the time because they were out of date. In the children's IC, everything is tailor-made for each child. There is stock for a maximum of 24 hours. The PICU does not use prefilled sterilised syringes.



Figure 7: syringes collected during the audit.



Figure 8: unused products found in the waste containers of one day



Conclusion

From this analysis, it can be concluded that the separation of general and specific hospital waste is not always done correctly. For example, syringes with blood were found in the general waste. This makes mechanical recycling of general waste impossible. However, the bags from the pharmacy and the bags which only contained food-related waste showed that separating regular waste from (infectious) specific hospital waste is certainly possible in certain areas of the hospital. This creates an opportunity for recycling general waste.

Requirements derived from this research:

- The waste must be properly separated to be able to mechanically recycle hospital waste.
- Waste separation regulations must be made clear to the staff.

Figure 9: set-up of the waste audit.

5. The syringe from a user's perspective

This section answers the following research question:

How and where is the syringe used by the staff?

Observations and interviews with the staff of the ICU are conducted to understand the use of a syringe from a user's perspective. The users are the staff of the ICU: a team of medical specialists, who are all described in appendix E. 4 nurses, 2 care assistants and 1 pharmacist were interviewed. The observation involved all of the staff members of the ICU. A use scenario, user journey and a workflow analysis are made to process the insights from the observations and interviews with the staff on the ICU.

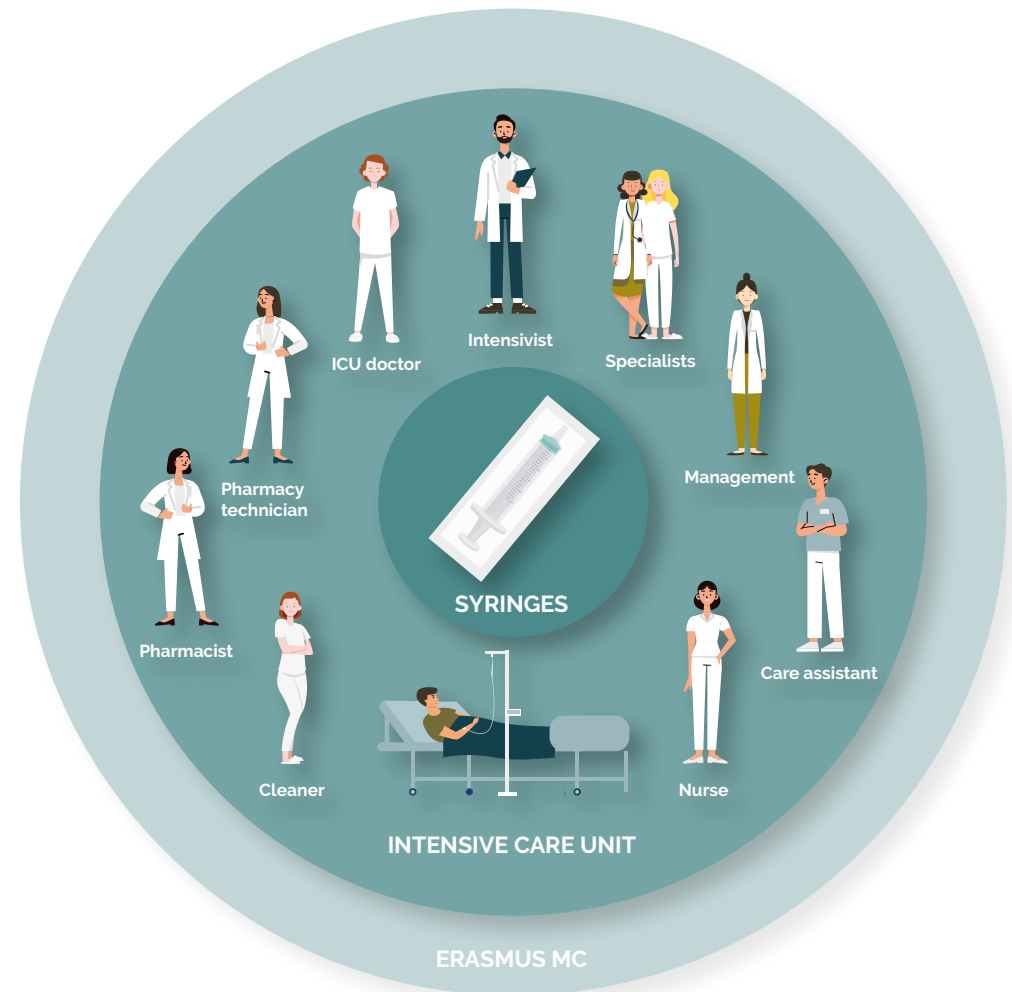


Figure 10: scope of the user research.

5.1 Use scenario

The steps for manually filling, using and disposing a syringe are shown in the use scenario (figure 11).

In total, it takes **28 actions** for the staff to prepare, use and dispose of a syringe.



1. The table is cleaned with alcohol. Supplies are laid out on the table.



2. The sticker is filled in with details about medication, patient's name, date and time.



3. The packaging with syringe is opened. The syringe is taken out without touching the tip.



4. The syringe is placed on the table in a way that the tip does not touch anything.



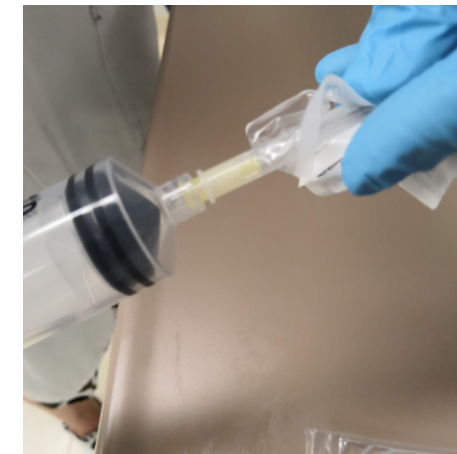
5. The infusion bag is opened.



6. The infusion bag is opened



7. A sterile needle is opened, without touching it.



8. The needle is screwed onto the syringe, without touching the needle. Only the packaging is touched.

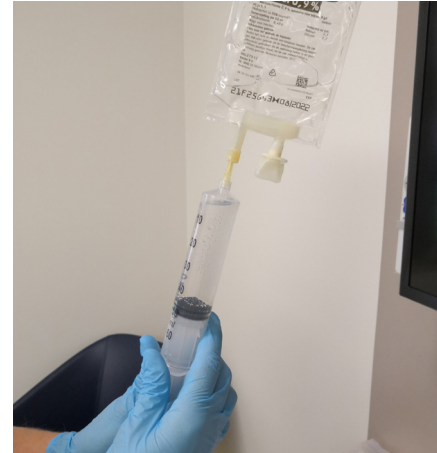
Figure 11: use scenario of the syringe.



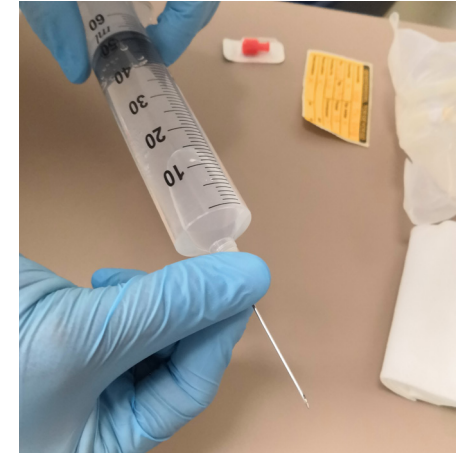
9. The syringe is placed in the infusion bag.



10. The needle is secured in the opening of the bag.



11. The medication is drawn up through the needle into the syringe



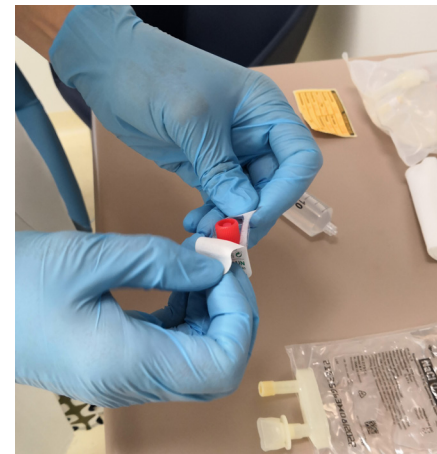
12. The syringe is full, needle can be taken off.



13. The needle is removed from the syringe.



14. The needle is disposed in the sharp infectious waste bin in the room.



15. A stopper is opened.



16. The stopper is placed on the syringe.



17. The sticker is placed onto the syringe in such a way that you can still see it when it is in the pump.



18. The red stopper is removed and the tube is attached to the syringe.



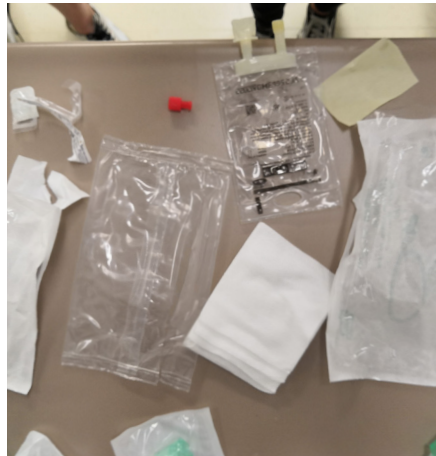
19. Pump is opened to make place for the syringe.



20. The syringe is placed into the pump. The pump is closed, and the display shows the type of syringe.



21. The extension line is connected to the patient.



22. The waste is collected and thrown away in the waste bin in the room.



23. The gloves can be taken off, and are disposed in the same bin.



24. The bin in the room is closed.



25. The waste bags from the room are placed in the green containers at the ICU by the care assistants.



26. The needle boxes from the room are placed in a cardboard box.



27. The containers are collected in the basement of the hospital.



28. The waste from the containers is pressed together and then incinerated.

Results

The use scenario demonstrates that most waste is produced during the preparation of the syringe (see figure 11). All products needed to fill the syringe are also single-use disposable items. Figure 12 shows the amount and type of disposed of products in each use phase. The height of the bar indicates the total number of pieces. Weighing the different products would have been more accurate, this was unfortunately not possible during the observation day.

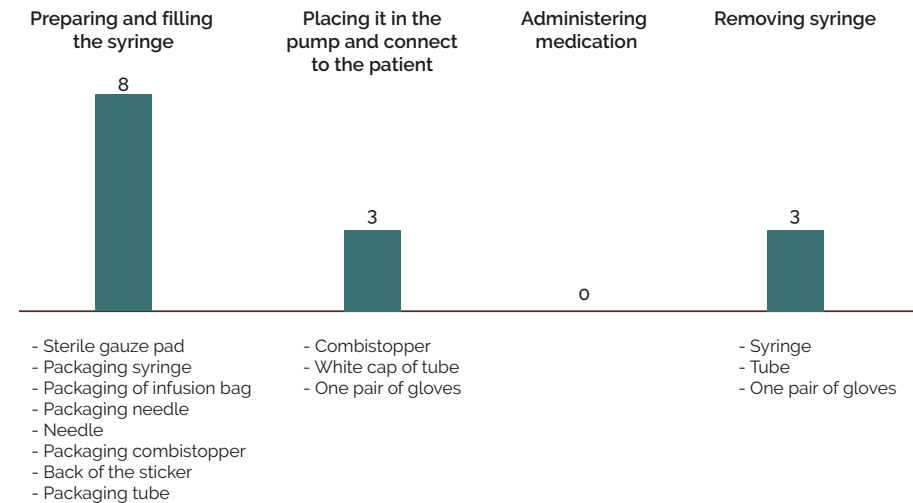


Figure 12: the amount of waste (in the number of pieces) during the use process.

5.2 Workflow analysis

The flow model

The flow model shows the communication, roles and responsibilities of multiple users within a work process (Holtzblatt & Beyer, 2017). Observing all users on the ICU showed who and what kind of actions with the syringe were performed (see figure 13).

The staff members interact with the syringes on different levels. The intensivists only communicate about the syringe by prescribing the

order. The pharmacy technician (PT 1) checks the order and arranges the logistics. Then a second PT (PT 2) prepares the syringes if needed. And PT 1 makes sure that the syringe is placed in the drawer of the patient. The nurses interact with the syringes and the patient, and the care assistant only interacts with the syringe before use and the cleaners after use.

As can be seen in figure 13, the nurse, pharmacy technician and care assistant have the most interactions with the syringe during patient-related activities and are therefore seen as the main users of the syringe.

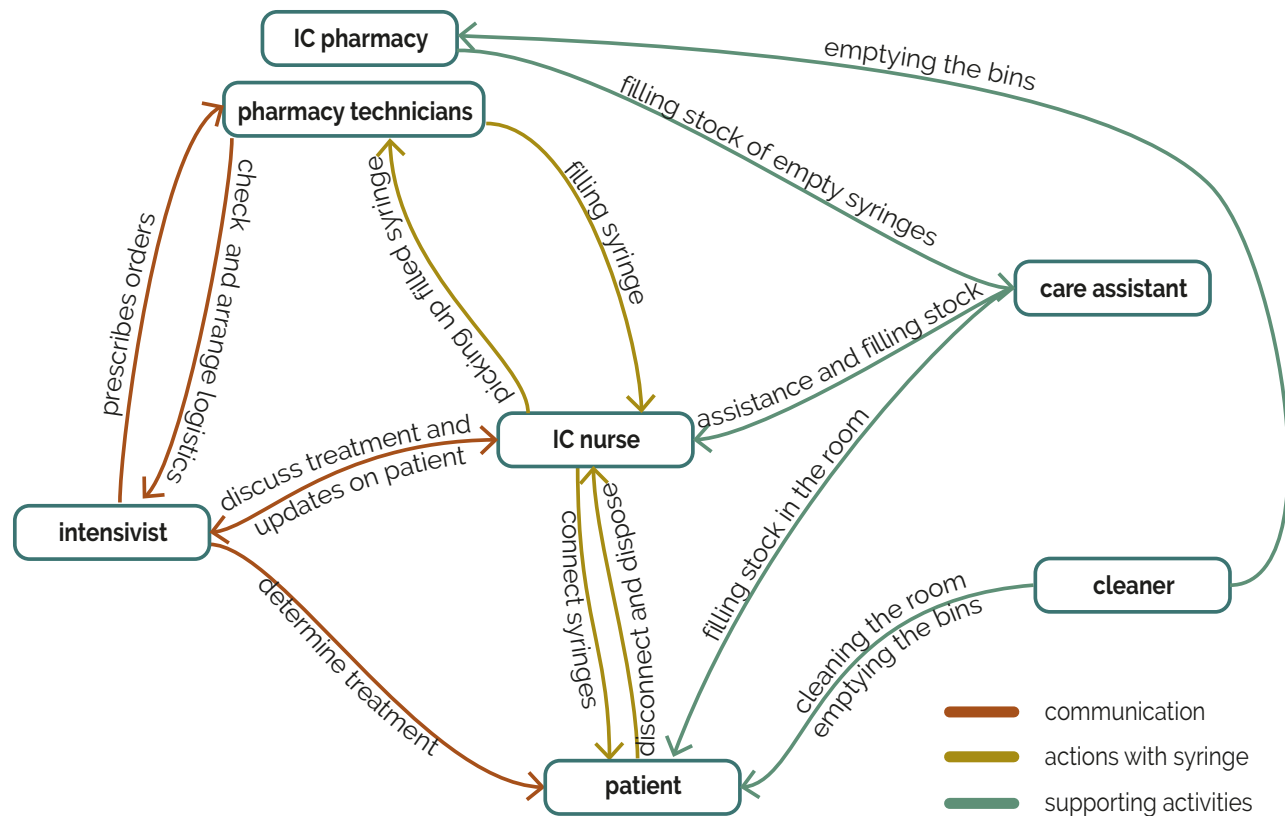


Figure 13: flow model of the users of syringes on the ICU.

The Physical Model

The physical model (see figure 14) shows how the environment is organised and where the activities of using a syringe take place (Holtzblatt & Beyer, 2017). It captures the structure of use and gives insights into the surroundings of using a syringe in the ICU. Observing and interviewing gave the following insights:

Care assistant

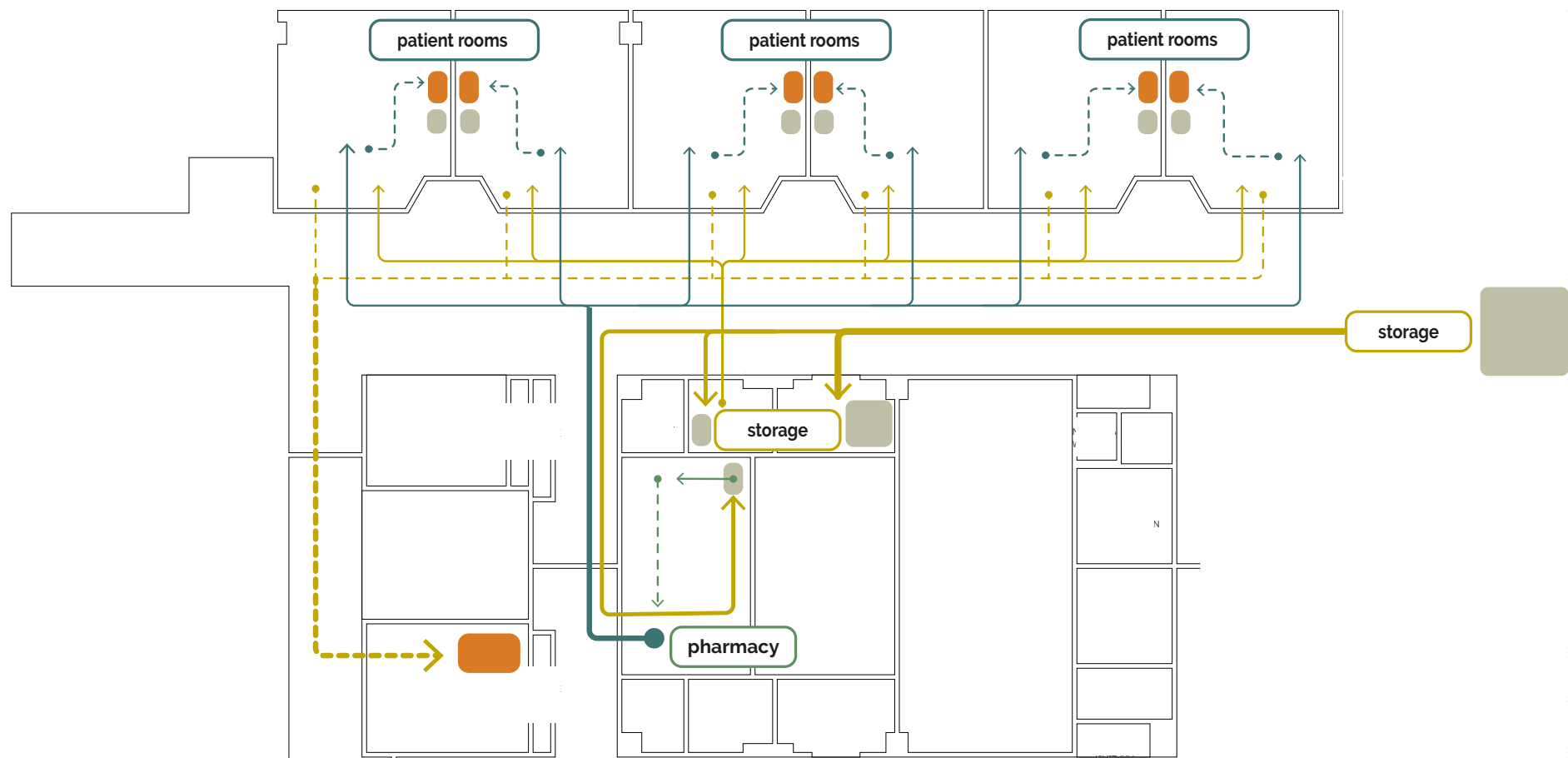
The care assistant (yellow line in figure 14) is responsible for replenishing the stock of empty syringes in the patient's rooms, the pharmacy and the different smaller storage rooms. This is done from the large storage rooms located in the ICU. In the rooms of the patient, there is a drawer filled with syringes. The drawer is topped up twice a day with two syringes of each size. When a patient leaves after a stay of at least 24 hours, the whole room will be emptied according to the infection prevention protocol. The care assistant or the cleaner takes out the trash bags to the waste container located on the ward.

Nurse

The nurse (blue line in figure 14) picks up the syringes filled with medicine from the pharmacy and brings them to the patient's room. Then the procedure of connecting a syringe to the pump and patient is executed. In the end, all the waste is disposed of in the room itself.

Pharmacy technician

The pharmacy technicians (green line in figure 14) have their pharmacy in the ICU and prepare syringes with medication specifically for each patient. They have a stock of empty new syringes in their room. Then they fill the syringes in this room and keep them in the fridge or a box with the patient's name on it until the nurses come to pick them up.



