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Environmental considerations along the life cycle of pharmaceuticals: Interview study on views regarding environmental challenges, concerns, strategies, and prospects within the pharmaceutical industry

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ABSTRACT

Environmental impacts of medicines arise throughout their entire life cycle. The pharmaceutical industry has a key role in reducing these impacts in early production phases, but currently has limited possibilities to reduce the environmental exposure arising from drug consumption and end-of-life. The aim of this interview study was to explore the current environmental actions within the industry, as well as the views and attitudes toward the strategies to address the environmental challenges and concerns. Semi-structured interviews were conducted among representatives (n = 15) from twelve pharmaceutical companies operating in Finland in February-May 2021. The data were analyzed using qualitative content analysis.

The representatives of pharmaceutical industry were overall well aware of the multifaceted environmental challenges related to the life cycle of pharmaceuticals and of their role in improving sustainability in production. Improving waste management and reducing impacts from companies' own operations were the most commonly mentioned actions already taking place within the companies (15/15). "Environmental impacts arising from drug consumption" (6/15) and "centralized drug manufacturing in countries with lax environmental regulation" (4/15) were most frequently brought up challenges difficult to resolve. "Development of environmentally more sustainable drug production in the company" was the most frequently raised key development need (5/15). To address this, establishment of tangible economic drivers, regulatory incentives, or reputational rewards were called for. "Incorporation of environmental aspects into decision-making in different situations" was suggested by 11/15 interviewees as a means to promote sustainable development, e.g. in selection of medicines by physicians and consumers. However, the attitudes towards the types of criteria and their evaluation differed between interviewees. Attitudes towards the "incorporation of environmental fate assessment into early phases of drug design and development" were mostly positive (10/11), suggesting that there is a keen interest in the industry to foster the introduction of new tools enabling the development of pharmaceuticals intrinsically less harmful for the environment.

1. Introduction

Environmental sustainability has become a central part of pharmaceutical business management, with respect to cleaner production, sustainable use of manufacturing materials, sustainability of the global supply chains, and human resources (Milanesi et al., 2020). In recent decades pharmaceutical residues in the environment have raised concern because of their reported adverse effects on wildlife (Brodin et al., 2017; Jobling et al., 2006; Oaks et al., 2004). Studies have reported substantial pharmaceutical pollution in surface waters worldwide (aus der Beek et al., 2016; Wilkinson et al., 2022). Most pharmaceutical residues in the environment originate from human excretion of pharmaceuticals and their metabolites to the sewage systems (BIO Intelligence Service, 2013). The highest environmental concentrations are typically measured in densely populated areas, or in developing countries with limited sanitation (Kairigo et al., 2020; Wilkinson et al., 2022).

To account for the environmental risks of medicines use, some

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countries have adapted environmental classification systems that rely on risk-based evaluation of active pharmaceutical ingredients (APIs), in accordance with the regulatory environmental risk assessment (ERA) guidance (EMA, 2006). In the EU, the ERA of new APIs has been a mandatory part of marketing authorization (MA) since 2005 (2001/83/EC Article 8(3)(ca)). Although publicly available ERA data are very limited, the MA holder can voluntarily provide it to the classification system, initially established as a part of the Swedish electronic product information system (Fass.se), and later adopted in Norway (Felleskatalogen.no) and Finland (Pharmacafennica.fi). This risk-based assessment accounts for both drug consumption and measured ecotoxicological hazard by comparing the predicted environmental concentration to the predicted no-effect concentration. The utility of ERA-based classification is, however, much debated because of a lack of comprehensive ecotoxicological data and the discrepancies within it (Ramström et al., 2020; Ågerstrand et al., 2009).

Moreover, pharmaceutical manufacturing can also be a major source of pharmaceutical pollution in areas where environmental legislation that affects permitting of pharmaceutical plants is lax. With the concentration of pharmaceutical raw material manufacture in low-income countries, the lack of regulatory enforcement has resulted in alarmingly high levels of pharmaceutical pollution, especially in Asia (Larsson, 2014). Besides environmental exposure by pharmaceutical residues, the environmental impacts of medicines also arise from drug production (e.g., energy and clean water consumption), distribution (including transportation and storage), and end-of-life (unused, discarded medicines).

To evaluate the environmental impacts occurring over the life cycle of medicines, dedicated life cycle assessment (LCA) approaches have been developed for pharmaceutical products and industries over the past ten to twenty years (DeSoete et al., 2017; Jimenez-Gonzalez and Overcash, 2014; Mata et al., 2012). Traditionally, the LCA of pharmaceuticals has focused on cradle-to-gate analysis (from resource extraction to the factory gates before distribution), which is typically performed for internal purposes, for example, to optimize and develop more cost-effective processes (DeSoete et al., 2017; Jimenez-Gonzalez and Overcash, 2014). Consequently, the LCA data are rarely publicly available, as they may contain information about proprietary processes or other classified material (DeSoete et al., 2017). In recent years, increasing emphasis has been put on establishment of cradle-to-grave approaches, to better account for the environmental impacts of also drug distribution and use as well as the end-of-life, and to find strategies to reduce the environmental impacts along the life cycle (Fig. 1). However, some of these operations are often organized and regulated on a local or regional level, which challenges their incorporation into a unified LCA assessment. This has triggered the development of national evaluation systems that aim to assess the environmental impacts of pharmaceutical products from a life cycle perspective (Pålsson et al., 2019) as well as approaches to identify potential levers in the life cycle of medicines to limit the adverse effects to the environment (van der Grinten et al. 2016).

However, the lack of publicly available LCA data is still a major barrier to the use of LCA approaches for environmental classification purposes or for policy and decision-making in the pharmaceutical sector (DeSoete et al., 2017). Moreover, the local waste management strategies for, e.g. wastewater purification and take-back of unused medicines, and the interlinked practices for the use of sewage sludge and recycling of the packaging materials (Fig. 1), also play a major role in delimiting environmental discharges. In Europe, Switzerland has taken on a pioneering role toward zero-pollution wastewater purification creating both legal and economic foundations for elimination of pharmaceuticals and other organic trace substances (AFRY, 2020). According to a study conducted in the Baltic countries, the national practices for take-back and disposal of unused medicines via designated collection points, instead of mixed household waste or flushing down the drain, varies greatly between countries (Mehtonen et al., 2020), with high take-back percentages typically reported in the Nordic countries (Louhisalmi et al., 2020; Mehtonen et al., 2020). Besides reactive measures, there are also proactive initiatives aiming to "*support the development of pharmaceuticals intrinsically less harmful for the environment and promote greener manufacturing*" (Fig. 1) in accordance with the European Commission's Strategic Approach to Pharmaceuticals in the Environment (COM, 2019). The insights of the pharma industry, which has a key role toward this aim, were recently evaluated through a structured questionnaire among the R&D and environmental experts from seven globally active pharmaceutical companies (Puhlmann et al., 2023). The outcomes of this study indicated that the R&D experts see many opportunities at different stages along the R&D process to include properties providing

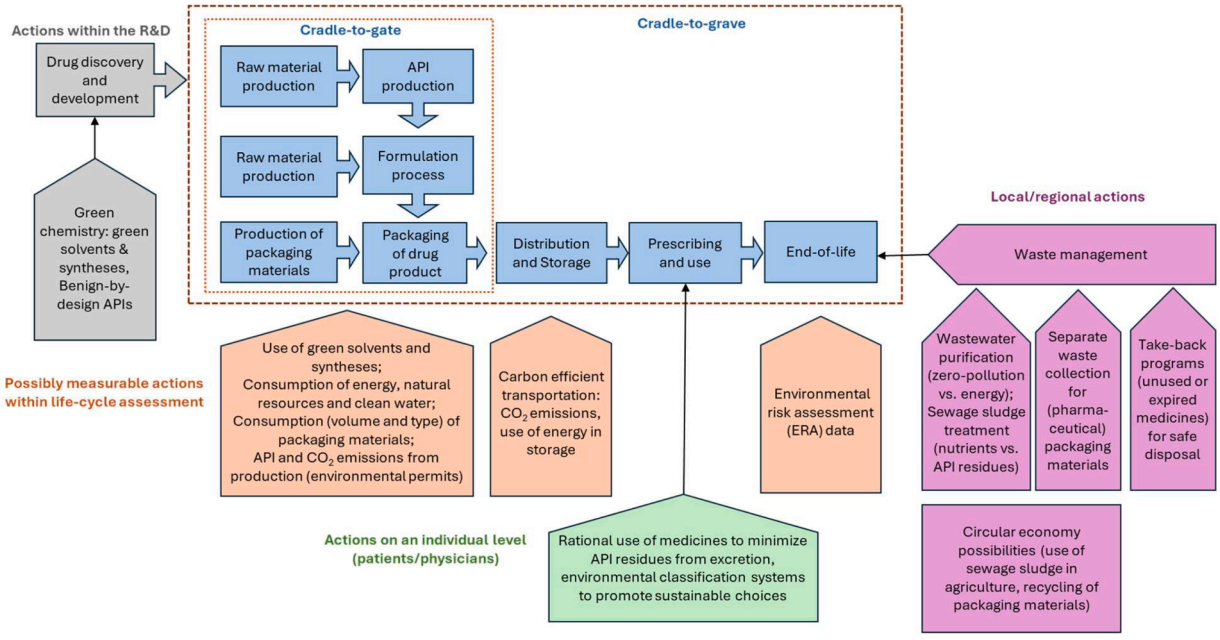

Fig. 1. Overview of the main elements of cradle-to-gate and cradle-to-grave life cycle assessments, and the key actions and strategies to delimit environmental impacts of medicines within the industry, by the drug consumers and physicians, and through strategic decision-making applied to waste management.

greener APIs.