- Care assistant ● Restock new syringes ● — → Cleaning and disposing
- Nurse ● Pick up filled syringes ● — → Removing and disposing syringes
- Pharmacy technician ● Filling syringes ● — → Placing filled syringe in fridge
- Storage of empty new syringes
- Waste bins for used syringes

Figure 14: the physical model of the use of a syringe.

5.3 User journey

The user journey (figure 15) is an overview of the different phases that the main users are going through when using a syringe. It gives a better understanding of the use process, as well as insight into interactions, emotions and frustrations of the users (Albayrak, 2021a). This map is made for the three main users of syringes in the ICU: the nurse, the pharmacy technician and the care assistant. These three staff members of the ICU have the most interaction with the syringe, which was concluded from the flow model. The patient is not actively interacting with the syringes and is thus left out of this journey map. All information is gathered during observations and interviews with the staff in the ICU.

Results

It was observed that the users feel bad about the amount of waste and that they are open to a change. During the interviews, different staff members mentioned their frustrations and possible solutions. The pharmacists mentioned that making batches of syringes with medication, instead of preparing only one syringe, saves packaging and products. A nurse mentioned using 100 cc syringes instead of two 50 cc syringes, to replace the syringes less and have less waste. According to the care assistant, nurses sometimes pick up multiple syringes when they only need one.

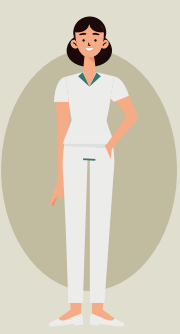







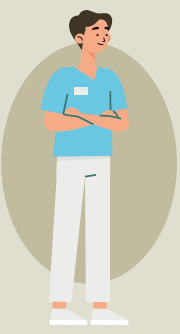



	Storage	Preparing the syringe	To the patient	Removing/replacing	Disposing
 <p>Nurse</p>	<p><i>task</i></p> <p>Picking up the filled syringe from the pharmacy. Picking up tubes etc. at the storage room.</p>		<p>Connecting the syringe to the tube, the pump and the patient.</p>	<p>Syringes need to be disposed or replaced after 24 hours or when empty. They are checked manually to see if they need to be replaced, whereas the replacement of tubes is notified in the computer.</p>	<p>Disconnecting the syringe and disposing it in the garbage bin in the room.</p>
	<p><i>emotion</i></p> <p> Relieved, because I don't need to prepare the syringes themselves.</p>		<p><i>emotion</i></p> <p> Content.</p>	<p><i>emotion</i></p> <p> Frustrated sometimes.</p>	<p><i>emotion</i></p> <p> Sad to throw unused products away.</p>
	<p><i>frustration / challenge</i></p> <p>Medication is needed in time, sometimes more is needed on short notice.</p>		<p><i>frustration / challenge</i></p> <p>Sometimes the syringes have double caps, which is not necessary, or the tips are different.</p>	<p>The syringes need to be replaced a lot, takes time and lines are sometimes mixed together.</p>	<p>Disposing unused syringes is a frustration. Also, the amount of packaging is a lot.</p>
 <p>Pharmacy technician</p>	<p><i>task</i></p> <p></p>	<p>Fill the syringes with medicine for specific patients. Doctors prescribe what needs to be made and when.</p>			<p>Dispose all parts used during the preparation in the pharmacy itself, and placing the full syringe in the fridge.</p>
	<p><i>emotion</i></p> <p></p>	<p><i>emotion</i></p> <p> Joy, 50 mL syringes are easy to work with</p>			<p><i>emotion</i></p> <p> A lot of packaging, bin is full quickly</p>
	<p><i>frustration / challenge</i></p> <p></p>	<p><i>frustration / challenge</i></p> <p>50 mL syringes are the easiest to work with. Making batches would be more efficient and has less packaging, but this hardly occurs.</p>			<p>A lot of different material is disposed (paper, glass, plastic)</p>
 <p>Care assistant</p>	<p><i>task</i></p> <p>Distribute the syringes over the different storage rooms, patient's rooms and the pharmacy</p>			<p>Refill the syringes in the drawers in the room twice a day. Two of each type of syringe are placed in the drawer.</p>	<p>Cleaning the room after a patient leaves. Need to throw everything away, even when it is still in the packaging.</p>
	<p><i>emotion</i></p> <p> Satisfaction</p>		<p><i>emotion</i></p> <p> Content</p>	<p><i>emotion</i></p> <p> Sadness, shame</p>	
	<p><i>frustration / challenge</i></p> <p>Nurses pick up too much syringes when they only need one.</p>		<p>Not always needed. Sometimes the syringes fall of the refill cart on the floor, but are placed in the room anyway.</p>	<p>Pain in stomach about the rule that the room needs to be emptied after the patient leaves.</p>	

Figure 15: user journey of using a syringe on the ICU.

5.4 Conclusion from a user perspective

The user research clarified how and where the syringes are used by different users.

Firstly, the use scenario showed that filling a syringe with medication and connecting it to the patient requires a lot more disposable products than only the syringe itself. Most of the additional products are used during the preparation and filling phase. This phase could be optimised to reduce the amount of waste.

Secondly, the flow model has visualised the interaction between staff members using syringes. All staff members interact with the syringes on different levels, so a redesign will affect each staff member differently. The nurse, pharmacy technician and care assistant interact most with the syringe and are therefore seen as the main users of the syringe. However, the intensivist gives the instructions to the nurse and pharmacy technician, and should therefore be taken into consideration during the design process.

The physical flow and user journey showed that the storage of new syringes in the rooms could be revised, as well as the infection prevention protocol. Decreasing the stock inside the rooms of the patient would lead to a decrease in unused disposed items. The user journey presented that the amount of disposed of unused syringes could be decreased by changing the habits of staff. For example, nurses sometimes pick up multiple syringes when they only need one. Teaching the staff to only pick the amount you are going to use could decrease the disposal of unused syringes.

Lastly, it was observed that there is no separation of waste based on materials. Changing the environment by placing different waste bins, in for example the pharmacy, to separate waste.

The main barriers to decreasing the impact of syringes are the infection prevention protocol and behaviour of the staff, causing syringes to be disposed of unused.

Design requirements based on the user research:

- The design must not increase the workload of the nurses, regarding time and number of actions. It must be as efficient (in time and number of actions needed) to attach to the patient as the current syringes.
- The design must remain safe for the staff and the patient.
- Syringes must be accessible close to or in the rooms, to ensure that the nurses can access them in a short time
- The design must fit the syringe pump of B-Braun
- The design must be able to be used for at least 24 hours straight
- The design must show what medication is in there, for who it is, the time and date it was placed in the pump
- The design must be usable with medical gloves
- The design must be able to be filled up to 50 ml of medication
- The nurses must be able to look through the material to see the fluid inside
- The design must be easy to replace after use
- The design must comply with the extension lines that connect to the patient
- The design must be able to be stored at room temperature (only if sterilised) or in the fridge (2°C-8°C)

6. The syringe from a product perspective

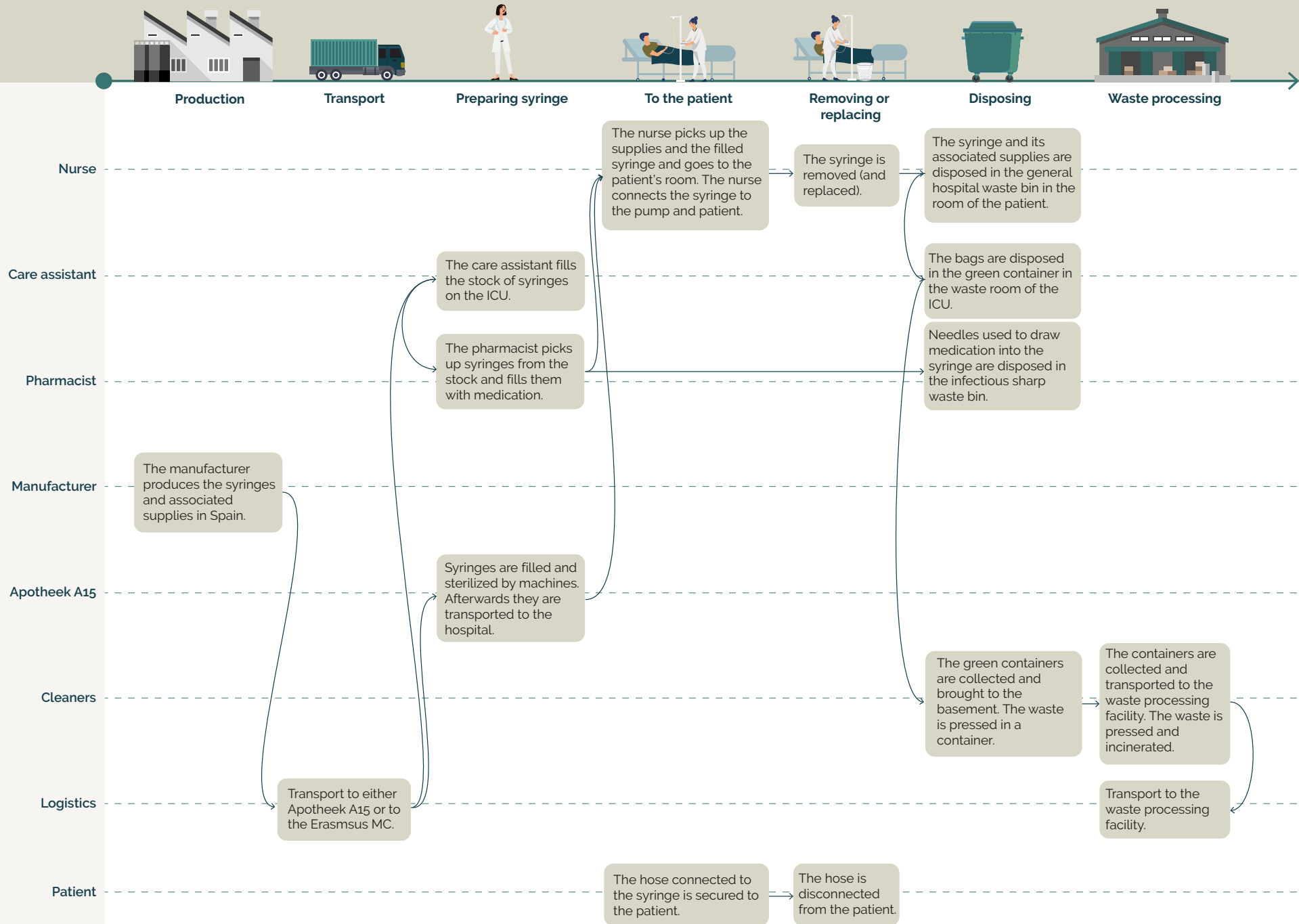
This section answers the following research questions:

- *What are the product specifications of a syringe?*
- *What processes does the syringe go through during its lifecycle?*
- *What are alternative life cycle scenarios for a syringe to reduce its impact?*

6.1 Product journey

The product journey is a representation of interactions between the product and the different stakeholders. All stakeholders interact with the product at another level and these interactions are most of the time-sequential (Albayrak, 2021b). The product journey of the syringe can be seen in figure 16. An explanation of the stakeholders involved can be found in Appendix F.

The product journey (figure 16) shows that the syringe goes through a linear life cycle and involves numerous different stakeholders. They do not operate at the same time and are at different locations. To achieve a reduced impact, all the stakeholders should be considered and taken into account when looking for solutions.



6.2 Life cycle analysis of a syringe

Metabolic has not investigated the impact of the syringes in detail. Therefore, this section determines the product specifications and analyses the life cycle of the 50 ml Luer-Lock syringes, the type of syringes that are used most in the ICU, in-depth.

Parts and materials

The plunger rod, barrel and stopper (see figure 17) are made from high purity processed materials (polypropylene (PP) and bromobutyl) and produced by injection moulding and assembled by an assembly line. The packaging consists of paper and a laminate of PA6 and LDPE. This is difficult to separate at the end-of-life and therefore not recyclable.

The barrel and plunger are made of PP for the following reasons:

- High transparency (needed for the medication to remain visible for the users),
- High chemical resistance, toughness and resistance to bacteria (Joseph et al., 2021).
- A relatively low cost in comparison to other plastics, for example, polycarbonate (PC), but similar performance in the case of single-use (Akre, 2012).
- It is a non-absorbable material; the medication is not absorbed by the material (Akre, 2012).

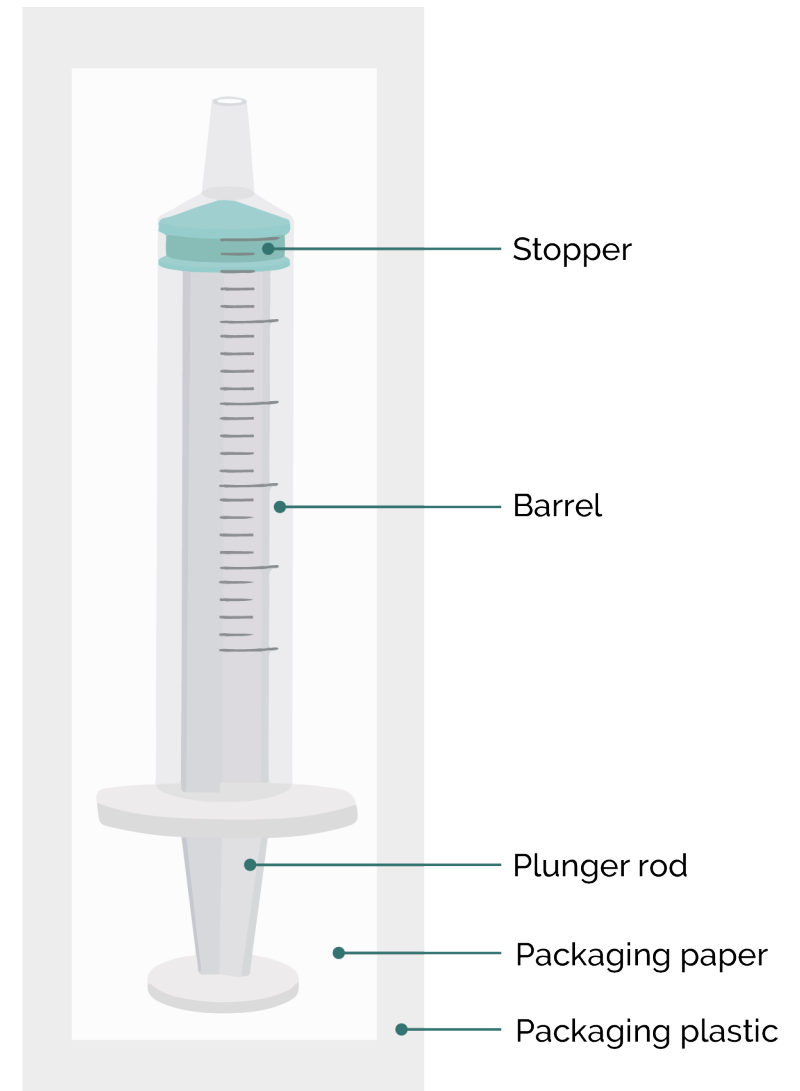


Figure 17: parts of the syringe.

Life cycle

The different stages of the life cycle of a syringe (figure 18) are described below. The hotspots (marked in bold in figure 18) are steps in the process that are estimated to have a high environmental impact compared to other steps in the process.

Impact of materials

Functional unit (FU) = syringes needed for 6 patients (24 per patient per day) for one week = 1000 syringes per week.

The material impact of each part is calculated relative to the weight (see table 4). The barrel, plunger and stopper have an impact of 0.86 Pt, 0.55 Pt and 0.38 Pt respectively, and are thus the hotspots concerning material and parts of the syringe. The packaging has a low weight compared to the other parts, and the total impact (0.12 Pt) is therefore neglectable.

Sterilisation

Empty syringes are sterilised using ethylene oxide. The environmental impact of sterilising syringes with ethylene oxide is significant, due to the energy-intensive process (Ghannadzadeh & Meymivand, 2019). More sustainable ways of sterilisation should be considered, such as gamma sterilisation. The manufacturer (BD Plastipak) already has gamma sterilisation facilities, so a transition to gamma sterilisation is possible.

Transport

The syringes are produced in a manufacturing site in Madrid, whereafter they are brought to Rotterdam. This means that the syringe travels at least 1750 km from the manufacturing site to the hospital. It is assumed that the transportation is done by truck.

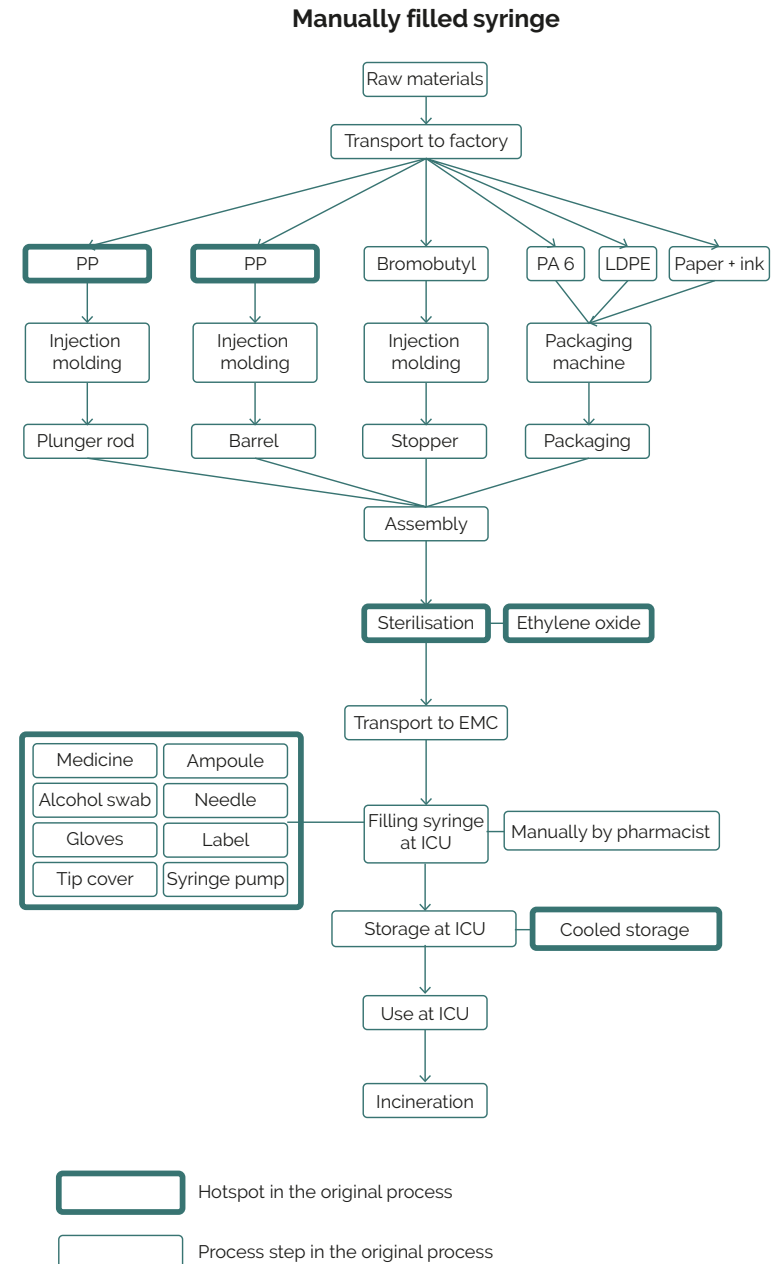


Figure 18: life cycle of the manually filled syringe.

Additional products

The syringe is filled manually at the pharmacy. Manually filling each syringe requires several different additional products, as can be seen in figures 18 and 19.

Cooled storage

The syringes need to be stored in a fridge until use. Cooling the syringes requires a significant amount of energy since the fridges are on day and night and is thus considered as an impact hotspot.

End of life (EoL)

The syringe ends up being incinerated either together with all the other hospital waste or with the specific hospital waste. The incineration generates electricity, but also produces carbon emissions and toxic gas and is the most harmful disposal method in terms of CO₂ emissions (Global Alliance for Incinerator Alternatives, 2019).

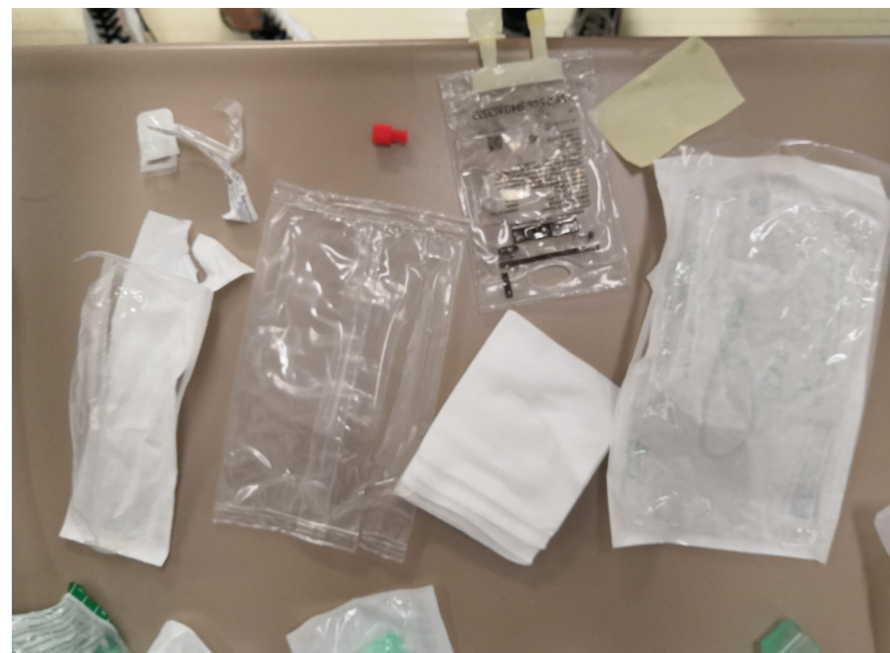


Figure 19: additional products needed for filling syringes manually.

Table 4: calculating the total ReCiPe endpoint per part of the syringe.

Part	Material	ReCiPe Endpoint (Pt/kg)	Weight (g)	Weight per FU (g)	Total ReCiPe endpoint (Pt)
Plunger rod	Polypropylene (PP)	0.05	11.0	11.000	0.55
Barrel	Polypropylene (PP)	0.05	17.2	17.200	0.86
Stopper	Bromobutyl rubber	0.12	3.2	3200	0.38
Packaging plastic	20% Polyamide 6 (PA 6)	0.16	0.20	200	0.03
	80% Low-density polyethylene (LDPE)	0.05	0.80	800	0.04
Packaging paper	Paper with medical-grade, printing ink	0.05	1.0	1000	0.05
Syringe total	-		33.4	33.400	

Conclusion

This section gave insight into the product specifications, life cycle and impact hotspots of the manually filled syringe. It became clear that the packaging of the syringe is only a small percentage of the total weight of the syringe. The impact of the packaging is almost negligible due to the small share in the total weight of the syringe.

The following hotspots of manually filled syringes were defined in this section:

- The barrel, plunger and stopper due to their weight compared to the packaging
- The sterilisation process (ethylene oxide)
- Additional products needed per syringe during the filling process
- Cooled storage at the pharmacy

A cause of the hotspots is the need for safety and sterility. Ethylene oxide sterilisation has a significant impact on the environment, but sterilisation is required to deliver sterile syringes to the hospital. Also, all the protective products needed at the pharmacy (alcohol swab, sterile gloves, tip cover) are there for preserving the sterility of the syringes. Sterility and preventing infections during the production and the filling process are the main barriers to decreasing the impact of the production and manual filling process of syringes, as well as the fact that each syringe is filled one by one per specific patient.



Figure 20: the syringe in its packaging.

6.3 Comparing different life cycle scenarios

Section 6.2 showed the life cycle of manually filled syringes. In this chapter, the following scenarios that could decrease the impact are reviewed:

- Prefilled sterilised syringes (PFSS)
- Recycling
- Sterilisation and reuse
- Using other materials.

These scenarios (see figure 21) derived from previous research; the literature review, user research and product research. Each scenario is compared to the current life cycle (manually filled syringes).

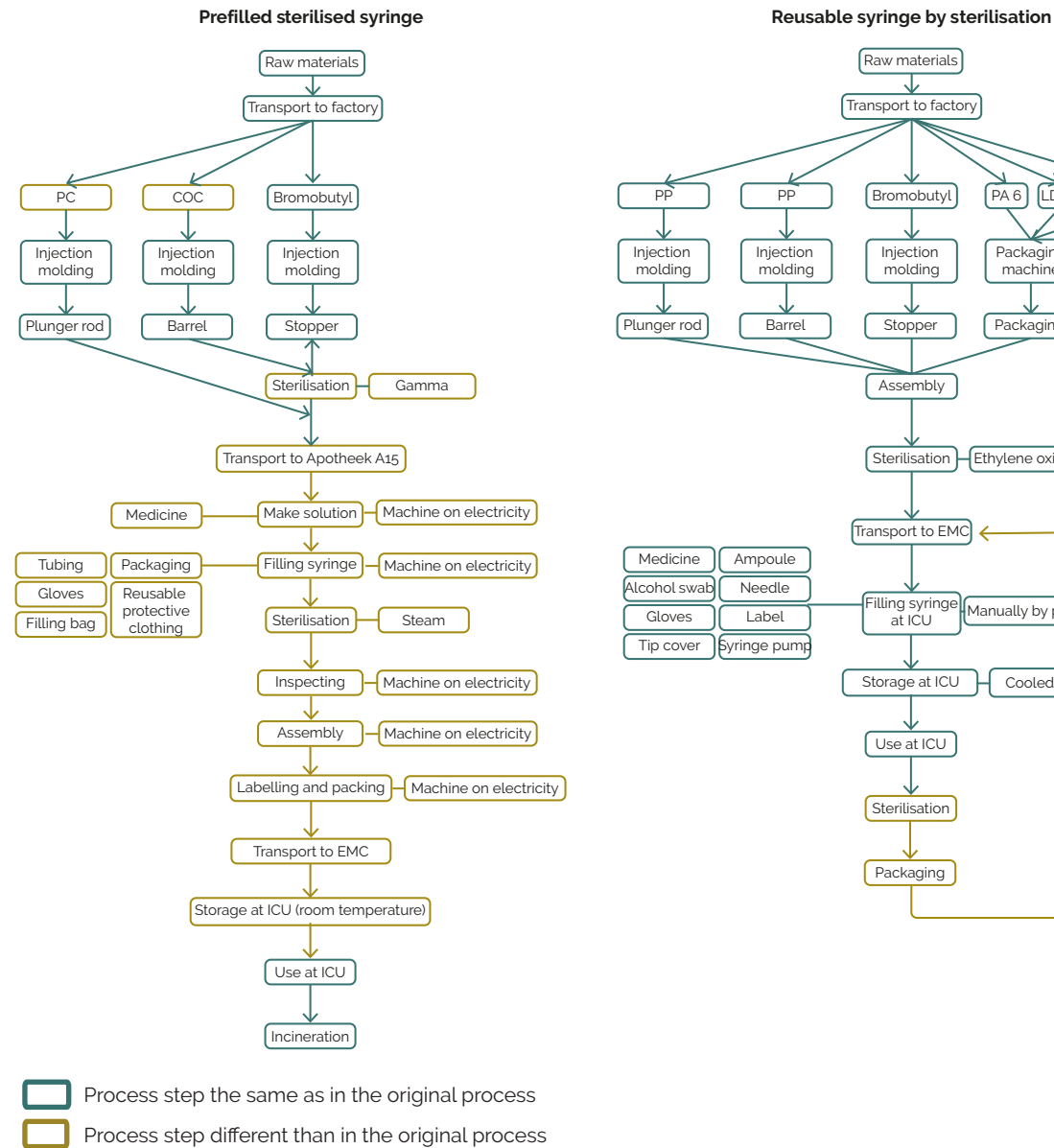
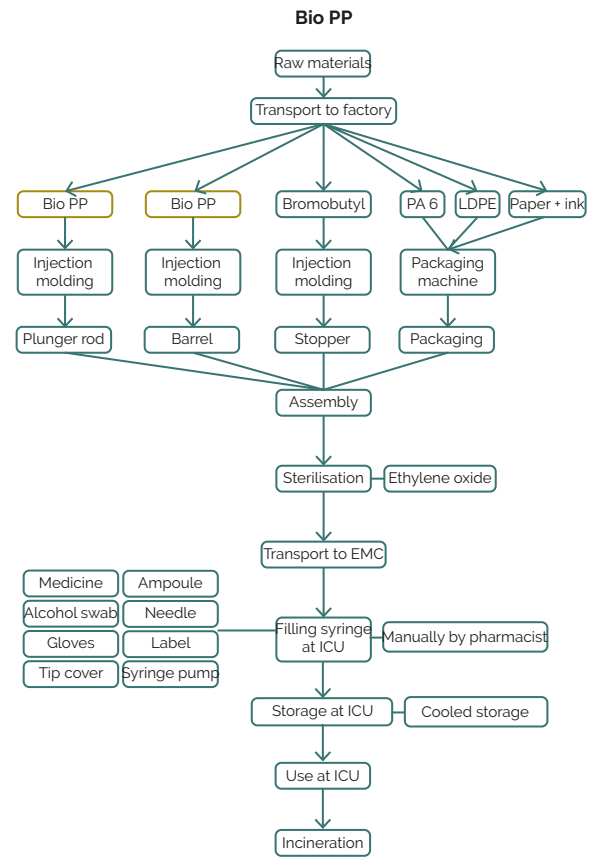
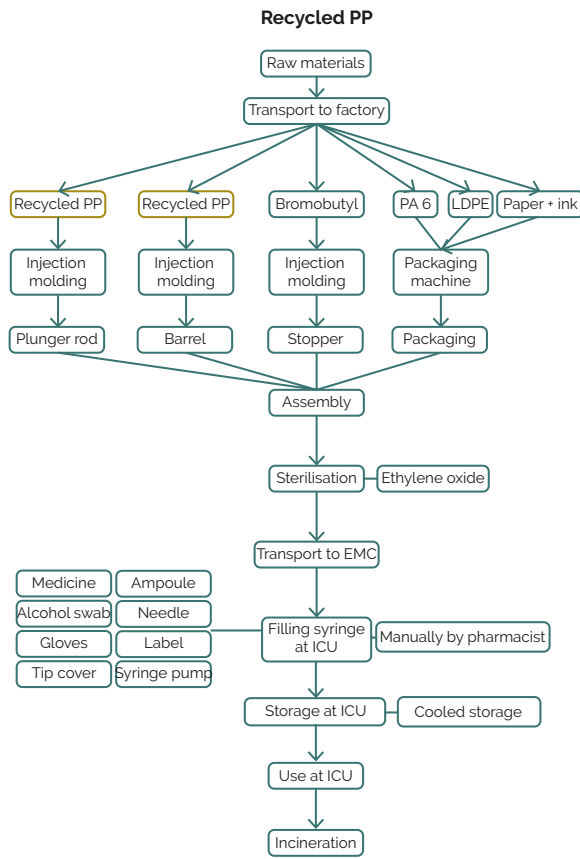
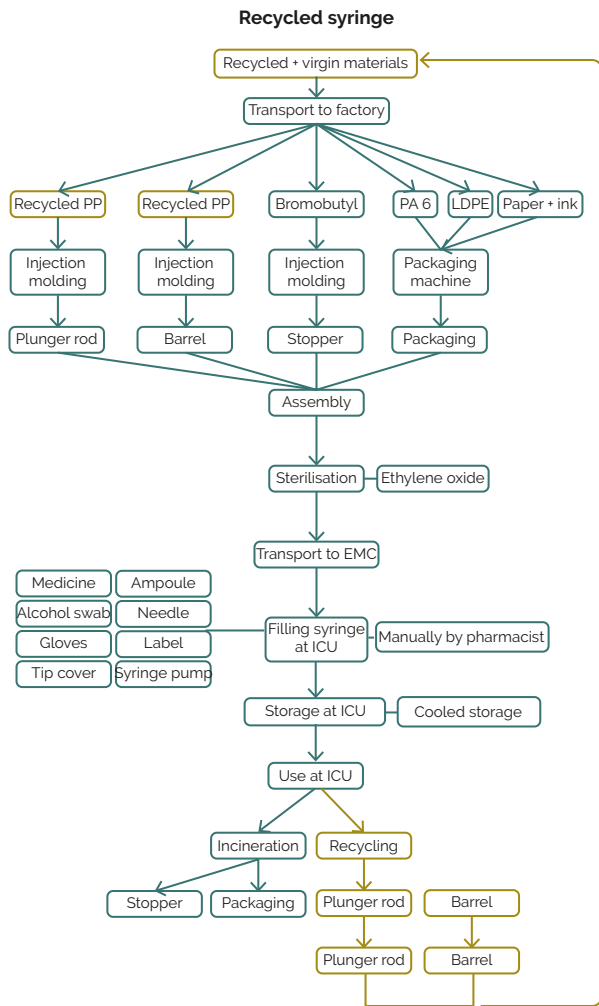


Figure 21: an overview of all different possible scenarios.



Prefilled sterilised syringes (PFSS) vs. manually filled syringes

Prefilled syringes are syringes filled with medicine by an external company, in this case, Apotheek A15. Erasmus MC uses a combination of prefilled (70%) and manually filled (30%) 50 ml syringes.

The goal of comparing is to see the difference in material and energy use. Impact hotspots of the filling process at Apotheek A15 are marked with bold lines in figure 22. The yellow lines indicate a difference between manually filled syringes and PFSS, blue lines indicate that there is no difference.

The functional unit (FU) = one full cart of 50 ml syringes placed in the autoclave = 1000 syringes per cycle.

Filling the syringe

Using prefilled syringes saves additional products needed during the filling process compared to manually filled syringes because the syringes are filled in batches. Manually filling syringes requires products such as ampoules, needles, alcohol swabs, labels, tip covers and gloves. Apotheek A15 uses additional products for filling such as the tube, filling bag and reusable protective clothing. These are not considered as a hotspot, since the same products are used throughout the whole day of filling and are neglectable per functional unit (1000 syringes). Even though the impact is not calculated specifically, it is clear that needing fewer materials to prepare a syringe will contribute to reduce the impact (Cheetham & Johnson, 2013).

However, approximately 20 kg of drug solution is left after a day of filling syringes. 4 g of this is the actual drug, the rest is sterile water for injection. The 300 L pharma vessel containing the drug solution needs to be cleaned after use: three times with water.

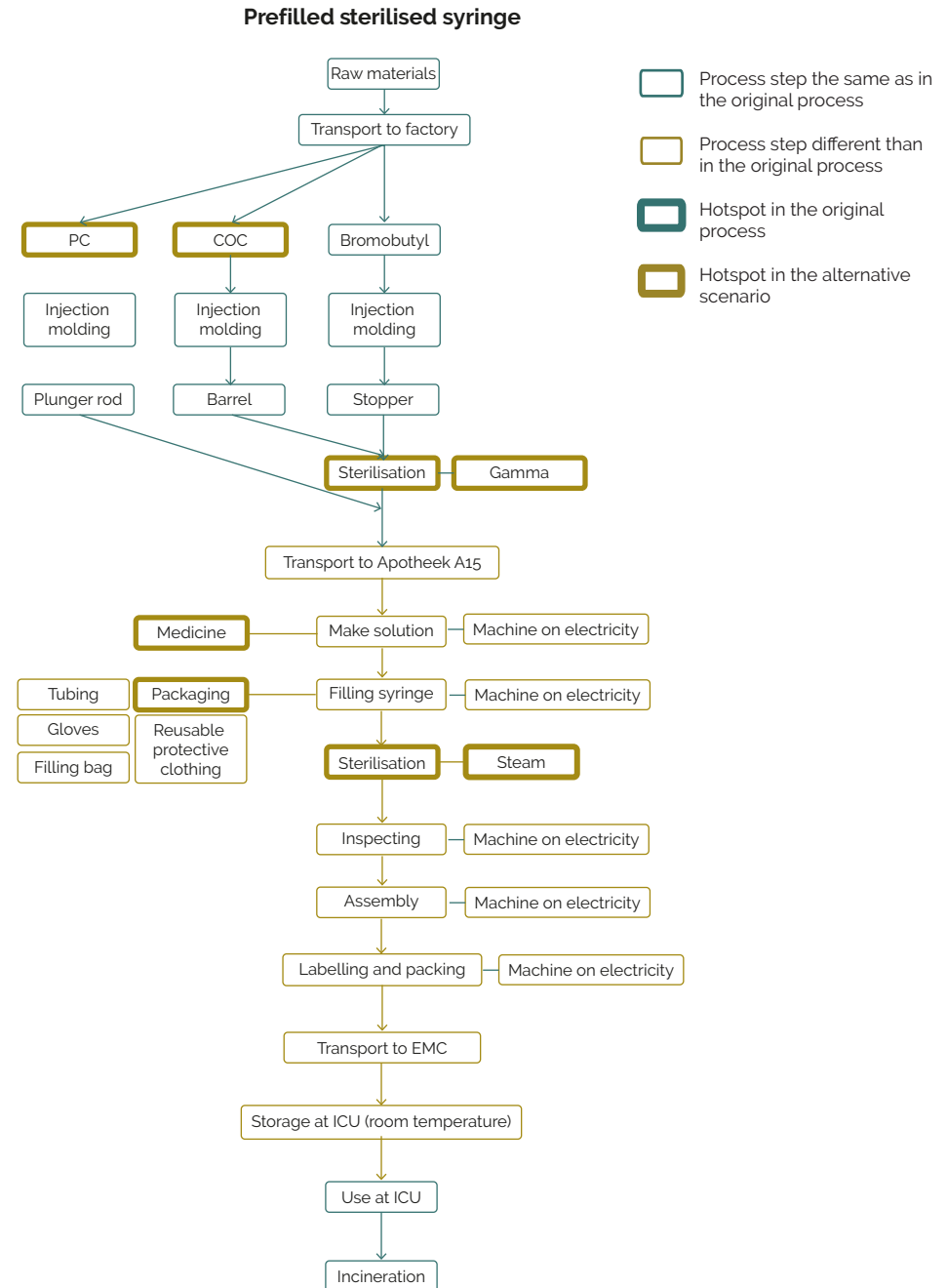


Figure 22: hotspots in life cycle of PFSS.

Furthermore, the empty barrels come in white plastic boxes, which are all disposed of after taking out the empty barrels (20 per box). During the filling process, stoppers are manually added to the machine. Occasionally these stoppers are stuck in the machine and a filled syringe will not be closed off with a stopper. This syringe is then considered as a production failure and is thrown away.

Material impact

Table 5 shows the impact per material relative to the weight. The material impact of cyclic olefin copolymer (barrel) was missing in the Ecolvent database, therefore the impact of the barrel is unknown. The impact of the plunger (1.02 Pt) and stopper (0.77 Pt) of PFSS are significantly higher than the impact of the plunger (0.55 Pt) and stopper (0.38 Pt) from the manually filled syringe. The packaging has a ReCiPe endpoint of 0.58 Pt, whereas the packaging of the manually filled syringe has a value of 0.12 Pt.

Table 5: calculation results of the ReCiPe endpoint of the syringe per FU.

Part	Material	Material impact ReCiPe endpoint (Pt/kg)	Weight per piece (g)	Weight per FU (g)	Total ReCiPe endpoint (Pt)
Plunger rod	Polycarbonate (PC)	0.08	12.8 g	12.800	1.02
Barrel	Cyclic olefin copolymer (COC)	unknown	21.4 g	21.400	unknown
Stopper	Bromobutyl rubber	0.12	6.4 g	6400	0.77
Packaging box	Polystyrene (PS)	0.06	192 g per box (20 syringes in one box)	1000 syringes = 50 boxes = 9600 g	0.58
Total	-		-	50.200 g	



Figure 23: machine for filling PFSS.

Sterilisation

PFSS are sterilised twice, once by the manufacturer (gamma sterilisation) and once by Apotheek A15 (steam sterilisation). This is done to ensure safety, sterility and to prolong the due date to up to 2 years instead of 24 hours. However, different studies show that sterilisation contributes significantly to the environmental footprint. Thiel et al. (2017) show that in the life cycle of reusing metal surgery instruments, sterilisation was one of the biggest impacts.

Leiden, Cerdas, Noriega, Beyerlein, and Herrmann (2020) also show major environmental impacts in the lifecycle of reusable surgery sets resulting from the sterilisation phase, due to energy use. In their study, the reusable instruments were sterilised three times in one life cycle, 2x steam sterilisation (before and after surgery) and 1x gamma sterilisation (after production). This resulted in the outcome that disposable instruments, sterilised once after production (gamma), were more sustainable than the reusable set (see figure 24).

A sensitivity analysis shows that steam sterilisation has a ReCiPe endpoint of almost 2.2 Pt (light blue bar in figure 24), whereas gamma sterilisation has a ReCiPe endpoint of 0.1 Pt (light green bar in figure 24). This is because the energy and water demand for steam sterilisation is considerably high. Other studies also confirmed that the impact of steam sterilisation is significantly high compared to the rest of the life cycle (McGain, Moore, & Black, 2017). Reducing the impact of sterilisation should be focused on decreasing water and energy usage (McGain, McAlister, McGavin, & Story, 2012).