Overall, the previous literature has established an understanding of the current challenges and the different prospective solutions necessary to increase the environmental sustainability of the pharmaceutical business. However, the previous research has mostly focused on specific development needs, such as cleaner production, green supply chains, or design of greener pharmaceuticals, usually by reviewing the available data readily published by the companies (Kaenzig et al., 2011; Veleva et al., 2003) or acquired through structured surveys or interviews (Li and Hamblin, 2016; Masri and Jaaron, 2017; Puhlmann et al., 2023). However, little is known about the views and attitudes within the pharmaceutical industry regarding the priorities towards the different reactive and proactive solutions and strategies to address environmental challenges. This study aimed to investigate the current status of environmental actions within the pharmaceutical industries through semi-structured interviews, to obtain data about views towards the priorities about environmental challenges facing the pharmaceutical business as a whole as well as about attitudes towards different proposed solutions and incentives necessary for addressing these challenges.

2. Materials and methods

2.1. Study context

This study was limited to pharmaceutical companies operating in Finland, many of which have only branch offices in the country. This enabled shedding light on possible specific sustainability challenges experienced by companies operating in small market segments. According to the Finnish Medicines Agency (Fimea, 2022a), there are currently 97 pharmaceutical wholesale license holders and 34 medicinal product manufacturer's license holders in Finland. Only three of these manufacture pharmaceuticals in large-scale manufacturing plants in Finland (Pharma Industry Finland, 2022). Additionally, there are some companies with smaller-scale operations and a few contract manufacturers. Most of the companies operating in Finland are therefore affiliated branches or sales and marketing offices of global pharma companies. Compared with global business, the Finnish pharmaceutical market is small, comprising approximately 0.3 % of the global and 1.2 % of the European pharmaceutical markets (EFPIA, 2016). In 2020, the total sales of pharmaceuticals on the Finnish market were 3518 million euros (Finnish Medicines Agency and Social Insurance Institution, 2021). Most of the medicines in the Finnish market are imported. In 2020, Finland's pharmaceutical imports were worth 2091 million euros and exports were worth 829 million euros (Pharma Industry Finland Statistics 2020).

2.2. Study setting

The study was conducted between February and May 2021 as semi-structured interviews with representatives from the pharmaceutical companies operating in Finland. The semi-structured interview method was chosen because it allows studying perceptions and attitudes with open-ended questions (Smith, 2002), which is especially valuable when previous research on the topic is scarce.

Altogether 41 pharmaceutical companies operating in Finland were invited to participate in the study. Interview invitations were sent to all the pharmaceutical companies that are member organizations of the Pharma Industry Finland ($N = 30$) and Finnish Generic Pharmaceutical Association ($N = 8$), the Finnish interest groups of the originator and the generic industry, respectively. Additionally, the invitations were sent to three pharmaceutical companies (one originator and two generic) that are not members of the respective industry associations, but are important actors in the pharmaceutical market in Finland. Industry associations first informed their member organizations of the upcoming study after which the invitations were sent to the country managers or the chief executive officers of the companies via email. The recipients were encouraged to forward the invitations inside the company, as necessary, to the most suitable person for the interview to respond to questions on environmental sustainability actions. One researcher (SR) arranged the dates and times for the interviews and conducted them via Zoom or Teams. The interviews lasted between 20 and 54 min, with an average of 38 min, and were recorded with a digital voice recorder. The interviews were held in Finnish or in English.

2.3. Interview guide

The interview guide consisted of three themes, including main questions and their respective sub-questions (Table 1). Interview guides were sent to participants prior to the interview. All the main questions were asked of all interviewees, but the sub-questions were asked depending on the course of the interview and the interviewee's role in the company. Development of the interview guide was based on existing scientific literature about studies on sustainability of the pharmaceutical industry and environmental impact assessments of pharmaceutical products (De Soete et al., 2017; Milanesi et al., 2020; Pålsson et al., 2020, 2019) and on the authors' prior experiences on the topic; this adhered to the methodology of semi-structured interviews. Four pilot interviews were conducted with representatives of pharmaceutical companies in different positions (research and development, R&D; environment, health and safety; regulatory affairs; management) to test the suitability of the questions for a diverse group of industry experts. On the basis of these pilots, no changes were made to the interview guide, and the pilot interviews were also included in the study material.

2.4. Data analysis

The recorded interviews were transcribed word for word (SR) and anonymized, after which the material was subjected to a qualitative content analysis (Berg and Lune, 2017; Hsieh and Shannon, 2005), where the study material was systematically arranged according to chosen principles to enable the description of phenomena in generalized and compacted form. In this study, both deductive and inductive approaches were used. The analysis began with reading the transcripts and

Table 1
The interview guide with the themes and main questions.

Theme	Main questions of the theme
Environmental sustainability within the pharmaceutical industry	What are the most important procedures already carried out in your company to promote environmental sustainability? What are the key areas for development in your company that will further improve the environmental sustainability of your operations?
The environmental impacts of pharmaceuticals during their life cycle and ways of reducing them and promoting environmental sustainability in the pharmaceuticals business	Which environmental impacts during the different stages of life cycle of pharmaceuticals ("cradle to grave") do you consider the easiest to overcome? Which life cycle impacts do you find the most challenging? What actions or incentives do you think would improve environmental sustainability in the pharmaceuticals business the most?
Solutions from research to the environmental challenges facing the pharmaceuticals business	What new study methods, tools or incentives would be needed to promote environmental sustainability in the pharmaceutical industry? What kind of study data on the views of the general public could the industry benefit from when developing more environmentally sustainable operations? What do you regard as the biggest environmental challenge facing the pharmaceuticals business as a whole?

deductively encoding the answers under the aims and related research questions in a tabular form using Microsoft Word 2016. An analysis unit could be a sentence or a group of sentences describing the idea relating to the study questions. Accordingly, the interviewee's response could include many units, which were then separated into several analysis units. Next, these units were simplified, compared, and sorted into emerging subcategories named according to all simplifications of the respective subcategory. Finally, similar subcategories were combined into main categories, which were named accordingly, so that the name was descriptive of all subcategories. The analysis was conducted by one researcher (SR), but the grouping and categorizations were discussed by all authors.

2.5. Ethical statement

The study setting and the overall research process were in compliance with national ethical instructions for human sciences research (Finnish National Board on Research Integrity TENK, 2019). According to TENK instructions, this study required no ethical review. The participation was voluntary, and the interviewees gave their written consent for participation via email and for recording at the start of the interview. The anonymity of the interviewees was protected so that neither individual participants nor companies could be identified from the data. No incentives were provided to the participants.

3. Results

A total of 14 interviews were conducted with 15 representatives from 12 different companies (nine originators and three generics) comprising approximately 30 % of the invited companies. Four companies declined the invitation because of lack of either a suitable interviewee or time. Four companies requested more information on the study or forwarded the invitation to another person in their organization but did not return to participate. About 50 % (21 companies) of the invited companies did not respond at all to the invitation or the reminder invitation sent two weeks later.

Two of the companies had more than one participant each. In one interview, two people from the same company participated in the interview together upon their own request, but their responses were nevertheless analyzed separately ($n = 2$). All other 13 interviews were conducted individually. The results are presented under three themes: 1) The current status of environmental actions in the companies and the interviewees' views on the environmental life cycle impacts that are easiest to overcome. 2) Main environmental challenges facing the pharmaceutical business and identified development needs. 3) Plausible solutions to overcome the current environmental challenges. Direct citations from the interviews are presented under each theme as examples. The quotes from interviews held in Finnish were translated from Finnish to English.