Changing steam sterilisation to gamma at Apotheek A15 presents sustainability benefits since no energy is required for the process itself. However, gamma sterilisation uses 60Co, and therefore high safety standards are needed to ensure that no radiation can leave

the sterilisation location (Leiden et al., 2020). These standards include specific requirements for the location, such as a 2m thick building shell and a large water basin to store the 60Co pencils safely (Sandle, 2013). This means that changing steam sterilisation into gamma sterilisation for environmental benefits requires a major change in the environment and facilities for Apotheek A15.

UV sterilisation is also a sustainable way of sterilisation, but is not suitable for prefilled syringes, as it does not sterilise the inside of the barrels. UV sterilisation is however an option for sterilising surfaces.

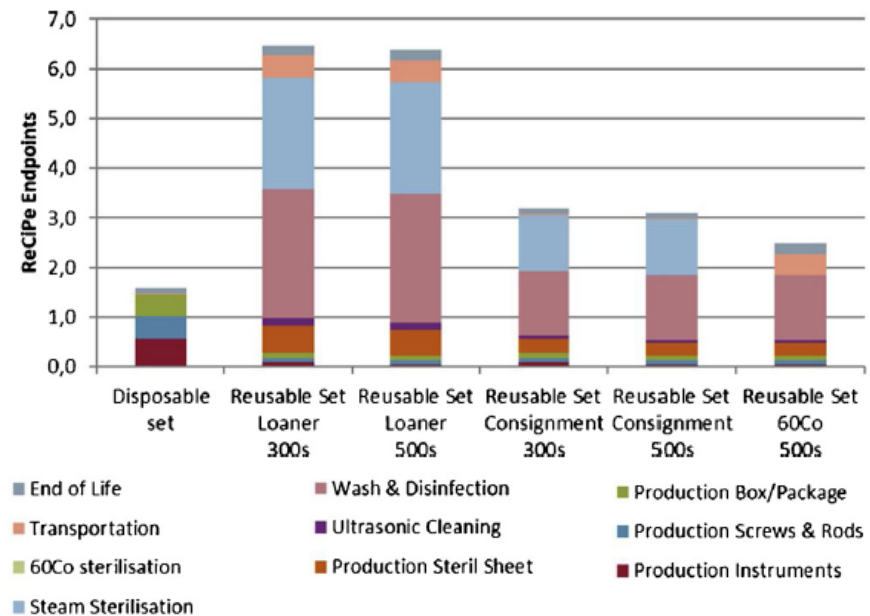


Figure 24: sensitivity analysis showing different scenarios and corresponding ReCiPe Endpoint scores (Leiden et al., 2020).



Figure 25: prefilled syringes in storage in the ICU.

Steps not defined as hotspots

- Machines are used to inspect the syringes on mistakes, to assemble the plunger onto the stopper and to label the syringe. These machines all run on electricity. The amount of energy used is neglectable compared to for example the sterilisation process, and therefore the use of the additional machines are not defined as hotspots in the process.
- Transport: the impact of transport (trucks) is also neglectable due to the small impact transport would have compared to other hotspots.
- Storage: the syringes are stored at room temperature instead of in a fridge. Therefore, this step in the process is not energy-intensive and thus not defined as a hotspot.

Conclusion

The filling process of PFSS saves a lot of products and material during the filling process compared to manually filled syringes. Needing fewer additional products to prepare a syringe reduces the environmental impact (Cheetham & Johnson, 2013). Furthermore, PFSS do not need to be stored in a fridge, as manually filled syringes do.

On the other hand, prefilled syringes have a higher impact on a product material level, since the syringe is made of materials with a higher ReCiPe endpoint than the manually filled syringe. Furthermore, the production process of PFSS involves energy and water consuming sterilisation process after filling, which is not the case for manually filled syringes.

In conclusion, the PFSS are more sustainable than manually filled syringes in terms of less waste. But the impact hotspots of the sterilisation process, leftover medication and materials are points of improvement to make the PFSS an actual sustainable alternative for manually filled syringes.

Recycling vs incineration

All of the hospital waste is currently incinerated. When infectious waste is separated properly from the general waste, other scenarios than incineration can be considered. The environmental impact of different hospital waste management scenarios is determined to investigate which scenarios would decrease the impact of the end-of-life of the syringe.

A study by Ali, Wang, and Chaudhry (2016) investigated the environmental footprint of hospital waste disposal by doing an LCA of different waste treatment scenarios. Three scenarios were compared to each other. The first scenario (A) included incineration and landfill of general hospital waste at an external company. The second scenario (B) involved incineration of mixed (infectious + general) hospital waste at an external company. The last scenario (C) included composting, incineration and recycling of segregated waste. The scenarios were only assessed on greenhouse gas (GHG) emissions (kg of CO₂ equivalent per tonne of hospital waste), other factors such as human toxicity, acidification potential etc were not taken into account. The reason for this was not mentioned. The study showed that landfilling and incineration are the most unfavourable option and that composting and material recovery presented a reduction in emissions. Of all scenarios, a combination of composting, incineration and material recycling turned out to be the best solution (see figure 26), since it could lead to a reduction of GHG emission and prevention of pollution.

This means that changing the end of life from incineration to a combination of incineration and material recovery by recycling would reduce the impact of the syringes in terms of GHG emissions. However, syringes in the category 'infectious waste' cannot be recycled like any other type of waste, due to the possible threat to the health of people

working with the waste. General hospital waste can only be mechanically recycled when the waste is separated properly so that there is no contaminated material present. This requires a behavioural change of the staff working in the ICU.

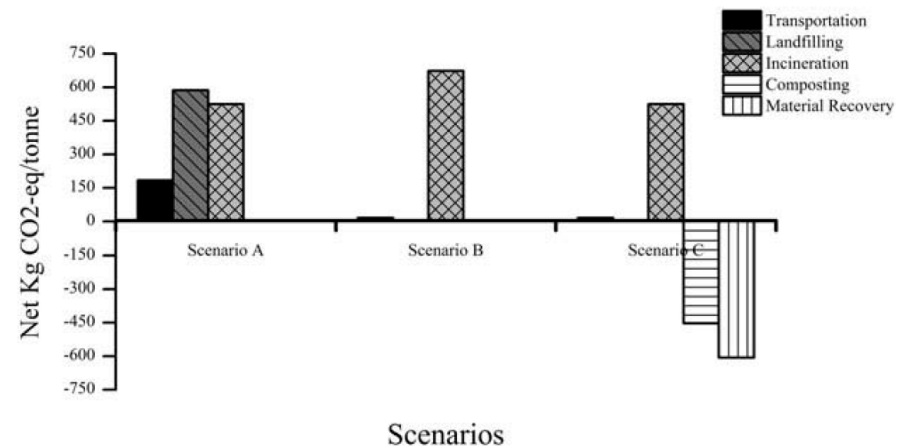


Figure 26: results of the LCA (Ali et al., 2016).

Sterilisation and reuse vs single-use

Sterilisation of highly critical and low-value single-use products is often not considered an option of recovery, because of the costs of sterilisation and safety issues. Safety issues include potential cross-infection, inability to clean and decontaminate, residues from chemical decontamination agents, material alteration, mechanical failure and reactions to endotoxins (Medicines and Healthcare Products Regulatory Agency, 2021). Furthermore, prion diseases are resistant to all common methods of decontamination. Due to minimising the risk of transmission, it is stated by the Medicines and Healthcare Products Regulatory Agency (2021) that 'devices designated for single episodes of use must not be reused under any circumstances whatsoever.'

On the other hand, van Straten et al. (2021) investigated the carbon footprint and costs impact of reprocessing face masks compared to new single-use face masks. They found out that the carbon footprint is 58% lower for reprocessed face masks (used 5 times) than new face masks (used once). The cost price of the reprocessed masks was also lower than the new masks, 1.40 euro and 1.55 euro respectively. However, they did not mention if this includes the costs of collection and logistics of the masks. Van Straten et al. (2021) concluded that reprocessing face masks has a lower environmental impact (carbon footprint) and lower costs than new face masks.

Therefore, reprocessing low-value products should certainly be investigated further. However, the design of the product plays a big role in the risk of potential cross-infection after sterilisation. Narrow or long lumens, coils, type of material and acute angles make it difficult to clean and decontaminate the product (Medicines and Healthcare Products Regulatory Agency, 2021). Syringes have narrow tips and acute angles which could make them hard to clean properly. Therefore, the

barrier to reuse by sterilisation is the shape of the syringe and the need for absolute sterility, since the fluid inside the syringes comes in direct contact with the bloodstream.

Furthermore, the eco-costs of reprocessed syringes should be investigated by an LCA to see if it is actually more sustainable than single-use syringes.



Figure 27: sterilisation autoclave.

Circular materials vs virgin materials

The barrel and plunger of the syringe are made of petroleum-based PP. To decrease the impact of the syringe, this can be replaced with a more sustainable material. A study by Galve, Elduque, Pina, and Javierre (2021) showed that for example recycled PP has a significantly lower environmental impact compared to virgin PP. The overall environmental impact (ReCiPe endpoint) was 29.8% lower and the carbon footprint was reduced by 42.8% (Galve et al., 2021). Therefore, changing the material from virgin PP to recycled PP is a good strategy to reduce the impact of the syringe.

Another option is to replace PP with bio-based PP, which is (partially) made from biomass. Bio-based plastics are more environmentally friendly than petroleum-based plastics (Atiweh, Mikhael, Parrish, Banoub, & Le, 2021). A study by Saidani, Pan, and Kim (2020) compared the global warming potential (GWP) of bio-PP with petroleum-based PP. It showed that bio-PP has a significantly lower GWP than petroleum-based PP. So bio-PP is a great alternative to reduce the impact of syringes. One disadvantage is that currently, the cost of bio-PP is higher than petroleum-based PP (Saidani et al., 2020). Chemically there is no difference between petroleum-based PP and bio-PP.

Until now only PP is discussed because the syringes are currently made of this material. However, other materials than PP could also be considered. For example 'unique' biobased polymers, or plastics that can be chemically recycled such as PET, PC and PMMA. The material properties of sustainable alternatives should still meet the requirements of materials for syringes: high transparency, high chemical resistance, toughness, non-absorbable and resistance to bacteria (Joseph et al., 2021).



Figure 28: Bales of used plastic packed for their journey to be recycled (Martin on Unsplash, 2021).

6.4 Conclusion from a product's perspective

Looking at the syringe from a product's perspective resulted in an understanding of the syringe on a product level. The life cycle analysis of the syringe showed the following hotspots:

- The barrel, plunger and stopper (compared to the packaging)
- The sterilisation process (ethylene oxide)
- Additional products needed per syringe during the filling process
- Cooled storage at the pharmacy until use

Reducing the impact of the packaging would be almost negligible due to the small share in the total weight. Sterility and preventing infections during the production process are the main barriers to decreasing the impact of the production and manual filling process of syringes.

Comparing different life cycle scenarios showed various possibilities to adapt the linear product life cycle towards a more circular life cycle.

Possible solutions are:

- Using prefilled syringes instead of filling syringes manually
- Changing the end of life from incineration to recycling
- Sterilise the syringes after use to reuse
- Change the material from petroleum-based PP to recycled or bio-based PP or another more sustainable material.

Each of these solutions is of interest to investigate further.

Requirements derived from a product's perspective:

- The material must be non-absorbable, and not reactive with medication.
- The design must be able to be mass-produced at least 300.000 per year only for Erasmus MC ICU.
- The design must withstand a sterilisation process (type of sterilisation is to be defined), and not deform or melt in any way.
- The material properties must be high transparency, high chemical resistance, toughness, and resistance to bacteria (Joseph et al., 2021).
- The design must anticipate developments in sustainable materials, to avoid lock-in situations.
- The stakeholders must all be considered to reduce their impact, instead of only looking at Erasmus MC.

7. Design vision and program of requirements

7.1 List of requirements

The conclusions from the analysis are transformed into design criteria. The complete list of requirements can be found in appendix G. The short version is stated below. The requirements are used to evaluate concepts.

- The product must decrease the overall impact of the syringe in the short and longer-term.
- The product must change the linear life cycle into a more circular life cycle.
- The product must not increase the workload of the nurses, regarding time and number of actions. It must be as efficient (in time and number of actions needed) to attach the syringe to the patient as the current syringes.
- The product must be safe for both the patient and staff to work with
 - The product must meet the rules of the infection prevention protocol.
 - The product's sterility and safety must be guaranteed by following the current regulation.
- The product must be able to be mass-produced: 300.000 per year
- The product must (in the end) be financially viable for Erasmus MC and potential stakeholders.

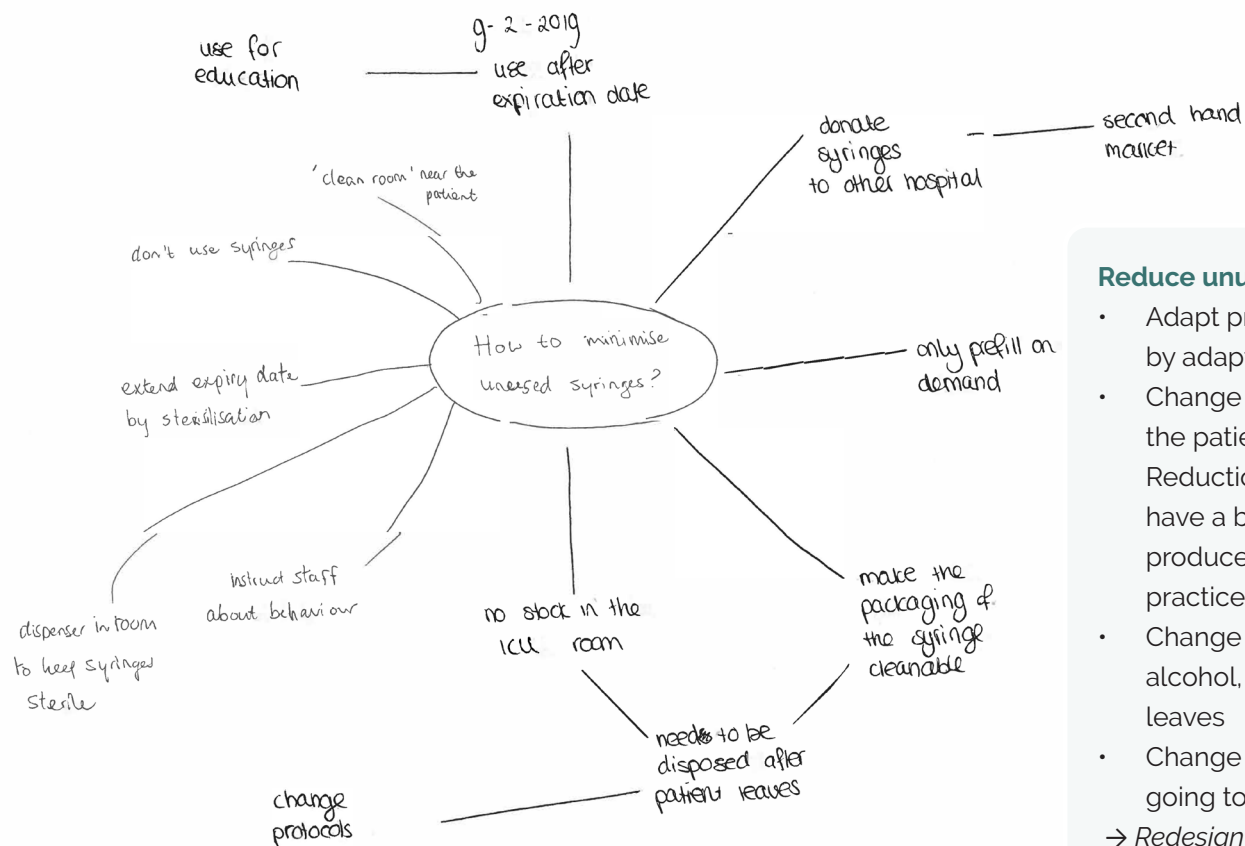
7.2 Design vision

The following vision is derived from the research phase and is used to guide the design process:

*"I want to reduce the **environmental impact** of syringes, without increasing the **workload** of the staff of the ICU, by applying circular design strategies that in the end **reduce** the amount of **waste** and use of **resources**."*

8. Ideation of possible interventions

With the design vision in mind, ideas were generated. This is done by doing creative sessions. Drawings made during the ideation phase can be found in appendix H. All insights and ideas are clustered and divided into categories based on circular R-strategies. For each category, the consequence for a redesign is mentioned.



Reduce unused disposed syringes

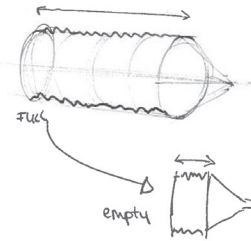
- Adapt protocol: decrease the amount of unused disposed items by adapting the infection prevention protocol
- Change environment: decrease the stock inside the rooms of the patient to decrease the amount of unused disposed items. Reduction of stocked syringes inside patient rooms could have a big impact on the amount of unused hospital waste produced. This demands a change in the working culture and practice of the staff.
- Change packaging: design packaging that can be cleaned with alcohol, so that the syringes can stay in the room after a patient leaves
- Change habits of staff: only pick the number of syringes you are going to use, instead of grabbing a handful.

→ Redesign the protocol, behaviour and environment of the ICU

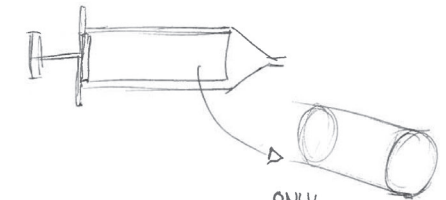
Reduce products on a system level

- Use prefilled syringes instead of manually filled syringes
 - Change workflow: minimise packaging and products used in the pharmacy by making larger batches of filled syringes
 - Change product or workflow: for example, use bigger syringes (100 ml instead of 50 ml) so the nurses need to replace the syringes less often.
- Redesign the process and system of filling a syringe

1. FOLDABLE SYRINGE

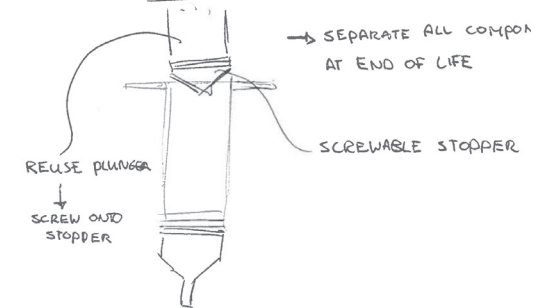


2. CARTRIDGE SYSTEM

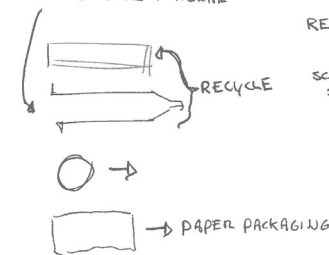


IDEAS
PRODUCT BASED

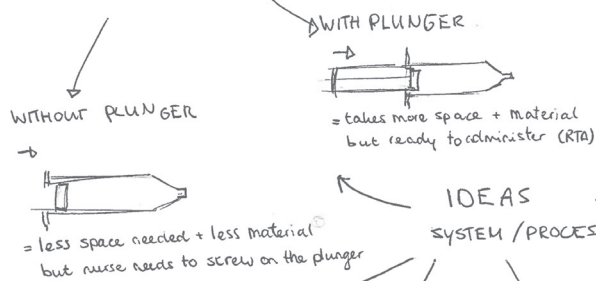
3. MODULAR SYRINGE



4. PLUNGER AND BARREL IN ONE MATERIAL

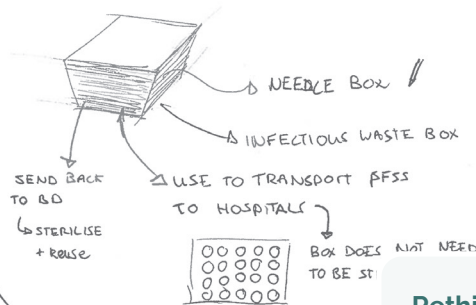


1. USE PREFILLED STERILISED SYRINGES



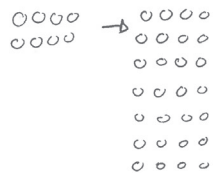
IDEAS
SYSTEM / PROCES

2. REPURPOSE PACKAGING OF PFSS



5. PRODUCE IN LARGE BATCH

→ less waste + costs

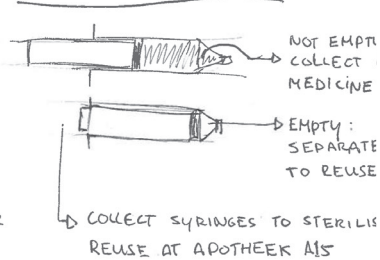


STERILISE WASTE FOR RECYCLING

4. RECYCLE



3. COLLECT USED SYRINGES



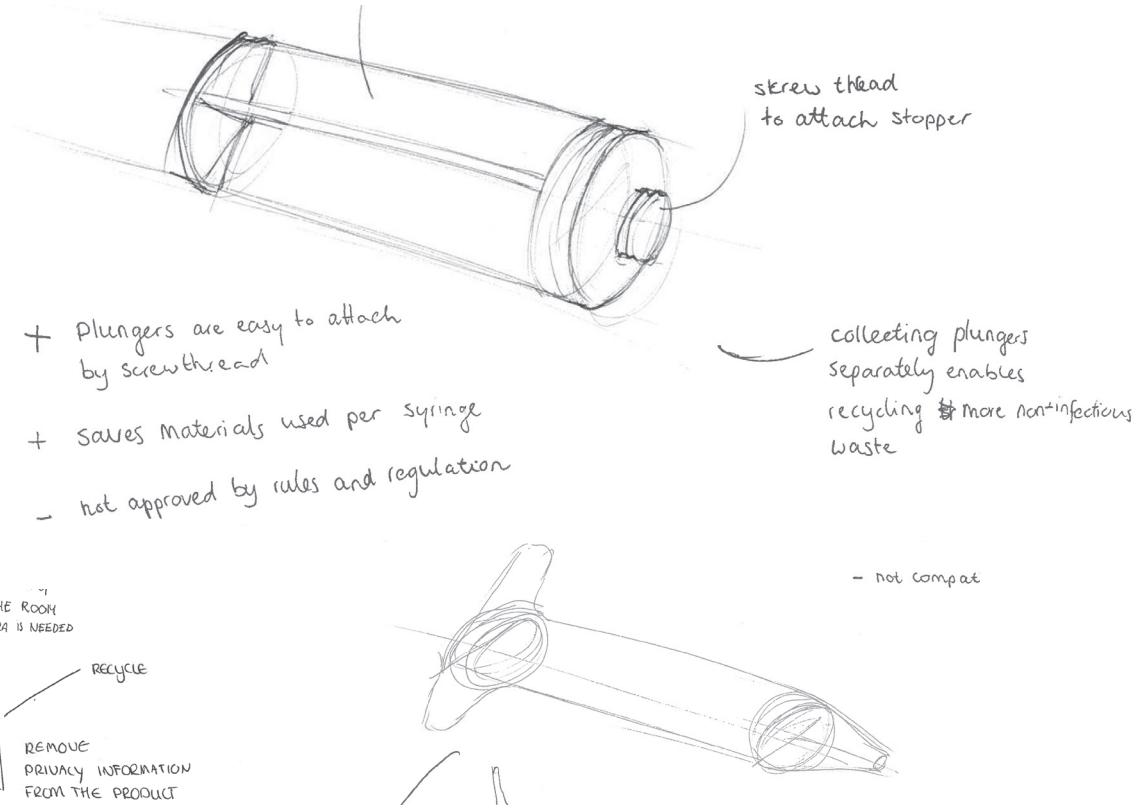
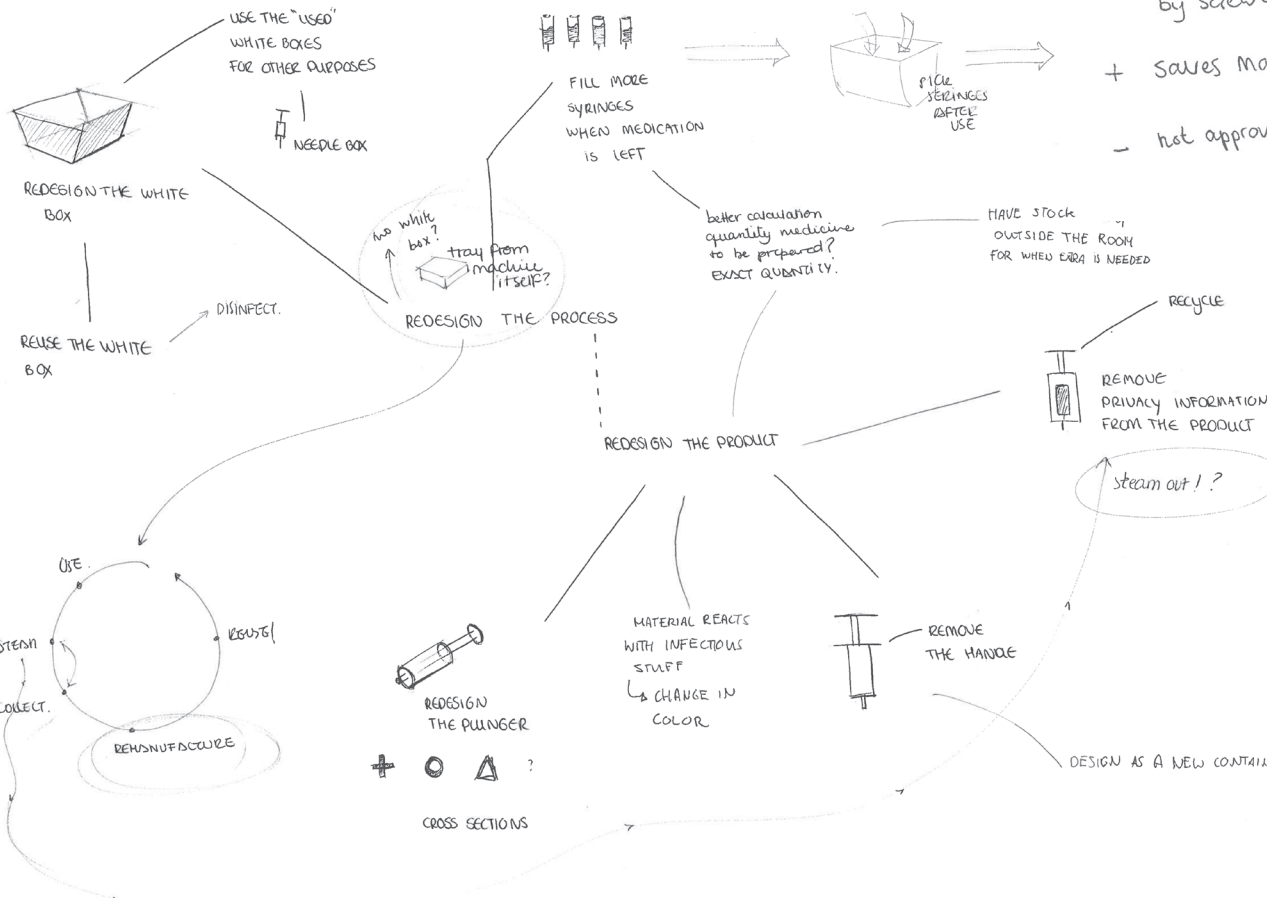
Rethink materials and shape of the syringe

- Change material from virgin PP to a more sustainable material (biobased, biodegradable, compostable, unique biobased polymers, glass).
 - Redesign the shape for saving material or space: decrease the wall thickness, make a modular syringe with a cartridge system, remove the flange
- Redesign syringe in terms of material, shape and end of life

Recycle: separating wasting for recycling

- Change environment: place different waste bins to separate waste, for example in the pharmacy
- Reduction in waste by behavioural change
- Redesign for recycling and separating the components more easily

→ Redesign for waste management and behaviour of the staff



Remanufacture and reuse

- Reuse by sterilising the syringe; use, collect, sterilise, refill and reuse.
- Reuse plungers (plungers do not come in contact with the patient or medication, and are thus not considered infectious)

→ Redesign the form and material of the syringe for sterilisation and reuse

9. Design conceptualisation

9.1 Choosing a design direction

A design direction is chosen to further elaborate during the project.

This is done in consultation with the staff of the ICU. The choice is made based on the list of requirements, the design vision and a discussion with the staff of the ICU.

Four directions based on the ideas (see figure 29) were discussed during a meeting with the project leader Sustainability/Green Team Intensive Care Adults and the Team Manager of the ICU. It became clear that the staff of the ICU and the green team can realise adapting protocol and behaviour change themselves in the short term. The unit infection prevention will take a look at the storage of syringes in the rooms, and adapt the protocol where possible. The nurses are instructed to be aware of how many syringes they pick up and how much they really need.

Concepts on a product and system level were discussed to be of interest for this project. This will affect the behaviour and protocols as well, but the redesign decreases the environmental impact instead of the other way around.

The concept phase will thus be focussed on decreasing the impact on both a system and product level.

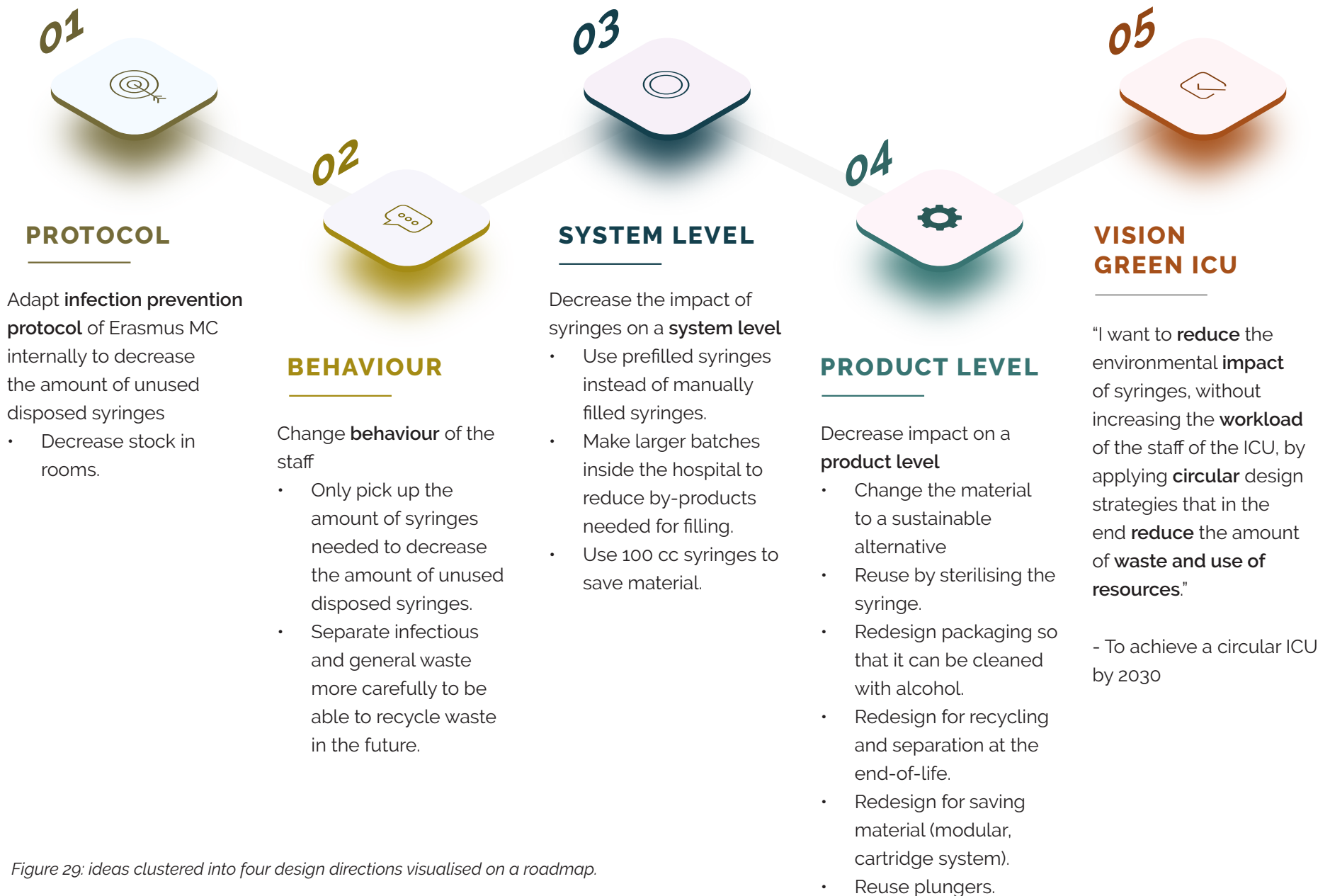


Figure 29: ideas clustered into four design directions visualised on a roadmap.

Concept 1 modular syringe

Reduce the environmental impact by reusing the plunger and the tip and only replacing the barrel. Designed to separate the materials at the end-of-life to enable recycling.

Advantages of modular syringes

- Easy separation of materials to be able to recycle
- Cartridge system (only replacing the barrel for use) saves material
- Reuse the plungers multiple times

Product improvements to be made

- Design components in such a way that they can be assembled and separated easily (screw thread for example)
- Design a new workflow for the staff that does not increase the workload

Influence on stakeholders

Manufacturer: adapt production process

A15: adapt production process (fill barrels only)

Erasmus MC: adapt workflow (extra work to disassemble and separate waste) + add recycle possibilities

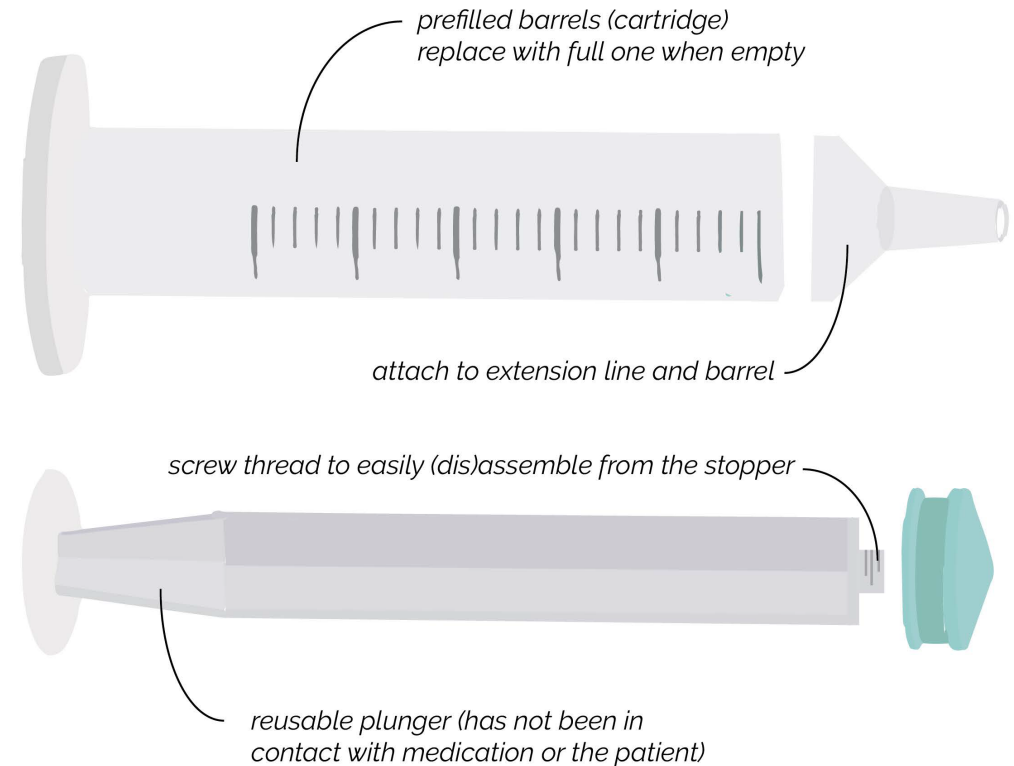


Figure 30: concept 1.

Concept 2 optimise filling process PFSS

Optimise the filling process to reduce losses during production of prefilled sterilised syringes.

Advantages of prefilled sterilised syringes

- Reduced amount of waste by filling the syringes at Apotheek A15 (mass production) instead of manually in the ICU
- Longer shelf life (up to 2 years on room temperature)
- Takes off workload of nurses/pharmacists
- Guaranteed quality of medication

Production process improvements to be made

- Reduce losses in production process
- Repurpose packaging box as needle container in the hospital
- Use renewable energy
- Optimise use of machines and sterilisation phase

Influence on stakeholders

Manufacturer: t.b.d.

A15: adapt production process

Erasmus MC: t.b.d.



Figure 31: concept 2.

Concept 3 sterilisable syringe

Decrease the impact by reusing and refilling the syringe through sterilisation.

Advantages of sterilisable syringes

- Save material and production processes by reusing the syringe multiple times before disposal
- Add as a product-service system with Apotheek A15

Product improvements to be made

- The shape must be redesigned to enable proper decontamination: avoid acute corners and narrow coils.
- Safety must be guaranteed for reuse

Influence on stakeholders

Manufacturer: adapt product and production process

A15: for a product service system: adapt production process; collect empty syringes + extra round of sterilisation

Erasmus MC: adapt workflow (extra work separate empty syringes from other waste)

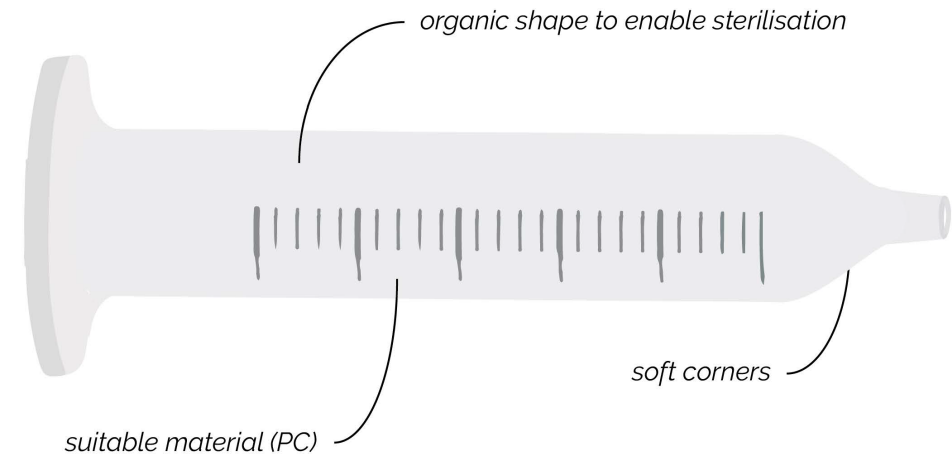


Figure 32: concept 3.

Overview of the three concepts

The impact of each concept is placed on the product journey. The first one shows the original product journey of manually filled syringes. The

boxes around a step in the process indicate that this step is different than the original. The arrows indicate that material is going back in the loop.

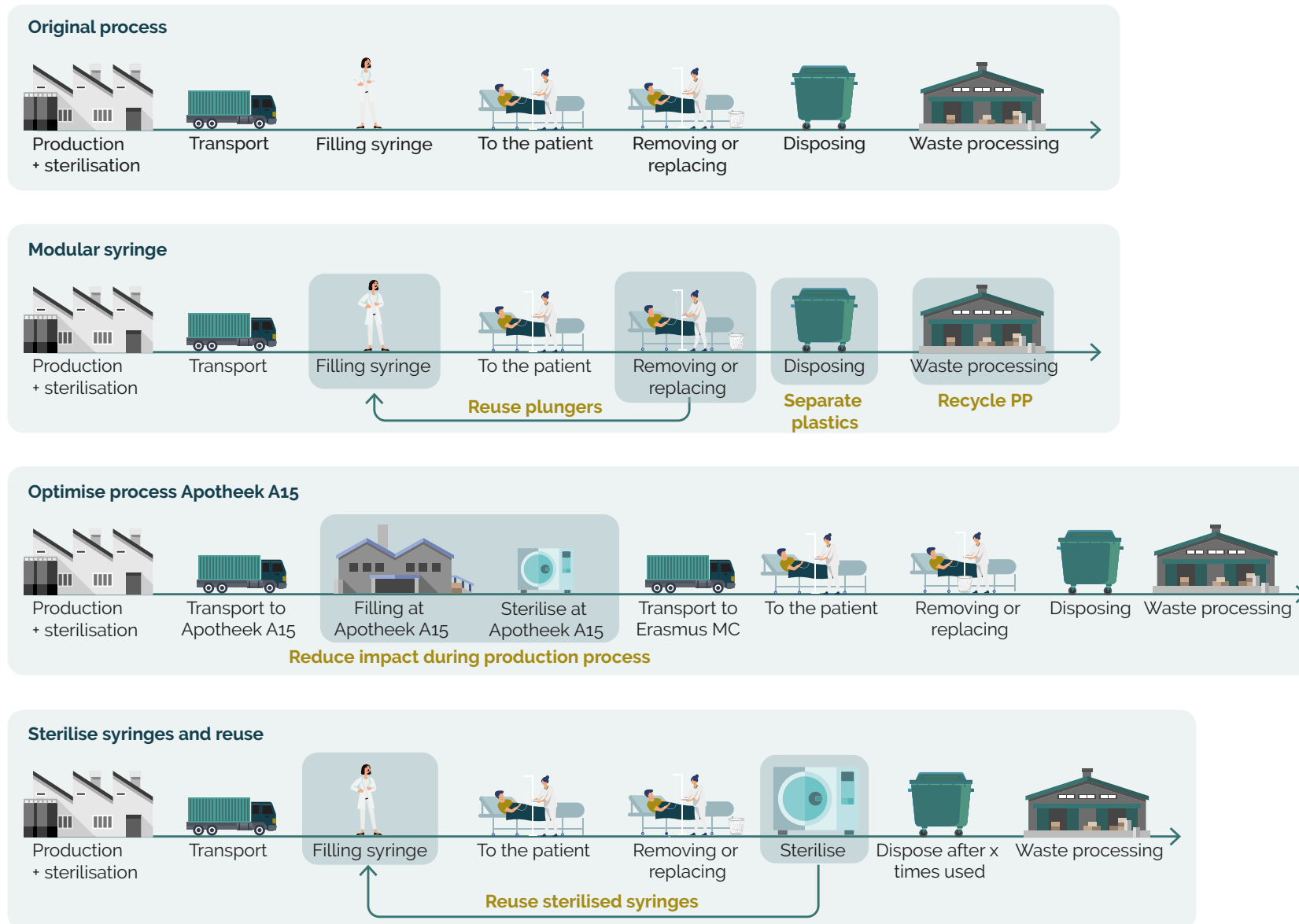


Figure 33: an overview of the three concepts compared to the original process.