3.1. Current status of environmental actions and views on the environmental life cycle impacts easiest to overcome in the pharmaceutical companies

When asked about environmental sustainability, all interviewees mentioned actions that had taken place in their company to reduce environmental impacts resulting from their operations. Most of these procedures were related to waste management, such as reduction and proper disposal of generated waste (8/12 companies), reducing emissions from commuting (5/12) or production (4/12), or implementation of sustainable energy solutions (4/12). Several companies had also established environmental programs or strategies (5/12) or set specific environmental targets (5/12), such as carbon neutrality goals. Interviewees from three companies mentioned that their company had already worked to develop more sustainable pharmaceutical products. The examples given on actions toward "greener products" were development of environmentally more sustainable and recyclable packaging and development of a reusable medical device to replace a disposable one. In addition to the improvements made in their companies' operations, interviewees from five companies also mentioned actions to pursue increased environmental sustainability in the pharmaceutical sector as a whole, by demanding environmental responsibility from their contract manufacturers (3/12) or by participating in global initiatives (2/12), such as AMR Industry Alliance or Pharmaceutical Supply Chain Initiative (PSCI), that aim to increase sustainability of the pharmaceutical industry and transparency in the production chains (AMR Industry Alliance, 2017; PSCI, 2006).

> *"…and if the waste is created, it would be recyclable or disposable so that there would be as little impact as possible to the environment…" (Interviewee 2)*

When asked about the environmental life cycle impacts of pharmaceuticals, the interviewees (10/15) most frequently cited impacts arising from the company's operations, such as production or energy and water usage, as the easiest to overcome, as these are subject to internal action. Other life cycle impacts mentioned as easily resolved related to optimization of pharmaceutical packaging size and use of environmentally friendly materials (5/15) and to environmental emissions resulting from improper disposal of medicines by consumers (2/15) and medicine waste (2/15).

> *"…energy solutions are, at least in my opinion, sort of (solutions) that you can affect yourself, and and, even if they cost, and so on, at least they are realizable…" (Interviewee 1)*

3.2. Main environmental challenges facing the pharmaceutical business and development needs

The interviewees' views on the environmental challenges facing the pharmaceutical business, and the identified key points of development to improve environmental sustainability, were divided into six categories, and further into subcategories, as described in Table 2. Controlling the life cycle impacts of pharmaceuticals was considered challenging by most of the interviewees (12/15) and clear development needs were identified (Table 2). Environmental impacts resulting from drug consumption were mentioned repeatedly (6/15); these are considered particularly challenging because the environmental load is largely due to human excretion and thus expected to increase due to aging and growing populations. It was noted that, even if the industry works to improve the situation, for example by developing environmentally less hazardous pharmaceuticals, the challenge is complex and cannot be fixed by the industry alone. Inevitably, based on their mode of action, pharmaceutical residues will impact the environment, and it is impossible to discontinue the use of medicines.

> *"…if we talk about like about the pharmaceutical residues that come through the end user, then then… It is probably the challenge that, I imagine, that the solution would be very difficult, difficult and expensive to develop relative to how important the treatments are…" (Interviewee 5)*

Environmentally more sustainable drug production was also raised (5/15) as a key needed development, suggesting that much more could be done to reduce the impact arising from production, although this was also considered one of the easiest goals to achieve, as it is entirely in the hands of the producer.

> *"…of course we can, like, improve the energy efficiency and that's what we must do by the law as well… But on the other hand we eventually hit a barrier there, as we need to ensure the GMP. We have clean rooms that require* e.g. *certain air exchange rates. So we have like fairly tight frames where we can carry out that (energy efficiency improvements)…" (Interviewee 9)*

Table 2
Views of the interviewees on the main environmental challenges facing the pharmaceutical business and the key identified development needs.

Main category Subcategory	Interviewees ($n = 15$)
Controlling the life cycle impacts of pharmaceuticals	**12**
Environmental impacts resulting from drug consumption	6
Development of environmentally more sustainable drug production	5
Comprehension of the life cycle impacts of pharmaceuticals	3
Identification of the environmentally most significant targets for development along the life cycle for action prioritization	3
Development of more environmentally sustainable transportation	2
Development of more environmentally sustainable pharmaceuticals	1
Lack of transparency and need to improve environmental sustainability in the production chains	**9**
Production concentrated in countries with weak environmental regulation	4
Ensuring the environmental sustainability of subcontractors	3
Lack of transparency in the production chain	3
Limited possibilities for individual companies or countries to influence global markets and trends	2
Lack of binding systems and surveillance in the purchasing and production chains	2
Legislative challenges	**6**
Lack of legal framework to guide and require more environmentally sustainable operations in the pharmaceuticals business	3
Legal framework in Finland that is slow to change and requires decision-making at the EU level	2
Challenges resulting from changes in legislation	2
Advertising restrictions that prevent informing consumers about prescription medicines	1
Environmental load resulting from the mandatory reserve supplies	1
Developing more environmentally sustainable mode of operations in the company	**5**
Development of environmental management system in the company	2
Environmental evaluation of the mode of operations and target-oriented development	2
Environmental impacts of commuting	2
Identification of the needs and demands of the stakeholders	1
Global pandemics threatening human health	**3**
Antimicrobial resistance	3
Global pandemics	1
Pandemics resulting from climate change	1
Others	**4**
Development of instructions on how to recycle or dispose of medicines and medical devices	2
Changing the mindset of people	1
Finding common ground between the industry and the environmental groups	1
Using recycled materials in medicinal products	1

The lack of transparency in the production chains and the need to improve their environmental sustainability was frequently mentioned (9/15). Considered especially problematic were the challenges arising from production centralized in countries with lax environmental regulation and the lack of means to ensure and assess the environmental sustainability of subcontractors. A range of legislative challenges was raised by some interviewees (6/15), with the lack of a legal framework to guide and require environmentally sustainable operations as a key challenge (Table 2). Additionally, one-third of the interviewees (5/15) brought up the need to develop environmentally more sustainable modes of operation within the company (Table 2), suggesting that these are still lacking in some companies, even though many have already established their own environmental programs or strategies.

> *"…the API production being localized in countries with weak regulation, or weaker regulation, that is one of those big global problems, which causes that, well, most certainly some adverse environmental impacts arise there…" (Interviewee 14)*

3.3. Plausible solutions to overcome current environmental challenges

Open-ended questions were used to ascertain what solutions, actions, and incentives the interviewees would raise themselves for dealing with the environmental challenges facing their business. The actions and incentives that the interviewees spontaneously introduced were divided into eight categories (Table 3). Next, their views on specific actions and/or incentives were asked with a set of sub-questions compiled from the data, and based on the answers, the attitudes were categorized as "positive," "reserved," or "negative" (Fig. 2). Examples of responses relating to the categorized attitudes of the interviewees are compiled in the Supplementary material.

3.3.1. Incorporation of environmental aspects into decision-making in different situations

Nearly all of the interviewees (11/15) brought up the need for the incorporation of environmental aspects into decision-making, emphasizing its effectiveness in tackling environmental challenges (Table 3). The suggested mechanisms included aspects relating to environmental

Table 3
Interviewees' suggested actions and incentives toward the environmental challenges facing the pharmaceutical business.

Main category Subcategory	Interviewees ($n = 15$)
Incorporation of environmental aspects into decision-making in different situations	**11**
Increasing transparency in the production chains to guide decision-making	3
Raising public awareness of the environmental impacts of pharmaceuticals so that consumers can include environmental aspects in their decisions	3
Incorporation of environmental criteria into public procurement processes in hospitals	3
Competitive pressure to guide focusing on environmental issues	2
API-based environmental classification to help physicians in decision-making when prescribing medication (when acceptable from a therapeutic point of view)	2
Incorporation of environmental aspects in production as criteria in choosing medicines	2
Incorporation of environmental aspects into reimbursement discussions	1
Raising awareness on environmental issues and influencing the general atmosphere in society	**8**
Raising awareness on environmental issues	4
Raising awareness on correct ways to dispose of medicines	3
Affecting consumers and the general atmosphere in society	2
Global uniform and equal environmental criteria and standards based on international cooperation	**7**
Global uniform and equal environmental standards	3
Global cooperation	3
Sustainability/responsibility criteria to assess the performance of the companies and to encourage doing well	2
Incorporation of environmental assessments and sustainability considerations in drug design and development	**5**
Environmental effect assessments of drug design and development	4
Sustainability considerations regarding drug design and development	1
Removal of pharmaceuticals from wastewaters	**5**
Targeted and more effective treatment of wastewaters to remove pharmaceuticals	3
Dedicated collection of bodily excretions containing harmful pharmaceuticals	2
Legislative means	**4**
Improving the mandatory reserve medical supplies system	2
Environmental criteria (on production) incorporated into marketing authorization approval or in the good manufacturing practice (GMP) norms	2
Changes to pharmaceutical legislation	1
Rational use of medicines	**3**
Rational use of medicines	3
Other	**4**
Incentives and actions to support recycling of medicinal package materials	2
Switching to renewable energy in the company	1
Resolving the emissions from company's production	1
Incentives from easy tools	1