9.3 Selecting one concept

The concepts are evaluated with a Harris profile; a visual representation of the strengths and weaknesses of the concepts (van Boeijen, Daalhuizen, Zijlstra, & van der Schoor, 2013). The main design requirements are used to evaluate the concepts relative to each other. The requirements are ranked in order of importance, the top being the most important. The concepts are compared in terms of performance in each requirement. The black blocks need to be imagined as a tower; by looking at which way the tower falls a decision can be made.

Comparing the three profiles shows that improving the filling process has the most favourable profile (see figure 34). The concept scores high on safety and on not increasing the workload for the staff in the ICU. Each requirement with argumentation for scoring the concepts is given below:

Safety

All concepts could be developed safely for both the patient and the staff. However, the automated process at Apotheek A15 has a reduced chance of human mistakes as opposed to the modular and sterilisable syringe.

Decreasing the environmental impact

The modular syringe and improved filling process score the same on decreasing the environmental impact and implementing circular strategies. Modular syringes decrease the impact by reusing parts of the syringe. Improving the filling process reduces material use in the filling process. The sterilisable syringe scores badly since sterilising and cleaning (contaminated) syringes is an energy-intensive process.

Workload

The modular syringe and sterilisable syringe require more time and actions from the nurses than currently used syringes, for example, to

separate the materials and collect syringes for sterilisation. The syringes from Apotheek A15 are produced for 'ready to use' (RTU) and require the least amount of time and actions for the staff in the ICU. Furthermore, as little need for change in behaviour from the staff as possible will result in higher acceptance of the solution

Viability

Financial viability is difficult to predict in this stage, but it is assumed that the sterilisable and modular syringe would be more viable than the syringes from Apotheek A15. The manufacturer of the syringes changes the production process and sells these syringes worldwide. Apotheek A15 only serves a group of academic hospitals in the Netherlands and has therefore a smaller range of clients.

Large scale

The modular and sterilisable syringe would be produced by the manufacturer, who already produces syringes on a large scale and thus has the facilities. Apotheek A15 is dependent on the demand from the hospitals. Nonetheless, Apotheek A15 is already expanding their building to prepare for delivering syringes on a larger scale.

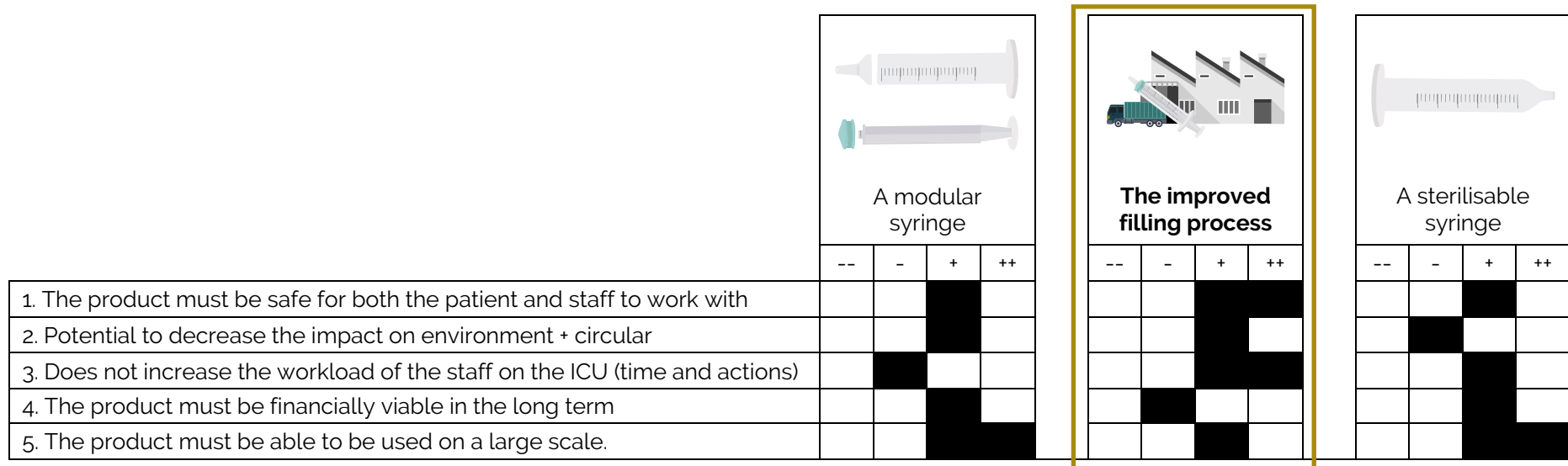


Figure 34: Harris profiles for the three concepts.

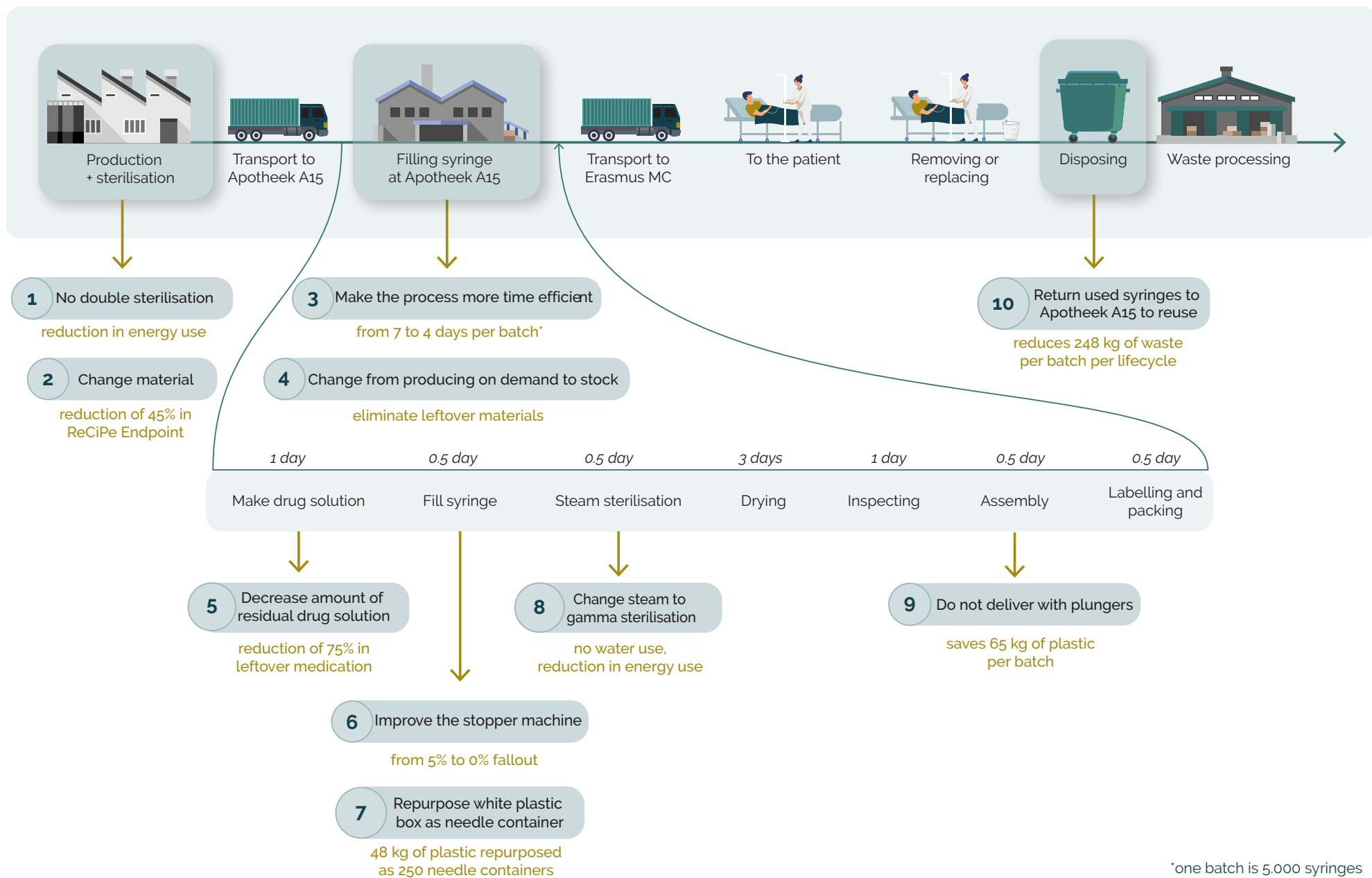


Figure 35: Overview of interventions on decreasing the impact of the filling process of PFSS at Apotheek A15, visualised on the product journey.

10. Detailing the concept: optimising the filling process of PFSS

The final concept is a process optimisation for the entire filling process of prefilled sterilised syringes at Apotheek A15. All steps in the filling process of syringes have been reviewed with the design vision in mind. This resulted in a holistic concept that reduces the environmental impact of syringes without increasing the workflow of the staff in the ICU.

PFSS are produced in large batches and require fewer additional products per syringe than manually filled syringes. Therefore, PFSS are assumed to have a lower impact than manually filled syringes. However, the impact hotspot analysis of PFSS (section 6.3) showed that the materials used, sterilisation and leftover products contribute significantly to the environmental impact. This makes it less environmentally friendly than existing studies assumed.

Therefore, the design concentrates on decreasing the environmental impact of the hotspots in the filling process of PFSS. Figure 35 shows an overview of 10 interventions that reduce the impact of the filling process.

The 10 different interventions are based on circular design strategies and have the following effect:

- **Reduce waste** (interventions number 4. deliver from stock, 5. decrease the amount of drug solution, 6. improve stopper machine, 7. repurpose packaging, 8. reuse plungers and 10. reuse syringes)
- **Reduce energy and water usage** (interventions number 1. double sterilisation and 8. steam to gamma)

- **Reduce material impact:** (intervention number 2. change to a sustainable material)

Furthermore, the final design also improves the workflow efficiency. In the next section, all 10 interventions are explained separately.

10.1 Explanation per intervention

All 10 interventions are explained in this section.

1. Eliminate the first sterilisation

Sterilisation takes place twice, at the manufacturer (gamma sterilisation), and at Apotheek A15 after filling the syringes (steam). The first sterilisation could be left out since the syringes are already sterilised after filling.

- Impact: reduction in energy use and materials (Co60) needed for gamma sterilisation.
- Drawback: syringes need to be produced as sterile as possible. Eliminating the first sterilisation increases the risk of microorganisms and endotoxins in the syringe.
- The consequence for the ICU: this will formally not have an impact on the ICU.
- Future actions to take: research the safety of this intervention to ensure that there are no microorganisms and endotoxins present after filling and sterilisation at Apotheek A15.

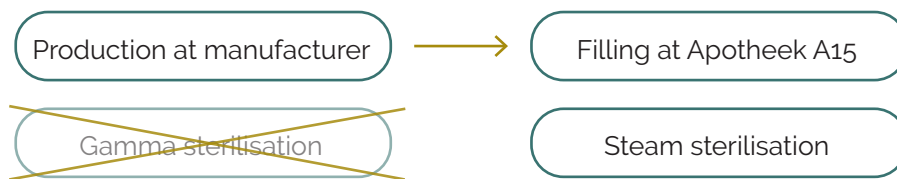


Figure 36: eliminating the first sterilisation.

2. Change material

Change COC and PC to materials with a lower impact, but the same properties, to decrease the overall impact per syringe. To avoid lock-in situations in the future, the manufacturer should look into plastics that will be sustainable in the far future, such as 'unique' biobased polymers. The material should also withstand current and future sterilisation processes.

- Impact: material impact decreases per syringe. For example, changing PC to bio-PP decreases the impact by 45% in ReCiPe Endpoint concerning the material.
- Drawback: The costs of sustainable plastics is currently higher than petroleum-based plastics.
- The consequence for the ICU: A material change might affect the settings of the infusion pump. The speed of the pump is based on the friction between the stopper and the barrel. The lead time of the new syringe must be tested.
- Future actions to take: Research sustainable alternatives for the future with the required material properties.

3. Reduce the amount of time needed to fill one batch

The filling process takes a week for one batch, as can be seen in figure 37. The drying process after steam sterilisation is the bottleneck (takes 3 days). Replacing steam sterilisation with gamma sterilisation eliminates the drying process, and makes the process more time-efficient. The process would then only take 4 instead of 7 days.

- Impact: increased workflow efficiency, so more production is possible in the same amount of time.
- Drawback: no direct influence on reducing the impact of the syringes.
- The consequence for the ICU: the pharmacy technicians experience less time between ordering and receiving the syringes.
- Future actions to take: try out different schedules during the filling process to find out which one is the most efficient.

4. Change from producing on-demand to producing from stock

Currently, the demand of the different academic hospitals is combined and one big batch is made for all hospitals together. It takes a relatively long time from ordering to delivery to the ICU.

Making larger batches provides the possibility to deliver from stock. This reduces the time between the request and actual delivery and prevents having leftover medicine. The production could continue until the pharma vessel is empty.

- Impact: increased workflow efficiency and no leftover medicine
- Drawback: space needed to store all the syringes
- The consequence for the ICU: the pharmacy technicians would experience less time between ordering and receiving the syringes. Express deliveries are then possible as well.
- Future actions to take: determine where the syringes can be stored after production, how many syringes need to be produced per batch and how long it takes to sell the whole batch.

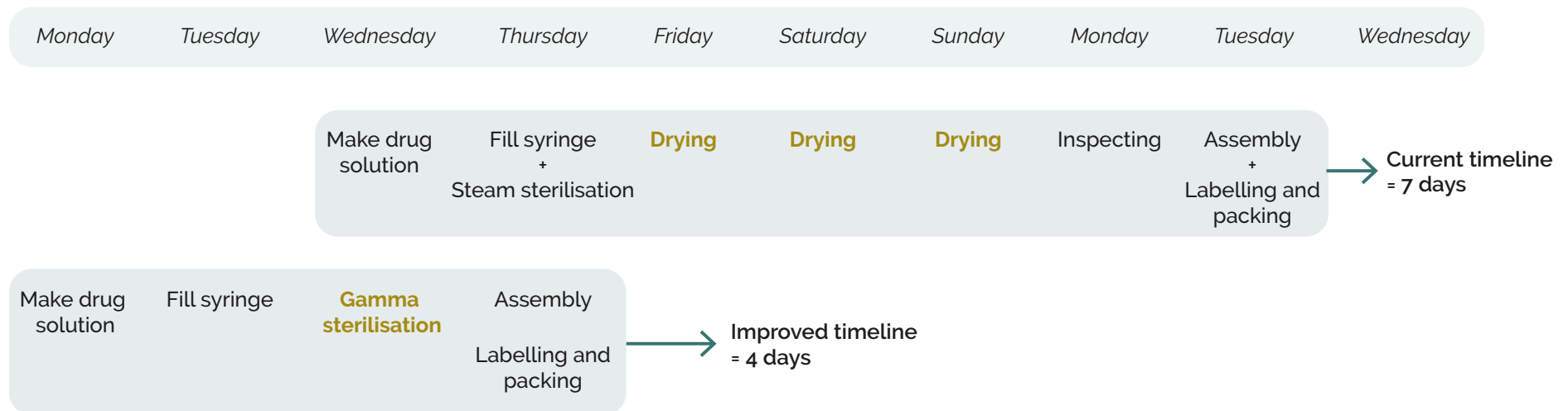


Figure 37: current and improved timeline of filling syringes at Apotheek A15.

5. Decrease the amount of residual drug solution

Around 20 L of 300 L medication solution is left and disposed of after filling a batch of syringes. This could be reduced to 5 L, which is the dead volume of the pharma vessel. This is a 75% decrease in left-over medicine.

- Impact: decreased environmental impact by reducing the amount of leftover medicine.
- Drawback: no room for mistakes (spilling medicine solution), because then the pharma vessel will be empty before the batch is finished.
- The consequence for the ICU: this intervention will not have an impact on the ICU.
- Future actions to take: calculate the exact amount of drug solution needed to fill x number of syringes with a safety margin for mistakes and calibration of the machine. Measure how much is left over after a day of filling and optimise the safety margin.



Figure 38: staff manually adding the stoppers into the machine.

6. Improve the stopper machine

The filling machine places stoppers into the barrels to seal off the liquid. The stoppers are manually supplied to the machine (see figure 38). The stoppers occasionally get stuck in the machine, resulting in filled barrels without a stopper. These filled barrels are disposed of because the stoppers cannot be inserted manually. A solution to this problem decreases the number of disposed of syringes during the process.

- Impact: decrease environmental impact by reducing errors in the stopper machine.
- Drawback: -
- The consequence for the ICU: this intervention will not have an impact on the ICU.
- Future actions to take: measure the number of syringes that come out of the machine without a stopper per batch. Find out why the stoppers get stuck and find a solution. Measure the number of syringes without stopper again to see if the problem is solved.



Figure 39: supply of stoppers in the machine.

7. Repurpose the white plastic packaging box as needle containers for the hospital

The empty barrels from the manufacturer are delivered to Apotheek A15 in sterile white plastic boxes (20 barrels per box), see figure 40. The boxes are only used for sterile transport. When the barrels are taken out, the boxes are disposed of. The boxes are designed to protect the barrels from being damaged on transport and are therefore quite heavy and firm. Repurposing the boxes as sharps waste containers for the ICU extends the lifetime of the box and eliminates the need for the current sharps containers. The logistics are already there.

- Impact: decrease the impact of the by-products of the filling process by repurposing it as a needle container

- Drawback: increased workload in either Apotheek A15 or the hospital, since the lids need to be assembled onto the containers.
- The consequence for the ICU: the new boxes will not affect the workflow of the staff on the ICU. Currently, the lid and box of the sharps container are also assembled by the staff of the ICU when they pick up a new box. As long as the lid has the same functionalities, the staff will not be affected by this intervention.
- Future actions to take: design a lid and test it in the user environment.

Appendix I shows the design process of designing the lid.

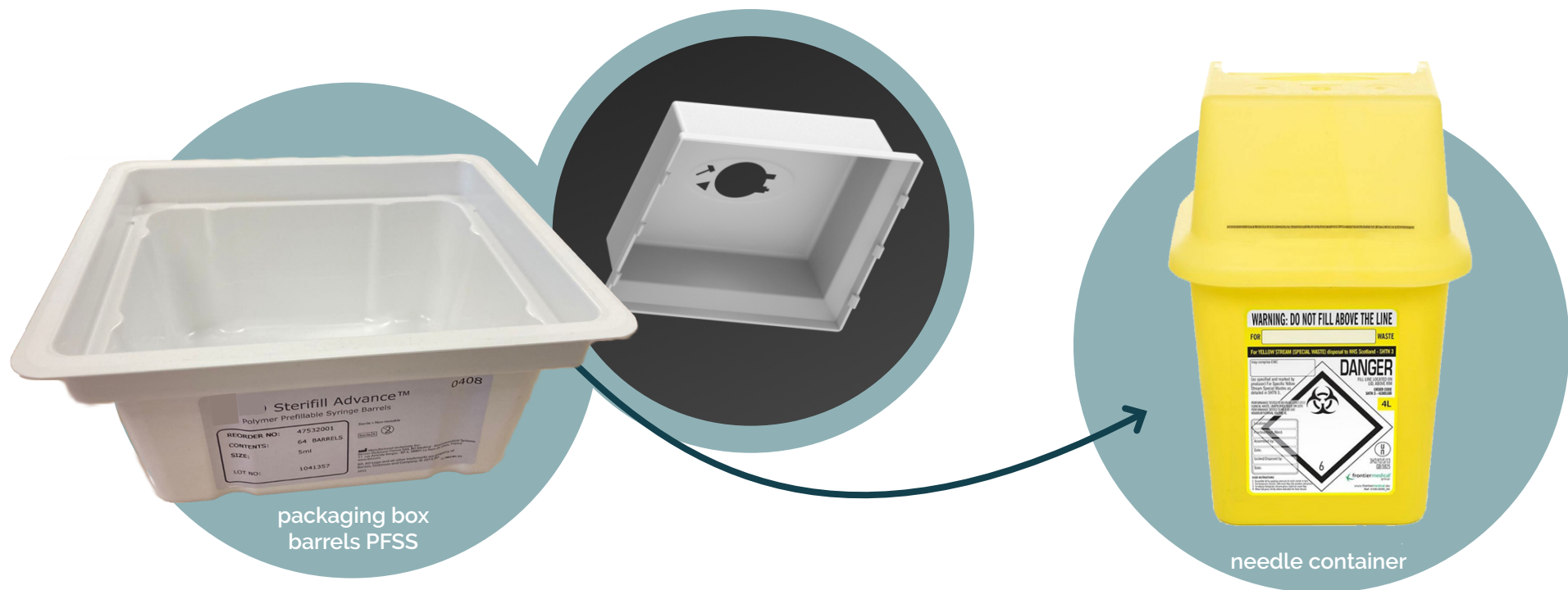


Figure 40: packaging boxes and a designed lid used as a needle container.

8. Gamma sterilisation instead of steam

Using gamma sterilisation at Apotheek A15 would reduce the environmental impact of the process significantly since gamma sterilisation require less water and energy than steam sterilisation. However, gamma sterilisation requires a drastic change in the building of Apotheek A15, due to the safety regulations. A 2m thick building shell and a large water basin to store the 60Co pencils safely (Sandle, 2013) would be needed. Therefore, this is a long term solution. Furthermore, it needs to be tested whether the medication inside the syringes could withstand gamma sterilization.

- Impact: major reduction in impact in the sterilisation phase.
- Drawback: comes with a cost to introducing this in the building
- The consequence for the ICU: this intervention will not have an impact on the ICU.
- Future actions to take: research the possibilities of gamma sterilisation in combination with medication and the feasibility and viability of replacing the autoclave with a gamma sterilisation installation.

9. Do not deliver with plungers and reuse plungers

The plungers are assembled to the syringe in the last phase by a separate machine. Eliminating this step results in syringes taking up less space during storage and transport (see figure 41). The plungers can be assembled at the hospital, where they can be stored as well. When the syringe is empty, the plunger can be reused for the next syringe.

- Impact: decrease in impact by reusing plungers (less material used per syringe). Less space is needed during storage and transport.
- Drawback: possible contamination of plungers. Reusing might not be safe.
- The consequence for the ICU: increased workload on the staff of the hospital to assemble plungers. Also, when the nurses are in a hurry, the syringe needs to be ready to use. They will not have time to assemble a plunger.
- Future actions to take: investigate whether it is safe (regarding infections) for the patient and nurse to assemble and reuse a plunger in the ICU. Research who should assemble the plungers; staff on the ICU, or at the pharmacy etc.

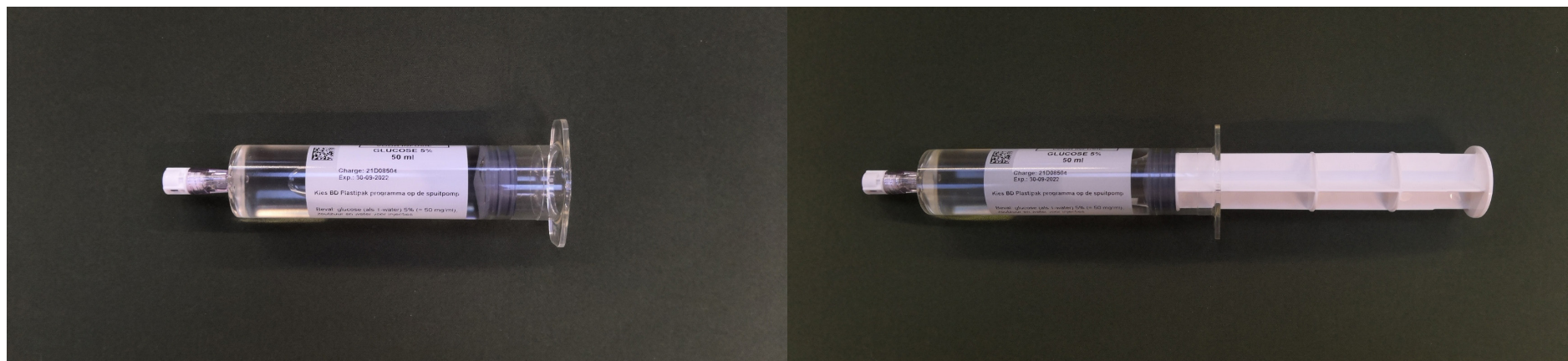


Figure 41: prefilled syringe without (left) and with the plunger (right).

10. Return used syringes to Apotheek A15 to reuse after sterilisation

Syringes are only used once before disposal. However, reusing syringes decreases the environmental impact. The only requirement is that the syringes must be sterile again.

Apotheek A15 already has the machines and infrastructure for sterilising new syringes, it would not be a major change to also sterilise used syringes. Apotheek A15 would collect the syringes from the hospitals, sterilise and decontaminate them and finally reuse and fill them with medicine.

From earlier research, steam sterilisation appeared to be the greatest contributor to the environmental impact of the filling process. Therefore, steam sterilisation should not be considered to remanufacture the syringes. If gamma sterilisation is introduced at Apotheek A15, remanufacturing syringes would be an intervention to look into. Before sterilising the syringes, a sustainable cleaning phase to remove all leftover liquids should be performed.

- Impact: reduced impact by using fewer materials by reusing the syringes. This would save material used per lifecycle of a syringe.
- Drawback: sterilisation and decontamination increase the impact

significantly. Furthermore, the safety of remanufactured syringes must be guaranteed before use. Further studies should investigate the safety of remanufactured syringes, specifically if liquids and microorganisms are still present after the cleaning and sterilisation process. Also, the number of cycles possible should be determined. Each cycle affects the material and product integrity could be affected.'

- The consequence for the ICU: increased workload on the staff of the ICU. Reusing syringes demands a proper collection of syringes by the nurses, since sterilisable syringes need to be separated from the single-use syringes.
- Future actions to take: research the safety of this intervention and the practical aspects; How many times can a syringe be sterilised and reused? How do you know the syringe has lost its integrity and needs to be disposed of? What is a sustainable way of cleaning before sterilisation?

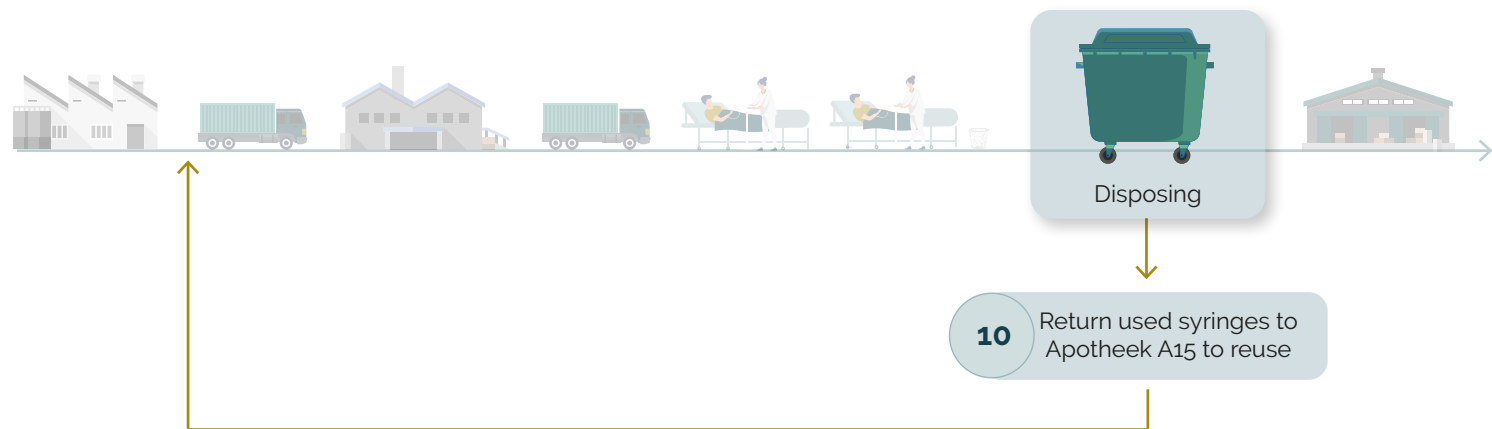


Figure 42: illustration of returning used syringes to reuse again.

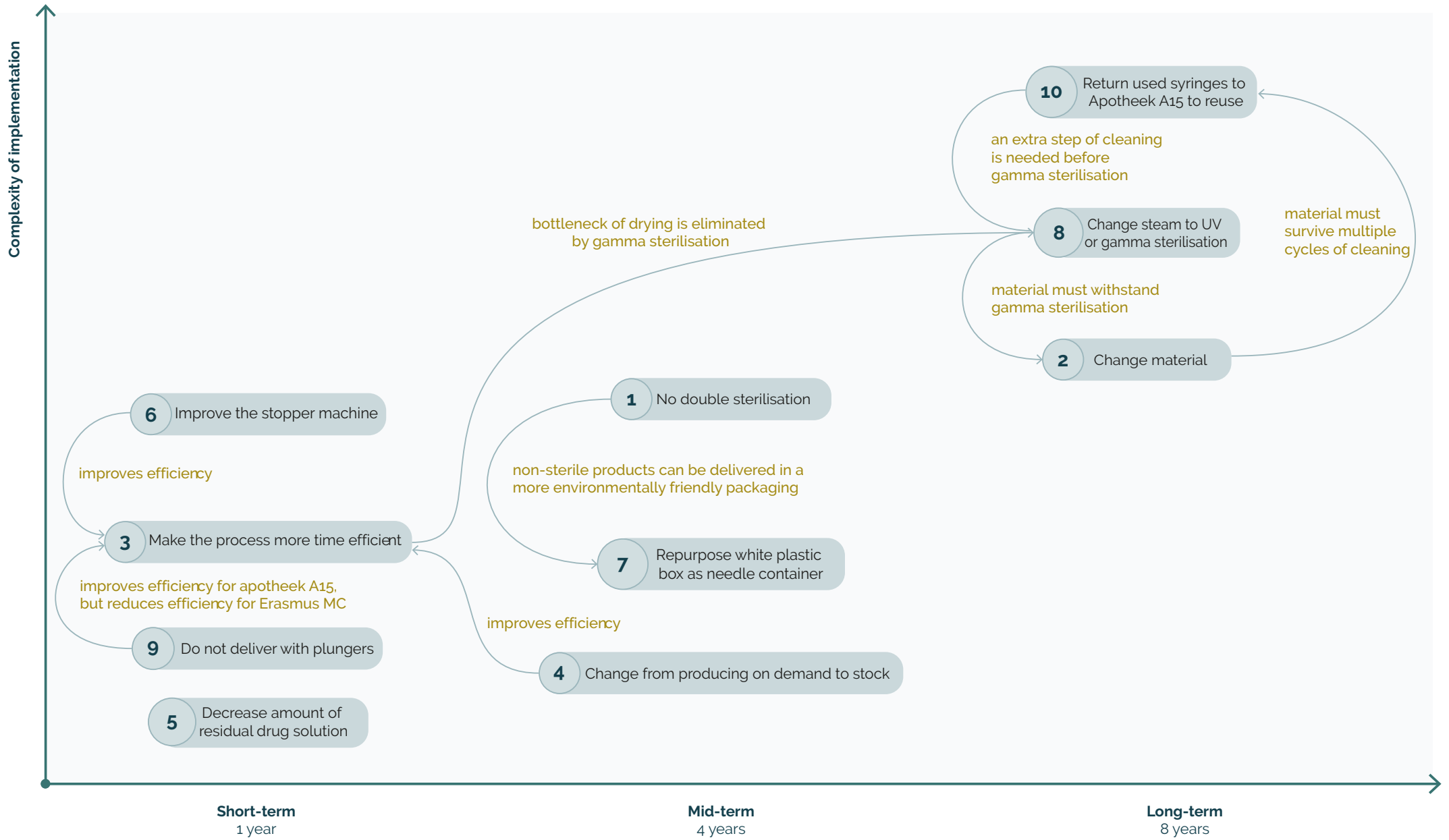


Figure 43: Roadmap and relations between interventions.

10.2 Coherence between interventions

The interventions interrelate with each other and should be considered together to achieve an overall reduced impact in the long term. Figure 43 shows the different interventions on a roadmap (x-axis). The arrows indicate relations between the different interventions and the y-axis indicates the complexity of implementation.

Firstly, changing steam to gamma sterilisation interrelates with interventions 2 (change material), 10 (reuse syringes) and, 3 (increase efficiency).

- The material choice not only depends on a reduced impact but also on gamma sterilisation capabilities and remaining its product integrity after a certain amount of cycles.
- If syringes are reused, gamma sterilisation will not be enough to clean the syringes. An extra step of cleaning is needed.
- Gamma sterilisation will increase the efficiency of the process since the bottleneck of the drying process is not present anymore.

Secondly, eliminating the first sterilisation at the manufacturer could result in a different packaging of empty barrels. The barrels do not need to be transported sterile anymore and could be transported in packaging that costs less material. This also influences the intervention of repurposing the packaging as a needle container, which would then not be needed anymore.

Lastly, several interventions contribute to making the process more time-efficient at Apotheek A15: intervention 6 (improve stopper machine), intervention 4 (produce for stock), intervention 9 (deliver without plungers) and intervention 8 (change to gamma sterilisation).

10.3 Evaluation

The concept is evaluated by discussing with the following stakeholders:

- Apotheek A15: senior pharmacist production
- Erasmus MC: pharmacist and project leader Sustainability/Green Team ICU

The main question to be answered is:

How feasible/viable/desirable are the interventions?

During the discussion, the concept was explained and the stakeholders were able to express their opinion per intervention.

Results:

The results of the evaluation can be seen in table 6. Even though the interventions are not detailed in-depth, the contacted stakeholders were able to evaluate each intervention to a certain extent.

Table 6: evaluation of interventions with Apotheek A15 and Erasmus MC.

Interventions	Evaluation with Apotheek A15	Evaluation with Erasmus MC
1. No double sterilisation	Apotheek A15 needs as sterile as possible syringes to work with. Working with syringes with bacteria results in endotoxins present in the fluid inside the syringe. This is not desired.	Formally this does not influence the ICU. However, the sterility of syringes must be guaranteed for the ICU to use them.
2. Change material	This should be done by the manufacturer. Apotheek A15 will do a qualification examination with the new material to see if it reacts with the medicine.	A validation with the B-Braun infusion pump must be performed to test the new material with the speed of the pump.
3. Make the process more time-efficient	Currently, it takes 3 days to dry the syringes. The drying process is the bottleneck to a shorter process.	This only affects the time from order to delivery.
4. Producing from stock	Good idea. This also eliminates the transport between hospitals, who deliver PFSS to each other as well when a certain hospital is in need.	This only affects the time from order to delivery.
5. Decrease amount of residual drug solution	The vessel is filled with 300 L, of which 20 L is left. This could be reduced to 5 L, which is the dead volume of the vessel. However, a full cart of syringes in the autoclave and having leftover medicine is preferred over no medicine left and a half-full cart for the autoclave.	No impact for the ICU.
6. Improve stopper machine	This is a good idea.	No impact for the ICU.
7. Repurpose syringe packaging as needle container	Good idea. The information of the box cannot be taken off due to regulations, it must remain visible what was in there. This idea will be passed on to the R&D department.	The staff would not mind this change. The workflow remains the same, as the staff currently also picks up a lid and a box separately. An explanation of the new boxes is enough for the nurses to know to use it.
8. Change steam to gamma sterilisation	All the products are currently designed for steam sterilisation. It will not be possible in the short term.	No impact for the ICU.
9. Do not deliver with plungers	Beneficial for Apotheek A15, it saves space and a machine. However, the goal of PFSS was to deliver ready to use products and to reduce the workload of the hospital staff.	This is not desirable since it increases the workload of the staff in the ICU.
10. Sterilise used syringes to reuse	Safety needs to be guaranteed. For reuse, Apotheek A15 does not have the facility to attach the silicone oil layer to the inside of the barrel, which is essential for the syringe to close smoothly.	This will demand a change in workflow of the nurses to separate reusable syringes from disposable syringes, but it is possible.
Overall	Great overview of what possibilities there are to improve the process. It would be nice to have a step-by-step plan of how to implement these solutions so we can start to reduce the impact on the filling process.	Impact of PFSS on the staff: For the nurses, there will be no changes. It saves a lot of time for the pharmacy assistants (prepare-make-finish) to switch to prefilled sterilised syringes. For the pharmacist, it saves 5 minutes per batch (check protocol), since the PFSS are already inspected. The syringes are ordered by the pharmacy procurement and are stored at the stockroom of the pharmacy, and a small amount in the ICU.

Conclusion

Evaluating clarified that the final design provides an added value in either reducing the environmental impact or in making the workflow more efficient. However, some interventions require further research to investigate the feasibility and safety.

Firstly, eliminating the first sterilisation means that Apotheek A15 receives non-sterile empty barrels. Sterilising barrels with bacteria results in endotoxins inside the barrel. A high concentration of endotoxins could be harmful to the patient, as it will enter the bloodstream of the patient. Therefore, this should be validated before implementation. If double sterilisation turns out to be necessary, UV sterilisation of empty barrels should be considered, as this is the most environmentally friendly way of sterilising (but not possible for filled syringes, since UV sterilisation is only suitable for decontaminating surfaces).

Secondly, delivering the syringes without plungers is not desirable for Erasmus MC, as it increases the workload too much. This intervention will therefore not be implemented in the future. Reusing syringes will also require extra time from the staff, as the reusable syringes need to be separated from single-use syringes. However, the staff is open to separating waste, and therefore this intervention can be implemented in the future.

Compared to the original manual filling process in the ICU, the PFSS have an added value by decreasing the workload of the staff in the ICU. The workflow of the nurses, care assistants, intensivists, and cleaners will remain the same. The workflow of the staff of the pharmacy will change positively. The pharmacy assistants will save time since they don't need to prepare and fill the syringes anymore. For the pharmacists, it will also save time, namely 5 minutes per batch.

In conclusion, the final design reduces the environmental impact of syringes, by reducing the amount of waste, energy and water usage and material impact, without increasing the workload of the staff of the ICU.

Limitations

The concept was only evaluated by discussion and not tested in the real environment. Furthermore, the concept was not evaluated with manufacturers of syringes, who have a big impact on the material choice and packaging of the syringe. It might be of interest to involve the manufacturer in the design process in the future. This would result in a more holistic view of the concept.

11. Conclusion

The main research question to be answered during this project was:

How can the environmental impact of syringes be reduced by a redesign, according to circular design strategies, without increasing the workload of the staff in the ICU while remaining safe?

This question was answered by literature, user and product research. Findings resulted in different solutions to decrease the environmental impact of syringes. The project concluded with one final concept: an optimised filling process of prefilled sterilised syringes.

User and product research showed that decreasing the impact of syringes is not only about the product itself. Manufacturing, preparing, using and disposing of all contribute to the environmental impact of the syringe. The use scenario showed that filling a syringe in the ICU requires many additional products that also contribute to the environmental impact. Therefore, the system of the syringe was investigated and different lifecycle scenarios were analysed. It turned out that prefilled sterilised syringes require fewer additional products for filling, and are therefore assumed to be more environmentally friendly. However, a life cycle analysis of PFSS showed multiple new impact hotspots, such as the sterilisation phase, materials used, and left-over medication. The final concept, therefore, focused on optimising the filling process to reduce the environmental impact of these impact hotspots.

The final design is a process optimisation for the entire filling process of PFSS at Apotheek A15. All steps in the filling process of PFSS have been reviewed with the design vision in mind. This resulted in a

holistic concept based on circular design strategies that reduces the environmental impact of syringes without increasing the workflow of the staff in the ICU. Compared to the original manual filling process in the ICU, the concept has an added value by decreasing the workload of the staff in the pharmacy. The workflow of the nurses, care assistants, intensivists, and cleaners will remain the same.

In the end, the environmental impact of syringes is reduced by optimising the filling process of syringes. The optimised process reduces the amount of waste, energy and water usage and material impact per syringe.

However, the final design is not the only answer to the main question and not the only valuable aspect of this project. The research from different perspectives has revealed many pain points and possible solutions that could decrease the impact of syringes. The insights from the analysis phase and recommendations are also valuable for Erasmus MC and the transition to a circular ICU. These are discussed in the next chapter.