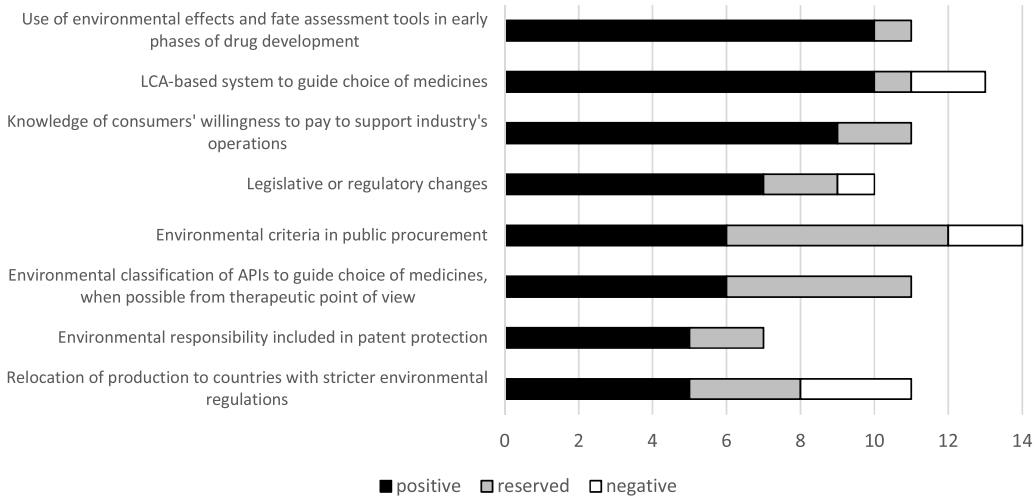

Fig. 2. Attitudes of the interviewees toward the different suggested actions and incentives to deal with the environmental challenges of the pharmaceutical business. The length of the bar indicates the total number of interviewees with an opinion of the given action or incentive. The number of interviewees per sub-question thus varies, since not all sub-questions were discussed with every interviewee (or not everyone had an opinion on each sub-question).

impacts of the APIs and to transparency and sustainability of production to guide decision-making by consumers, physicians, or hospital/institution drug buyers. However, the opinions about which criteria to use for decision-making, and who should make the decisions, varied substantially among the interviewees, although many suggested that incorporation of environmental aspects into decision-making would incentivize and guide the companies to put more focus on environmental issues. Some interviewees were concerned about whether patients would get the needed treatment if they made decisions about over-the-counter (OTC) drugs based on the environmental impacts of medication. It was also noted that the patients should not be exposed to choosing their medication on these grounds, but the decision should rather be made by the physicians only, who could evaluate the overall risk-benefit ratio of the treatment. Nevertheless, the interviewees' attitudes were mostly positive toward drug classification based on LCA of the pharmaceutical products (10/13) to guide the selection of medicinal products (Fig. 2 and Supplementary material). However, the attitudes toward drug classification based on environmental risks of APIs were more divided between positive (6/11) and reserved (5/11), but none were clearly negative, suggesting that acknowledging the environmental impacts of medicines, and minimizing the use of the most harmful ones, was generally considered important.

Ten interviewees considered an LCA-based system accounting for environmental and sustainability aspects of the whole product to be a good mechanism to guide decision-making and to support the development of sustainably produced medicines (Fig. 2 and Supplementary material). Although it was considered difficult to establish, such a system was perceived as an incentive for the companies to improve their operations. Two interviewees had negative attitudes toward the use of LCA data to guide the selection of drug products because of the challenges in producing comparable environmental footprint data for different products by different companies. Nevertheless, LCA data were considered valuable for identifying specific points in the production processes for further development. The challenges raised with the establishment of LCA-based assessment systems were the extensiveness of the data across the life cycle even for one product and the question of sufficient transparency to allow reliable third-party reviewing without compromising property rights. It was also pointed out that the assessment system would need a structure to enable all companies to participate, without categorically excluding any particular business sector, for example by unequal treatment of originators and generic companies.

Additionally, three interviewees cited the incorporation of environmental criteria in public procurement processes as another mechanism to promote environmental sustainability (Table 3). When specifically asked, six of the fourteen interviewees had positive attitudes toward this, considering environmental criteria in public procurement tenders as an incentivizing mechanism, whereas eight interviewees had a reserved or negative attitude with concerns about the criteria to be used (Fig. 2 and Supplementary material). This group of interviewees considered it important that the criteria would not only build on who can provide certain documents, but also guide the industry to enforce improved sustainability in their operations. Several interviewees emphasized that the criteria should be impartial, clear, and harmonized so that the same criteria could be used in several procurement regions in different countries without excluding any particular segment of the pharmaceutical industry from the tendering. Two interviewees were nevertheless skeptical of the success of weighing environmental criteria against price.

> *"…in some way getting the environmental issues included in the choosing of the medication process. No matter if it is in a hospital or outpatient care when choosing medicine. But that somehow it would be included. So, it could be one of the criteria, or one claim that the bidders would need to provide a report on how… umm the environmental issues have been taken into account in the production…" (Interviewee 2)*

3.3.2. Raising awareness on environmental issues, global environmental criteria and cooperation

The interviewees frequently (8/15) raised increasing awareness on environmental issues and affecting the general atmosphere in society, considering them important, although slow, means to improve environmental sustainability (Table 3). They advocated improvement in education and increased research on environmental impacts of medicines to increase discussion, to train professionals for the pharmaceutical sector, and to raise awareness on all levels, including drug consumers, who will have the ultimate impact on political decision-making and legislative actions.

> *"…of course it would be good to do awareness raising in all levels. And then I believe that the awareness would gradually increase and then the pressure perhaps also to political decisions and legislative guidance would increase…" (Interviewee 15)*

Information on consumer willingness to pay for more sustainably produced medicines was also considered important by nine interviewees, and a tangible incentive for the companies to invest in environmentally sustainable production and products (Fig. 2 and

Supplementary material). However, two interviewees had reservations about the incentivizing effect of this information, emphasizing the need for information on a society's willingness to pay, because, in many countries, much of the costs of prescription medicines is reimbursed by national health insurance agencies.

Raising awareness on correct disposal of unused and expired medicines (3/15) was also brought up as a concrete action on which consumers should be informed to avoid unnecessary environmental load. Public awareness campaigns targeted to drug consumers were proposed to address the general lack of awareness of the environmental impact of medicines.

> *"…I do strongly see that the awareness of people also on how to dispose of medicines… So, I think that can save or improve the situation (to reduce the load of pharmaceutical residues in the environment) a lot, that they are not thrown in the household waste nor flushed down the toilet…" (Interviewee 2)*

The interviewees frequently (7/15) brought up the need for global actions and incentives, including setting of equal environmental standards and criteria based on international cooperation, as mechanisms to increase effectiveness and transparency required for the highly interlinked international global pharma industry.

> *"…one really big challenge of course is, as I already mentioned earlier about the raw materials that are purchased around the world, that of course if there would be uniform environmental set of rules globally, then this problem would be solved. So probably cooperation in these issues is like really important and to have influence in that…" (Interviewee 1)*

3.3.3. Incorporation of environmental assessments and sustainability considerations into drug design and development

Incorporation of environmental aspects into drug design and development was spontaneously brought up by five interviewees as a means to reduce the environmental impacts of APIs and thereby increase the environmental sustainability of the pharmaceutical business (Table 3). Four interviewees noted that the environmental effects of pharmaceuticals should be assessed in early preclinical phases of drug design and development to avoid the use of environmentally harmful chemical structures, when possible, or to develop medicines that can be targeted more efficiently to their site of action to reduce the dose and thereby the amount of human excretion to the environment.

> *"…in terms of a development of a new drug and how we develop the new drug, the sustainability kind of component was not well enough reflected in the things that we want to put into that new drug. So I think that needs to be, just that needs to rise so, you know, in the R&D groups that discussing, so that… We have a molecule here, how do we bring it to the patient? I think the sustainability thinking needs to be there at every step, yeah?..." (Interviewee 12)*

When specifically asked for opinions on the use of environmental effect and fate assessment tools in early phases of drug discovery and development, ten interviewees had positive attitudes (Fig. 2 and Supplementary material). Although not all interviewees were participating in research and development, and some specifically implied that they were giving their personal perception, possibly differing from the company policy, all ten interviewees said they would welcome such tools and foresee their use even without regulatory requirements. However, one interviewee had reservations and, while considering these tools interesting and valuable for increasing knowledge on drugs' environmental impacts, was cautious about their hindering the development of very potent and inevitably harmful medicines, such as anticancer drugs.