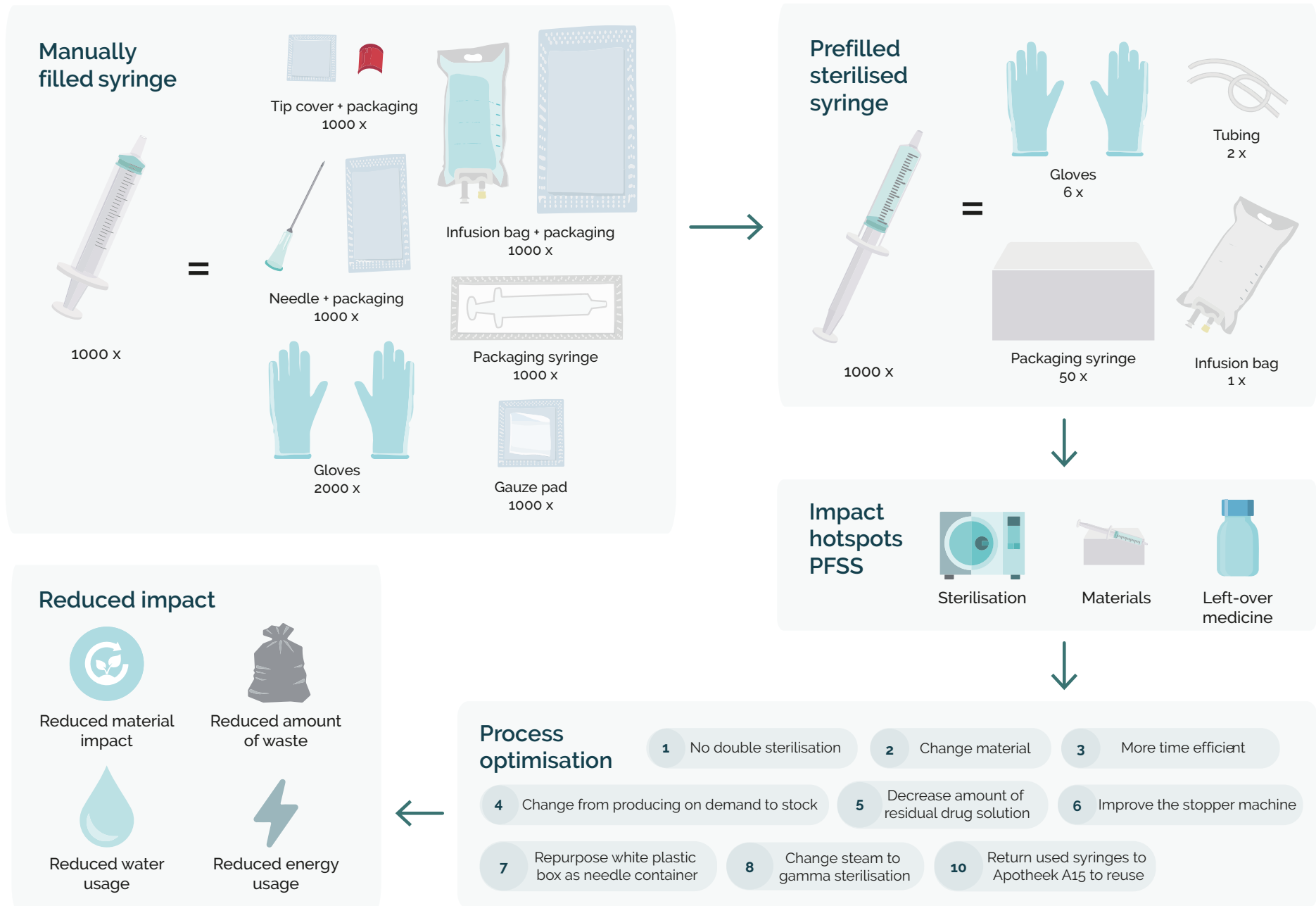


Figure 44: visualisation of the conclusion of the project.

12. Recommendations

This chapter gives recommendations for the final design, for reducing the impact of syringes in general and for future research. The following topics are recommended to be researched further to make substantiated decisions to be environmentally friendly in the long term.

Final design

Each intervention of the final concept (figure 35) should be tested and looked into further in terms of safety and quality of the syringes. Apotheek A15 should think in the long term on applying the final design to achieve a holistic result on reducing the impact of their filling process of PFSS. They should include the relations between the different interventions. Some interventions can be started right away, such as decreasing the amount of left-over medicine and improving the stopper machine.

Furthermore, a detailed LCA of comparing single-use PFSS and reusable PFSS would be of interest to make substantiated decisions for reusing syringes in the future. Different scenarios of decontamination must be included in the study, as the cleaning and sterilisation process often have a large share in the environmental impact of medical products. Unfortunately, it was not possible to perform a detailed LCA in this project, due to missing data and available time.

Reducing the amount of unused disposed syringes

User research showed that in the adult ICU, syringes are disposed of unused due to the infection prevention protocol and habits of the staff. The following could reduce this:

- Adapt the infection prevention protocol concerning the stock inside the patient rooms.

- Teaching the staff to only pick the required amount, instead of grabbing a handful. Nurses and other staff members should be instructed on the importance of decreasing the amount of unused disposed syringes.
- Syringes that are unused and still in their packaging, but need to be discarded due to the infection prevention protocol, can be sterilised using UV sterilisation. UV sterilisation is a sustainable way of sterilisation and is suitable for decontaminating surfaces. This makes sure that unused syringes do not need to be thrown away after a patient leaves the room. Or the packaging can be redesigned in a way that it can be cleaned with alcohol so that the syringes can stay in the room after a patient leaves.

Product level recommendations

Product research made clear that the product itself could be redesigned in several ways to reduce its impact:

- Redesign for cleaning and sterilisation after use. This means that the geometry and material of the syringe should be adapted so that proper decontamination can take place.
- Redesign the shape for saving material or space: decrease the wall thickness or design a modular syringe with a cartridge system.
- Redesign for recycling and separation of components to ensure that components can be disposed of separately at the end-of-life. This includes the packaging, which is currently made of a plastic laminate that cannot be separated.
- A material study into long term sustainable materials for syringes would be of interest, as it would result in a significant reduction in impact.

Separating and recycling waste

The waste audit made clear that infectious and general waste should be separated more carefully to make mechanical recycling of non-infectious waste possible. For recycling, it should be made easy for the staff to see what is considered infectious waste, what is not, and how and where to dispose of this. Furthermore, separating waste on type of material (paper, plastic, glass) could be of interest for the future in terms of recycling. In particular in the pharmacy and the break room/kitchen, where there is no patient-related waste.

Chemical recycling could also be of interest as an alternative end-of-life scenario since infectious waste can also be chemically recycled. During this project, chemical recycling was not researched in-depth but would be of interest for future research.

A future design project concerning the disposal of medical waste would be useful to investigate the possibilities of recycling. This project would include a behaviour study of the staff concerning (in)correct disposal, as well as a logistics study of how to deal with different waste streams.

Procurement

The procurement of syringes currently does not consider the eco-costs of products. An indication of the eco-costs of each type of product could help the procurement staff in taking more substantiated decisions concerning sustainability.

Furthermore, besides syringes, many disposable single-use products are used in the ICU. A critical investigation should be done to determine if this is really necessary, or if certain products can be replaced with reusable alternatives.

Norms and regulations

Norms and regulations concerning syringes do not include sustainability. Adding rules and regulations for syringes to be more sustainable would help a lot to get the manufacturers to change their products.

All in all, to achieve a decreased impact of syringes, a holistic long term solution is needed. The entire product journey and all stakeholders should be kept in mind during the design process to achieve a long term result.

13. Personal reflection

The project started with visiting the Erasmus MC and the intensive care. This was already quite impressive since I had never visited the hospital from the point of view of the staff. Spending time at the intensive care gave a lot of insights and helped me to understand the context and users of the project. It also allowed getting to know the people involved in the project.

Analysing the problem from different perspectives and combining the results was very valuable to put into practice. It was very valuable to learn so much about the medical field in combination with sustainability and circular design. On the other hand, the analysis resulted in a large amount of (complex) information. It was a challenge to reduce the complexity and communicate the findings in a clear way.

The ideation phase was the most difficult since I had the expectation to come up with a solution that solves the whole problem. The syringe seemed like a simple product in the beginning but was way more complex after realising that it is not only the syringe itself that has an impact, but the whole system around it contributes as well. Looking at the syringe from a system point of view steered me in the direction of optimising a process, something that I had not done before. This made it even more challenging, and I did not know where to start. Luckily my supervisors helped me with that. In the end, I think the final design is not the only valuable aspect of this project. The insights from the analysis phase and recommendations will also be very valuable for Erasmus MC and the transition to a circular ICU.

This project has taught me more than academic and design skills only. I've had the opportunity to improve my personal leadership skills by organising meetings with a lot of different people, presenting the project to for example the minister of education and by taking initiative in receiving feedback.

To conclude, I am thankful for having the opportunity to do a project for the Circular ICU of Erasmus MC and proud of being able to contribute to more sustainability in the healthcare sector.



Towards a circular ICU

Reducing the environmental impact of syringes in the Intensive Care Unit



The presented project addresses the environmental impact of syringes in the Intensive Care Unit (ICU) of Erasmus University Medical Centre (UMC) by developing solutions based on circular design.

Filling syringes by hand one by one in the ICU



Filling syringes by machine



Machine filling process



Waste



Next steps

- Engage with other hospitals
- Collaboration with industry
- Creating open access platform
- Funding

Health & Technology

ZonMw

ActiMP

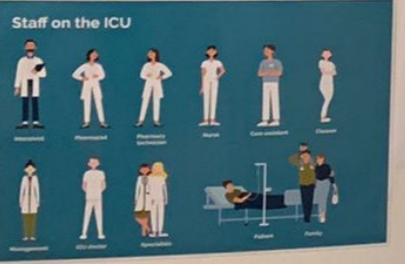


Figure 45: visit of the minister of education at Erasmus MC.

14. Acknowledgements

First of all, I would like to thank my supervisors for their guidance throughout the project. Armağan, thank you for the positivity you brought with you during the meetings, it really helped me to stay motivated. Also, your knowledge about user research in combination with the medical environment helped me a lot. Ruud, thank you for all the extensive feedback and all the sharp questions during the meetings. You really helped me to stay focused and to achieve a scientific result.

Furthermore, I would like to thank JC and Nicole for all their energy and time spent on the project. The weekly meetings on Monday morning were always a great start of the week. Also, your feedback and referrals to experts on the topic have helped me a lot. You also made sure that the project did not become dull, by inviting both the former and current minister of education, doing a TV interview, setting up a waste analysis and giving us access to work in the Green Room. It really made the project a lot more exciting!

I would also like to thank the staff of the ICU and PICU for showing their work to me and for participating in my research. It gave me a good understanding of your working environment and daily workflow.

Lisanne en Alicia, thank you for starting your graduation projects at the same time. It was a lot of fun to study together with you in the green room, and it was really nice to share experiences with you. The waste audit would also not have been the same without you.

Lastly, I would like to thank my family and friends for your support, involvement and interest in the project!

THE GREEN
WALL



MARGOT HONKOOP - TUDelft



WANNIE vd BERG - TUDelft



DOGA VILLE - TUDelft



NICOLE HUNFELD - EUSMUS HC



Baptiste Sené - VanBerlo



JODIEHL TU DELFT



SASCHA VERBRUGGEN - PICU



Suzan Cochijs - PICU



LEX BURGDORF - Sush Tokpaica



ARMAĞAN ALBAYRAK - TU DELFT

Sources

Akre, J. (2012). *What do we know about polypropylene?* Retrieved from <https://www.meshmedicaldeviceneWSdesk.com/articles/what-do-we-know-about-polypropylene-2>

Albayrak, A. (2021a). *Care pathways & patient journeys*. Retrieved from <https://brightspace.tudelft.nl/d2l/le/content/297878/viewContent/2097358/View>

Albayrak, A. (2021b). *Stakeholder map & product journey*. Retrieved from <https://brightspace.tudelft.nl/d2l/le/content/297880/viewContent/2130369/View>

Ali, M., Wang, W., & Chaudhry, N. (2016). Application of life cycle assessment for hospital solid waste management: A case study. *Journal of the Air & Waste Management Association*, 66(10), 1012-1018. doi:10.1080/10962247.2016.1196263

Ashby, M. F. (2016). Chapter 4 - Tools, Prompts and Check-Lists. In M. F. Ashby (Ed.), *Materials and Sustainable Development* (pp. 55-84). Boston: Butterworth-Heinemann.

Atiwesh, G., Mikhael, A., Parrish, C. C., Banoub, J., & Le, T.-A. T. (2021). Environmental impact of bioplastic use: A review. *Heliyon*, 7(9), e07918. doi:<https://doi.org/10.1016/j.heliyon.2021.e07918>

Browne-Wilkinson, S., Exter, P. v., Bouwens, J., Souder, J., & Chatel, É. (2021). *Circulaire Intensive Care Unit*. Retrieved from Metabolic.

Cheetham, B., & Johnson, A. (2013). *Syringes and sustainability: planet, people, profit*. Retrieved from The Royal Liverpool and Broadgreen University Hospitals NHS Trust: https://networks.sustainablehealthcare.org.uk/sites/default/files/resources/syringe_case_study_0_0.pdf

Cheng, Y. W., Sung, F. C., Yang, Y., Lo, Y. H., Chung, Y. T., & Li, K. C. (2009). Medical waste production at hospitals and associated factors. *Waste management*, 29(1), 440-444. doi:<https://doi.org/10.1016/j.wasman.2008.01.014>

Deloitte. (2020). 2016 Global health care outlook: Laying a foundation for the future. In: Deloitte Touche Tohmatsu Limited London.

Dhote, J. (2016). Review on the diseases caused due to improper handling of Biomedical Waste. *International Research Journal Of Science and Engineering 2322 -0015*, 4, 98-100.

Ellen MacArthur Foundation. (2019). Circular economy systems diagram. Retrieved from <https://ellenmacarthurfoundation.org/circular-economy-diagram>

Erasmus MC. (2014). *Afval informatiemap*. Retrieved from <https://docplayer.nl/47888859-Afval-informatiemap-erasmus-mc-versie-juli-2014.html>

Galve, J., Elduque, D., Pina, C., & Javierre, C. (2021). Life Cycle Assessment of a Plastic Part Injected with Recycled Polypropylene: A Comparison with Alternative Virgin Materials. *International Journal of Precision Engineering and Manufacturing-Green Technology*. doi:10.1007/s40684-021-00363-2

Gamba, A., Napierska, D., & Zotinca, A. (2021). *Measuring and reducing plastics in the healthcare sector*. Retrieved from Healthcare Without Harm: <https://noharm-europe.org/articles/news/europe/measuring-and-reducing-plastics-healthcare-sector>

Ghannadzadeh, A., & Meymivand, A. (2019). Environmental sustainability assessment of an ethylene oxide production process through Cumulative Exergy Demand and ReCiPe. *Clean Technologies and Environmental Policy*, 21. doi:10.1007/s10098-019-01748-3

Ghersin, Z. J., Flaherty, M. R., Yager, P., & Cummings, B. M. (2020). Going green: decreasing medical waste in a paediatric intensive care unit in the United States. *The New Bioethics*, 26(2), 98-110. doi:10.1080/20502877.2020.1767916

Global Alliance for Incinerator Alternatives. (2019). Fact sheet: Plastic and incineration. Retrieved from www.no-burn.org/fact-sheet-plastic-and-incineration/

Gluszynski, P. (2005). Waste Segregation Programme Nets Big Savings. In. *Health Without Harm*, Opole.

Hollander, M. C. d., Bakker, C. A., & Hultink, E. J. (2017). Product Design in a Circular Economy: Development of a Typology of Key Concepts and Terms. *Journal of Industrial Ecology*, 21(3), 8. doi:10.1111/jiec.12610

Holtzblatt, K., & Beyer, H. (2017). 8 - Traditional Contextual Design Models. In K. Holtzblatt & H. Beyer (Eds.), *Contextual Design (Second Edition)* (pp. 207-230). Boston: Morgan Kaufmann.

Huijbregts, M., Steinmann, Z., Elshout, P., Stam, G., Verones, F., Vieira, M., . . . Zelm, R. (2020). Correction to: ReCiPe2016: a harmonised life cycle impact assessment method at midpoint and endpoint level. *The International Journal of Life Cycle Assessment*, 25, 1-1. doi:10.1007/s11367-020-01761-5

Joseph, B., James, J., Kalarikkal, N., & Thomas, S. (2021). Recycling of medical plastics. *Advanced Industrial and Engineering Polymer Research*, 4(3), 199-208. doi:<https://doi.org/10.1016/j.aiepr.2021.06.003>

Kane, G., Bakker, C. A., & Balkenende, R. (2017). Towards design strategies for circular medical products. *Resources, Conservation and Recycling*, 135. doi:10.1016/j.resconrec.2017.07.030

Karliner, J., Slotterback, S., Boyd, R., Ashby, B., Steele, K., & Wang, J. (2020). Health care's climate footprint: the health sector contribution and opportunities for action. *European Journal of Public Health*, 30.

doi:10.1093/eurpub/ckaa165.843

Kirchherr, J., Reike, D., & Hekkert, M. P. (2017). Conceptualizing the Circular Economy: An Analysis of 114 Definitions. *SSRN Electronic Journal*, 127. doi:10.2139/ssrn.3037579

Lee Rushyuan, J., & Mears Simon, C. (2012). Greening of Orthopedic Surgery. *Orthopedics*, 35(6), e940-e944. doi:10.3928/01477447-20120525-39

Leiden, A., Cerdas, F., Noriega, D., Beyerlein, J., & Herrmann, C. (2020). Life cycle assessment of a disposable and a reusable surgery instrument set for spinal fusion surgeries. *Resources, Conservation and Recycling*, 156, 104704. doi:https://doi.org/10.1016/j.resconrec.2020.104704

McGain, F., McAlister, S., McGavin, A., & Story, D. (2012). A Life Cycle Assessment of Reusable and Single-Use Central Venous Catheter Insertion Kits. *Anesthesia & Analgesia*, 114(5). Retrieved from https://journals.lww.com/anesthesia-analgesia/Fulltext/2012/05000/A_Life_Cycle_Assessment_of_Reusable_and_Single_Use.23.aspx

McGain, F., Moore, G., & Black, J. (2017). Steam sterilisation's energy and water footprint. *Australian Health Review*, 41(1), 26-32. Retrieved from https://doi.org/10.1071/AH15142

Medbis. (n.d.). SHARPSAFE NAALDENCONTAINER. Retrieved from https://www.medbis.nl/html/catalog/home/product/450/Sharpsafe-Naaldencontainers.html

Medicines and Healthcare Products Regulatory Agency. (2021). *Single-use medical devices: implications and consequences of reuse*. Retrieved from https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/956268/Single_use_medical_devices.pdf

Ministerie van Algemene Zaken. (2021, April 14). Meer duurzaamheid in de zorg. *Duurzame zorg* Retrieved from https://www.rijksoverheid.nl/onderwerpen/duurzame-zorg/meer-duurzaamheid-in-de-zorg

Renewi. (n.d.). Specifiek ziekenhuisafval (sza). Retrieved from https://www.renewi.com/nl-nl/over-renewi/onze-rol/hergebruik-en-recycling/gevaarlijk-afval/specifiek-ziekenhuisafval

RIVM, Sterilisatie, (2018). Retrieved from https://www.rivm.nl/sterilisatie

Saidani, M., Pan, E., & Kim, H. (2020). *Switching From Petroleum- to Bio-Based Plastics: Visualization Tools to Screen Sustainable Material Alternatives During the Design Process*. Paper presented at the ASME 2020 International Design Engineering Technical Conferences and Computers and Information in Engineering Conference. https://doi.org/10.1115/DETC2020-22429

Sandle, T. (2013). *Sterility, sterilisation and sterility assurance for pharmaceuticals: technology, validation and current regulations*. Elsevier.

Stahel, W. (2010). *The performance economy*: Springer.

Thiel, C. L., Schehlein, E., Ravilla, T., Ravindran, R. D., Robin, A. L., Saeedi, O. J., . . . Venkatesh, R. (2017). Cataract surgery and environmental sustainability: Waste and lifecycle assessment of phacoemulsification at a private healthcare facility. *Journal of Cataract & Refractive Surgery*, *43*(11). Retrieved from https://journals.lww.com/jcrs/Fulltext/2017/11000/Cataract_surgery_and_environmental_sustainability_5.aspx

van Boeijen, A., Daalhuizen, J., Zijlstra, J., & van der Schoor, R. (2013). *Delft Design Guide: Design strategies and methods*. Amsterdam: BIS Publishers.

van Straten, B., Ligtelijn, S., Droog, L., Putman, E., Dankelman, J., Weiland, N. H. S., & Horeman, T. (2021). A life cycle assessment of reprocessing face masks during the Covid-19 pandemic. *Scientific Reports*, *11*(1), 17680. doi:10.1038/s41598-021-97188-5