3.3.4. Removal of pharmaceuticals from wastewaters and rational use of medicines

Five interviewees raised the possibility of removal of pharmaceuticals from wastewater as a means to reduce the environmental impacts of pharmaceuticals (Table 3); when asked for specific examples, they narrowed methods to targeted and more efficient removal processes for pharmaceuticals (3/15) and to dedicated collection of bodily excretions containing harmful pharmaceuticals (2/15).

> *"…And then, maybe, I don't know, treating of wastewater in general… … if there was some fine system developed to treat wastewaters, that would remove all those (residues), then that would be the best solution…" (Interviewee 1)*

Three interviewees additionally suggested rational use of medicines as an important action to reduce unnecessary and suboptimal drug consumption and thereby the environmental load and adverse impacts of pharmaceutical residues. It was also noted that physicians should pay attention to the amount of drugs prescribed at a time to avoid excess purchases.

> *"…probably the main thing is, what, what has like umm… been under discussion is of course reducing all kind of unnecessary use (of medicines) …" (Interviewee 5)*

3.3.5. Legislative means

Legislative actions were spontaneously raised and considered effective by five interviewees (Table 3) because once implemented, they are binding and require changes. One example presented (3/15) of specific legislative action to avoid unnecessary medicinal waste was targeting renewal of the legislation on obligatory storing of medicines based on the Finnish Act (979/2008) and Decree on Mandatory Reserve Supplies of Medicines (1114/2008) to enable recirculation of the stored medicines before they expire. Obligatory storing was considered necessary, but updated legislation could allow for flexibility to avoid unnecessary waste resulting from expired products. Another example, given by two interviewees, was the incorporation of environmental criteria (of production) into the marketing authorization or the GMP norms, to ensure that environmental impacts are considered in the context of pharmaceutical raw material production in low-income countries, where environmental regulation and its implementation might be inadequate (Table 3).

> *"…But then again, one (way) that for sure will work is (to include issues in) the pharmaceutical legislation. So that if something is required there, then that has to be enforced…" (Interviewee 6)*

Additionally, when specifically asked for their opinion on legislative or regulatory actions, seven interviewees had positive attitudes, two were reserved and one had a negative opinion (Fig. 2 and Supplementary material). The arguments in favor of legislative and regulatory changes emphasized that stricter policy instruments are needed despite the existing voluntary initiatives, such as the AMR industry alliance, and that changes in legislation could incentivize companies to relocate production facilities to Europe. For example, changes to the interpretation of Directive (2001/83/EC) on the Community code relating to medicinal products for human use, so that the companies would have to report the actual place of manufacturing (instead of the headquarter's address) in the package leaflets, may guide the selection of drug products and incentivize return of production to Europe. Other changes considered favorable are legislation enabling the companies to inform on the environmental impacts of prescription medicines, without this being interpreted as advertisement, or the replacement of the printed package leaflets with electronic ones, to reduce waste from pharmaceutical packaging. However, special requirements set on a national level were considered unrealistic for companies, and thus, to achieve bigger improvements, the environmental criteria and legislative changes would need to be implemented on the EU level.

The reserved (2/10) and negative (1/10) attitudes towards legislative changes (Fig. 2 and Supplementary material) were based on the opinion that current legislation in the EU is already sufficient regarding

environmental considerations. Stricter regulation and requirements were considered as possible risks to operational functionality of smaller companies, or as paths to price increases of drugs, such as generics critical to public health. Instead of strict environmental regulation or changes in legislation, one interviewee called for setting key performance indicators for environmental sustainability, perceiving that companies would follow them, not only because of goodwill, but also because of value-added investment as an incentive.

The attitudes varied in response to specific questions about relocation of drug manufacturing to countries having stricter environmental regulation (Fig. 2 and Supplementary material). Five interviewees regarded this positively as protecting the environment, while also securing the supply of medicine and raw materials. Three interviewees were reserved and considered actualization would require clear financial incentives or reputational advantages, and some questioned the willingness of societies to pay for presumably more expensive pharmaceuticals produced in Europe. Three interviewees argued that relocating the production to Europe is neither feasible nor the best solution, since Europe alone cannot provide medicines to the global market, and establishing new facilities in Europe would also have adverse environmental impacts. Instead, they suggested that the environmental impacts resulting from drug manufacturing outside the EU should be resolved by international cooperation, demanding similar environmental criteria as in the EU, permitting of non-EU producers, and contracting with responsible producers only. This approach was, however, perceived as challenging by another interviewee, who emphasized the limited ability to secure environmental sustainability of a subcontractor's operations despite periodic auditing. On the other hand, two interviewees raised the possibility of improving conditions by establishing the LCA-based assessment system to account for production location and methods of raw material production.

4. Discussion

4.1. Strengths and limitations of the study design

Out of the invited 41 companies, twelve (30 %) participated in this study. The participation rate in this study was lower (30% vs. 73 %) than in similar interview studies conducted for pharmaceutical companies, for example on the reasons behind medicine shortages (Heiskanen et al., 2017). This may be due to many different reasons. First, the business orientation for the companies operating in Finland focuses on sales and marketing only, whereas the environmental and sustainability actions are often considered to relate to manufacturing or strategic planning taking place at the headquarters. Thus, the invitees operating in the Finnish market might have found the interview themes difficult or irrelevant to their position in the company, lowering their interest in participating. Second, the interviews were conducted in the middle of the COVID-19 pandemic in spring 2021, which might have reduced the time and/or interest in participating. Despite the low participation rate, saturation of the data was achieved, and the number of interviewees was considered sufficient for drawing conclusions on their views and attitudes. In addition, the participation rate between originator and generic companies was equal (approx. 30 %) and therefore distortion in the results is not expected to arise from either sector's being over- or under-represented.

The study was conducted as a semi-structured interview, which enabled the participants to express their opinions and to bring up new aspects during the interviews for further discussions. In most cases, only one person per company participated in the interview and therefore the opinions and perceptions expressed did not necessarily represent the company policy. Instead, the results represent the views and attitudes of individuals acting in different positions in the companies, providing understanding of the daily environmental challenges facing the pharmaceutical companies, and including views on certain country challenges. Nevertheless, the actions and incentives proposed by the interviewees were prioritized to drive the environmentally sustainable development on a global level.

4.2. Current status of the companies regarding environmental actions

According to the interviewees, many improvements have already taken place in the pharmaceutical companies to increase the environmental sustainability of their businesses and of the sector as a whole. These include concrete actions in the companies such as generally improving waste management and reducing emissions from their operations and production; these were also considered the easiest life cycle impacts of pharmaceuticals to address. Similarly, Milanesi et al. (2020), based on managerial literature review, reported that cleaner production was the main topic associated with environmental sustainability. These results suggest that green production is one of the most intensively studied areas, where economic drivers (e.g., lower manufacturing cost) might already meet environmental incentives (e.g., reduced energy consumption). The international pharma industry has also many recent, voluntary initiatives aiming to improve the environmental sustainability of the pharmaceutical sector as a joint effort; these include the Eco-Pharmaco Stewardship program by European Federation of Pharmaceutical Industries (EFPIA) (EFPIA, 2015), the AMR Industry Alliance (AMR Industry Alliance, 2017), and the PSCI initiative (PSCI, 2006). Interestingly, these were noted by only two interviewees in this study, even though many of the companies were members of these initiatives, suggesting that participation is perhaps not considered as a concrete action on all levels of the business and that the interviewees' focus was on the more tangible operations.

Supporting the development of pharmaceuticals intrinsically less harmful for the environment and funding research and innovation to support "greener" pharmaceuticals are the action points in the EC's Strategic Approach to Pharmaceuticals in the Environment (PiE) (COM, 2019). Despite the regulatory support, the development of more environmentally sustainable pharmaceutical products was not commonly brought up by the interviewees as an action their companies had already begun, indicating that environmental fate of APIs and life cycle impacts of drug products are not yet an integrated element of the R&D in the participating companies, or if there are environmental aspects behind decisions in product development, these are not effectively communicated internally. The examples given by the interviewees focused largely on packaging materials and reducing waste by developing reusable medical devices. The examples given did not include designing of environmentally less harmful (e.g., readily biodegradable) APIs, indicating that "benign by design approach" (Kümmerer, 2007; Rastogi et al., 2014) is not yet a tangible goal. Although the companies had not yet adopted such pre-emptive approaches in drug design, several interviewees acknowledged this to be an interesting solution for the future and the attitudes were generally positive, which is well in line with the findings of Puhlmann et al. (2023).

4.3. Environmental impacts of drug manufacturing and transparency of production chains

Environmentally sustainable drug production was brought up by most interviewees as a key development need for the future. Lack of transparency in the complex production chains involving many, often dispersed, actors was overall the second largest challenge facing the pharmaceutical business according to the interviewees, with the most commonly mentioned challenge being the drug manufacturing centralized in countries with lax environmental regulation. The environmental challenges arising from centralized raw material manufacturing, and the industrial emissions from that, are a well-known issue (Larsson, 2014; Larsson et al., 2007), lacking economic and regulatory incentives to increase environmental sustainability of drug production. Any improvements toward, for example, adaptation of more efficient industrial wastewater treatment, were anticipated to raise production costs, and

therefore the interviewees considered that incorporation of environmental criteria into such aspects as public drug procurement or pricing and reimbursement are necessary incentives to help reduce discharges arising from drug production. The need for similar incentivizing acts for reducing discharges from antibiotic manufacturing have also been discussed by Larsson and Flack (2022). Environmental criteria in public procurement of medicines already exist in Sweden (Upphandlingsmyndigheten, 2015) and Norway (Sykehusinnkjöp, 2021). Although the use of environmental criteria in public procurement was generally supported by the interviewees of this study, their attitudes were partially reserved, with concerns relating to extra work with no clear rewards. Many interviewees considered that the cheapest bid would be the most competitive, despite environmental criteria. However, the interviewees perceived this mechanism as potentially incentivizing, provided that the criteria were harmonized, at least on the Nordic level, or preferably on the EU level, and appropriately weighed in the tendering. The importance of harmonized criteria has also been highlighted in previous studies as a factor to decrease the workload of both procurers and bidders and hence promote the use of environmental criteria in tendering (Miettinen, 2020). The use of procurement policy to encourage greener manufacturing is also one of the action points of the EC's Strategic Approach to PiE (COM 2019).

The interviewees noted that besides public drug procurement, increased transparency, and publicly available information regarding the origin of drug products could allow physicians and consumers to make informed choices (Larsson and Fick, 2009), as another means to foster environmentally sustainable drug production. The pressure from consumers is known to be a key driver for social and environmental improvements in companies as they can also be a reputational incentive (Lestari et al., 2021). According to recent studies, consumers are increasingly aware of the environmental impacts of pharmaceuticals (Alajärvi et al., 2021). The need for raising awareness of the environmental impacts of medicines in the society generally was also brought up by the interviewees. According to the recent studies carried out among a population in Finland, drug consumers expect sustainability from the pharmaceutical industry, and they are willing to pay more for environmentally sustainable pharmaceutical policies (Alajärvi et al., 2022, 2021). The information on consumers' valuations was generally perceived as positive by the interviewees, suggesting that consumer preferences and attitudes could hold a great incentivizing potential for the companies. In Sweden, the Välvald (" well-chosen") campaign has been developed to communicate the sustainability performance of the drug producers to the customers in community pharmacies in an effort to guide the customers' choices to increase transparency and support sustainable production (Swedish Pharmacy Association, 2022). The Välvald symbol is displayed next to the OTC medicines that meet the requirements set by the campaign. Currently, the requirements are that the companies must have an externally audited sustainability report, be a member of PSCI organization, and demand that the manufacture of the OTC products takes place with respect to human rights, workers' rights, the environment, and freedom from corruption. Additionally, the company must carry out and document risk analyses based on the PSCI principles for the supply chain relating to the OTC products. However, the information submitted by the companies is only handled by the Välvald office and therefore it does not provide information on the country of origin or production location to the customers. Välvald initiative is, however, a step forward as currently legal obligations to publish the country of origin are lacking.

Additionally, the interviewees discussed both global environmental standards and responsibility criteria developed with global cooperation, as well as stricter legislative actions, as means to reduce the hazards of raw material manufacturing in countries with weak environmental regulation. Nevertheless, relocation of manufacturing from low-income countries to Europe was not supported by all interviewees. Instead, legislative or regulatory changes that would obligate the companies to commit to environmentally sustainable operations independent of the manufacturing site were considered the most effective, and the attitudes toward legislative changes in this regard were positive, suggesting that industry prefers either tangible economic or regulatory incentives.

4.4. Environmental classification approaches

Controlling the multifaceted life cycle impacts of pharmaceuticals was the most commonly noted environmental challenge for the pharmaceutical business, and the impacts resulting from drug consumption were considered one of the greatest unresolved challenges. The suggested solutions included both preventive and reconstructive actions. Incorporation of environmental aspects to selection of medicines (e.g., physicians prescribing medicines or public drug procurements) was the most frequently proposed action to reduce environmental impacts of pharmaceutical residues, by promoting the use of either environmentally less harmful APIs or responsibly produced drug products. This approach would inevitably require an assessment system to enable comparison of APIs or drug products, based on their environmental footprint. However, the attitudes towards API-based environmental classifications were divided between positive and reserved. The interviewees anticipated that the impact of such a classification system on drug consumption and consequently on the environmental exposure would be small, and not the most effective means to overcome the challenge. Nevertheless, the interviewees considered that API-based classification could possibly incentivize companies to think about the environmental fate and effects of the APIs already in the R&D phase. Similar conclusions were also drawn in the report by the Swedish Environmental Research Institute (IVL), finding that the API-based classification of Fass had a limited impact on drug prescribing during 10 years since its introduction (Graae et al., 2017). On the other hand, the information collected for the "Pharmaceuticals and the environment" database of janusinfo.se has been used by the Swedish Drug and Therapeutics Committees when formulating recommendations for healthcare professionals (Ramström et al., 2020; The Wise List, 2015). Swedish physicians follow these recommendations in drug prescribing (Eriksen et al., 2017); this can affect the consumption of certain APIs and consequently, their environmental exposure levels. Nevertheless, fair comparison and substitution of APIs based on their environmental risks is challenging because of the limited data, lack of transparency, and discrepancies in the available environmental information (Ramström et al., 2020; Ågerstrand and Rudén, 2010).

The LCA-based environmental classification has been proposed as an alternative approach for favoring environmentally more sustainable pharmaceutical products, for example in public procurement of pharmaceuticals or in pharmaceutical benefits plans (Pålsson et al., 2020). This kind of environmental classification was also generally perceived as a positive development by the interviewees of this study, as incentivizing the companies to improve their operations. However, it was acknowledged by most of the interviewees that such a system is difficult to establish while not excluding any particular sector of the pharmaceutical business. Earlier literature (Larsson, 2014) has discussed challenges such as the difficulties in distinguishing which industrial discharges are associated with a particular product. On the other hand, for some products, the entire generic market relies on a single API manufacturer, making comparison based on industrial API emissions unfeasible. Similar concerns were also raised by the interviewees, emphasizing that companies might experience inequality if the requested API producer data is owned by a single company, which is also participating in the tendering. The challenges facing companies involving many suppliers and subcontractors in the production chain have been reviewed in more detail by Pålsson et al. (2019). Overall, the lack of primary process data and the challenges in sharing confidential data between companies are identified as key development needs for a fully functional LCA-based system for pharmaceutical products (DeSoete et al., 2017; Pålsson et al., 2019).

4.5. Country-specific issues

As an example of country-specific sustainability challenges, the mandatory reserve supply system of medicines, decreed by law in Finland, was introduced by two interviewees as a source of unnecessary medicine waste. The legislation in Finland aims to ensure the supply of medicines in circumstances when availability is restricted or prevented, e.g., as a result of suspended deliveries or serious crises (Fimea, 2022b). The legislation applies to pharmaceutical companies, importers, healthcare units, and the National Institute for Health and Welfare. The quantities to be stocked by pharmaceutical companies and importers are based on domestic sales and are equivalent to 3-, 6-, or 10-months' average consumption, depending on the type of medicine (Fimea, 2022c). While the mandatory reserve supply is critical to small markets, like Finland, these stored medicines are eventually incinerated as medicine waste, after the storage period ends. Similarly, the mandatory reserve stocks in hospitals are a significant source of medicine waste in Finland (Peltoniemi and Suomi, 2019). According to the interviewees, further investigation is necessary to understand how much medical waste is created solely because of this legislation and what mechanisms might reduce unnecessary waste.

5. Conclusions

Based on the outcome of this interview study, the pharmaceutical industry is well aware of the multifaceted environmental challenges relating to drug development, use, and end-of-life. Industry representatives identify their responsibilities for improving sustainability of drug production, and many improvements have already taken place in the companies. However, due to the lack of regulations and economic drivers or reputational rewards, incentives to promote environmentally sustainable drug production are unrealized. The environmental impacts arising from centralized API manufacturing are especially challenging and are mainly unaddressed. Therefore, the interviewees of this study called for global cooperation, including stricter legislative actions.

Overall, however, the environmental challenges relating to human excretion of consumed drugs and their metabolites were considered the most challenging. The most commonly mentioned actions to improve the environmental sustainability of the pharmaceutical sector were environmental criteria based on the active ingredients, drug products, and/or the company's environmental footprint, to guide the drug selection by consumers, physicians, and the healthcare system at large. This also highlights the importance of promoting awareness at all levels among professionals and drug consumers. The attitudes towards many of the different actions and incentives to solve the environmental challenges were, however, generally divided between positive, reserved, and negative. The only exception was the possibility of introducing environmental effects and fate assessment tools into the early phases of drug discovery and development, which received an almost entirely positive reception, although this is not yet a reality in the industry. These findings indicate that the benign by design approaches, whether focusing on the APIs or the drug products, comprise a strategy of clear interest to the industry for further proactive development to reduce the impact of future pharmaceuticals.

CRediT authorship contribution statement

Sanja Riikonen: Conceptualization, Methodology, Formal analysis, Investigation, Data curation, Writing – original draft, Visualization. **Johanna Timonen:** Conceptualization, Methodology, Formal analysis, Data curation, Writing – review & editing, Supervision. **Tiina Sikanen:** Conceptualization, Methodology, Writing – review & editing, Supervision, Project administration, Funding acquisition.

Declaration of competing interest

The authors declare that they have no competing interest that could have influenced the work reported in this paper.

Data availability

Data will be made available on request.

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Supplementary materials

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References

AFRY, 2020. Insights: Switzerland – pioneering in micropollutants removal from wastewater. https://afry.com/en/insight/switzerland-pioneering-in-micropollutants-removal-wastewater (accessed 3.3.2024).

Alajärvi, L., Timonen, J., Lavikainen, J., Martikainen, J., 2021. Attitudes and Considerations towards Pharmaceuticals-Related Environmental Issues among Finnish Population. Sustainability 13, 12930. https://doi.org/10.3390/su132212930.

Alajärvi, L., Lehtimäki, A.V., Timonen, J., Martikainen, J., 2022. Willingness to pay for implementation of an environmentally friendly pharmaceutical policy in Finland – a discrete choice experiment study. Int. J. Environ. Res. Public Health 19, 6535. https://doi.org/10.3390/ijerph19116535.

AMR Industry Alliance. 2017. https://www.amrindustryalliance.org/ (accessed 15.5.2022).

aus der Beek, T., Weber, F.A., Bergmann, A., Hickmann, S., Ebert, I., Hein, A., Küster, A., 2016. Pharmaceuticals in the environment – global occurrences and perspectives. Environ. Toxicol. Chem. 35, 823–835. https://doi.org/10.1002/etc.3339.

Berg, B.L., Lune, H., 2017. Qualitative Research Methods For the Social Sciences. Pearson Education Limited, Malaysia. Global Edition. 9. edition.

BIO Intelligence Service, 2013. Study on The Environmental Risks Of Medicinal Products, Final Report Prepared for Executive Agency for Health and Consumers. https://ec.europa.eu/health/system/files/2016-11/study_environment_0.pdf.

Brodin, T., Nordling, J., Lagesson, A., Klaminder, J., Hellström, G., Christensen, B., Fick, J., 2017. Environmental relevant levels of a benzodiazepine (oxazepam) alters important behaviour traits in a common planktivorous fish, (*Rutilus rutilus*). J. Toxicol. Environ. Health A 80, 963–970. https://doi.org/10.1080/15287394.2017.1352214.

COM, 2019. 128 final. Communication from the Commission to the European Parliament, the Council and the European Economic and Social Committee. European Union Strategic Approach to Pharmaceuticals in the Environment.

De Soete, W., Jimenéz-González, C., Dahlin, P., Dewulf, J., 2017. Challenges and recommendations for environmental sustainability assessments of pharmaceutical products in the healthcare sector. Green. Chem. 19, 3493–3509. https://doi.org/10.1039/c7gc00833c.

EFPIA 2016. European federation of pharmaceutical industries and associations: the pharma industry in figures – economy with a focus on market value. https://www.efpia.eu/publications/data-center/the-pharma-industry-in-figures-economy/market-value/ (accessed 9 June 2022).

EFPIA 2015. European federation of pharmaceutical industries and associations: Eco-Pharmaco Stewardship (EPS) a holistic environmental risk management program. https://www.efpia.eu/news-events/the-efpia-view/efpia-news/151009-eco-pharmaco-stewardship-eps-a-holistic-environmental-risk-management-program/ (accessed 14 June 2022).

EMA 2006. Committee for medicinal products for human use (CHMP), European Medicines Agency. Guideline on the environmental risk assessment of medicinal products for human use. EMEA/CHMP/SWP/4447/00 corr 1 01 June 2006.

Eriksen, J., Gustafsson, L.L., Ateva, K., Bastholm-Rahmner, P., Ovesjö, M.L., Jirlow, M., Juhasz-Haverinen, M., Lärfars, G., Malmström, R.E., Wettermark, B., Andersén-Karlsson, E., 2017. High adherence to the 'Wise List' treatment recommendations in

Stockholm: a 15-year retrospective review of a multifaceted approach promoting rational use of medicines. BMJ Open. 7, e014345 https://doi.org/10.1136/bmjopen-2016-014345.
Fimea, 2022. Finnish medicines agency: licences https://www.fimea.fi/web/en/supervision/pharmaceutical_industry/licenses (accessed 9 May 2022).
Fimea, 2022. Finnish medicines agency: mandatory reserve supplies. https://www.fimea.fi/web/en/supervision/mandatory_reserve_supplies (accessed 9 May 2022).
Fimea, 2022. Finnish medicines agency: reports on quantities to be stocked as mandatory reserves supplies. https://www.fimea.fi/web/en/supervision/mandatory_reserve_supplies/reports_on_quantities_to_be_stocked_as_mandatory_reserve_supplies (accessed 9 May 2022).
Finnish National Board on Research Integrity TENK, 2019. The ethical principles of research with human participants and ethical review in the human sciences in Finland, TENK guidelines. https://tenk.fi/sites/default/files/2021-01/Ethical_review_in_human_sciences_2020.pdf.
Finnish Medicines Agency and Social Insurance Institution, 2021. Finnish statistics on medicines 2020. https://urn.fi/URN:NBN:fi-fe2021122162437 (accessed 18 May 2022).
Graae, L., Westberg, E., Örtlund, L., 2017. 10 år med miljöklassificering av läkemedel på Fass.se. In: Dialogmöte i Stockholm 7:e november 2016. IVL Rapportnummer B 2274. (In Swedish. https://www.ivl.se/download/18.694ca0617a1de98f472b31/1628414077018/FULLTEXT01.pdf.
Heiskanen, K., Ahonen, R., Kanerva, R., Karttunen, P., Timonen, J., 2017. The reasons behind medicine shortages from the perspective of pharmaceutical companies and pharmaceutical wholesalers in Finland. PLoS One 12 (6), e0179479. https://doi.org/10.1371/journal.pone.0179479.
Hsieh, H.F., Shannon, S.E., 2005. Three approaches to qualitative content analysis. Qual. Health Res. 15 (9), 1277–1288.
Jimenez-Gonzalez, C., Overcash, M.R., 2014. The evolution of life cycle assessment in pharmaceutical and chemical applications – a perspective. Green Chem. 16, 3392. https://doi.org/10.1039/c4gc00790e.
Jobling, S., Williams, R., Johnson, A., Taylor, A., Gross-Sorokin, M., Nolan, M., Tyler, C. R., van Aerle, R., Santos, E., Brighty, G., 2006. Predicted exposures to steroid estrogens in UK Rivers correlate with widespread sexual disruption in wild fish populations. Environ. Health Perspect. 114 (Suppl1), 32–39. https://doi.org/10.1289/ehp.8050. Suppl 1.
Kaenzig, J., Friot, D., Saadé, M., Margni, M., Jolliet, O., 2011. Using life cycle approaches to enhance the value of corporate environmental disclosures. Bus. Strat. Env. 20, 38–54. https://doi.org/10.1002/bse.667.
Kairigo, P., Muriuki, C., Ngumba, E., Raude, J., Gachanja, A., Tuhkanen, T, 2020. Presence of antimicrobial pharmaceutical residues in various environmental compartments in selected Finnish, Kenyan and Zambian sites. Dosis, 3/2020. https://dosis.fi/front-page-dev/dosis-3-2020/.
Kümmerer, K., 2007. Sustainable from the very beginning: rational design of molecules by life cycle engineering as an important approach for green pharmacy and green chemistry. Green Chem. 9, 899–907. https://doi.org/10.1039/b618298b.
Larsson, D.G.J., de Pedro, C., Paxeus, N., 2007. Effluent from drug manufactures contains extremely high levels of pharmaceuticals. J. Hazard. Mater. 148, 751–755. https://doi.org/10.1016/j.jhazmat.2007.07.008.
Larsson, D.G.J., Fick, J., 2009. Transparency throughout the production chain – a way to reduce pollution from the manufacturing of pharmaceuticals? Regul. Toxicol. Pharmacol. 53, 161–163. https://doi.org/10.1016/j.yrtph.2009.01.008.
Larsson, D.G.J., 2014. Pollution from drug manufacturing: review and perspectives. Phil. Trans. R. Soc. B 369, 20130571. https://doi.org/10.1098/rstb.2013.0571.
Larsson, D.G.J., Flack, C.F., 2022. Antibiotic resistance in the environment. Nat. Rev. 20, 257–269. https://doi.org/10.1038/s41579-021-00649-x.
Lestari, E.R., Dania, W.A.P., Indriani, C., Firdausyi, I.A., 2021. The impact of customer pressure and the environmental regulation on green innovation performance. IOP Conf. Ser.: Earth Environ. Sci. 733, 012048 https://doi.org/10.1088/1755-1315/733/1/012048.
Li, X., Hamblin, D., 2016. Factors impacting on cleaner production: case studies of Chinese pharmaceutical manufacturers in Tianjin, China. J. Clean. Prod. 131, 121–132. https://doi.org/10.1016/j.jclepro.2016.05.066, 2016.
Louhisalmi, M., Alajärvi, L., Martikainen, J., Timonen, J., 2020. Finns return pharmaceutical waste to pharmacy – survey on the means of disposal of unused and expired medicines by the Finnish adult population. Pharm. Period. DOSIS 36, 384–397, 2020.
Masri, H.A., Jaaron, A.A.M., 2017. Assessing green human resources management practices in Palestinian manufacturing context: an empirical study. J. Clean. Prod. 143, 474–489. https://doi.org/10.1016/j.jclepro.2016.12.087, 2017.
Mata, T.M., Martins, A.A., Neto, B., Martins, M.L., Salcedo, R.L.R., Costa, C.A.V., 2012. LCA tool for sustainability evaluations in the pharmaceutical industry. Chem. Eng. Trans. (26), 261–266. https://doi.org/10.3303/CET1226044.
Mehtonen, J., Äystö, L., Junttila, V., Perkola, N., Lehtinen, T., Bregendahl, J., Leisk, Ü., Kõrgmaa, V., Aarma, P., Schütz, J., et al., 2020. Clear Waters from Pharmaceuticals (CWPharma) Activity 4.1 Report. Reports of the Finnish Environment Institute 34, 2020. http://hdl.handle.net/10138/319009.
Miettinen, M. 2020. Kestävien julkisten lääkehankintojen komponentit. Dosis 3/2020. (Summary in English). https://dosis.fi/front-page-dev/dosis-3-2020/.
Milanesi, M., Runfola, A., Guercini, S., 2020. Pharmaceutical industry riding the wave of sustainability: review and opportunities for future research. J. Clean. Prod. 261, 121204 https://doi.org/10.1016/j.jclepro.2020.121204, 2020.
Oaks, J.L., Gilbert, M., Virani, M.Z., Watson, R.T., Meteyer, C.U., Rideout, B.A., Shivaprasad, H.L., Ahmed, S., Chaudry, M.J.I., Arshad, M., Mahmood, S., Ali, A., Khan, A.A., 2004. Diclofenac residues as the cause of vulture population decline in Pakistan. Letters to Nature Nature 427, 630–633. https://doi.org/10.1038/nature02317.
Peltoniemi, T., Suomi, R., 2019. Eliminating medicine waste in a Finnish university hospital–a qualitative study. J. Pharm. Policy. Pract. 12, 27. https://doi.org/10.1186/s40545-019-0188-8.
Pharma Industry Finland Statistics, 2020. https://www.pif.fi/newsroom/statistics.html (accessed 9 June 2022).
Pharma Industry Finland, 2022. https://www.pif.fi/responsibility/pharmaceutical-manufacturing.html (accessed 9 June 2022).
PSCI 2006. Pharmaceutical supply chain initiative. https://pscinitiative.org/home (accessed 30 May 2022).
Puhlmann, N., Vidaurre, R., Kümmerer, K., 2023. Designing greener active pharmaceutical ingredients: insights from pharmaceutical industry into drug discovery and development. Eur. J. Pharm. Sci. 192, 106614 https://doi.org/10.1016/j.ejps.2023.106614, 2023.
Pålsson, A.C., Belleza, E., Ryding, S.O., Örtlund, L., Westberg, E., 2019. Environmental assessment model for pharmaceutical products. IVL Report No. B 2352. https://www.ivl.se/download/18.2299af4c16c6c7485d01de/1565693701749/B2352.pdf.
Pålsson, A.C., Bjerkesjö, P., Perjo, L., 2020. Reduce environmental impacts of pharmaceuticals along the value chain. IVL Report No. B 2395. https://www.ivl.se/download/18.4c0101451756082fbad80/1603698659379/B2395.pdf.
Ramström, H., Martini, S., Borgendahl, J., Ågerstrand, M., Lärfars, G., Ovesjö, M.L., 2020. *Pharmaceuticals and environment*: a web-based decision support for considering environmental aspects of medicines in use. Eur. J. Clin. Pharmacol. 76, 1151–1160. https://doi.org/10.1007/s00228-020-02885-1.
Rastogi, T., Leder, C., Kümmerer, K., 2014. Designing green derivatives of β-blocker Metoprolol: a tiered approach for green and sustainable pharmacy and chemistry. Chemosphere 111, 493–499. https://doi.org/10.1016/j.chemosphere.2014.03.119.
Smith, F., 2002. Qualitative interviews. Ed.: Smith F: Research Methods in Pharmacy Practice, 1st ed. Pharmaceutical Press, London, pp. 111–142.
Swedish Pharmacy Association 2022. Criteria Document Välvald, version 2.0. Date of entry into force: 6 February 2022. http://www.sverigesapoteksforening.se/wp-content/uploads/2021/11/Va%CC%88lvald-eng.pdf.
Sykehusinnkjöp, 2021. New environmental criteria for the procurement of pharmaceuticals in Norway. https://sykehusinnkjop.no/nyheter/new-environmental-criteria-for-the-procurement-of-pharmaceuticals (accessed 9 Jun 2022).
The Wise List, 2015. Region Stockholm. https://janusinfo.se/inenglish/thewiselist2015inenglish.4.2baa5e3e161e6f22189240.html.
Upphandlingsmyndigheten, 2015. The National Agency for Public Procurement in Sweden. https://www.upphandlingsmyndigheten.se/en/criteria/nursing-and-care/medicinal-products/medicinal-products/ (accessed 9 Jun 2022).
van der Grinten, E., Breure, A.M., Lambooij, M.S., Lette, M., 2016. RIVM Report 2015-0145. https://www.rivm.nl/bibliotheek/rapporten/2015-0145.pdf.
Veleva, V., Hart, M., Greiner, T., Crumbley, C., 2003. Indicators for measuring environmental sustainability - A case study of the pharmaceutical industry. Benchmark.: Int. J. 10, 107–119. https://doi.org/10.1108/14635770310469644. No.2.
Wilkinson, J.L., Boxall, A.B.A., Kolpin, D.W., Leung, K.M.Y., Lai, R.W.S., Galbán-Malagón, C., Adell, A.D., Mondon, J., Metian, M., Marchant, R.A., et al., 2022. Pharmaceutical pollution of the world's rivers. Proc. Natl. Acad. Sci. 119 (8) https://doi.org/10.1073/pnas.2113947119. Article e2113947119.
Ågerstrand, M., Wester, M., Rudén, C., 2009. The Swedish Environmental Classification and Information System for Pharmaceuticals – an empirical investigation of the motivations, intentions and expectations underlying its development and implementation. Environ. Int. 35, 778–786. https://doi.org/10.1016/j.envint.2008.12.001.
Ågerstrand, M., Rudén, C., 2010. Evaluation of the accuracy and consistency of the Swedish Environmental Classification and Information System for pharmaceuticals. Sci. Total Environ. 408, 2327–2339. https://doi.org/10.1016/j.scitotenv.2010.02.020.